DEPARTMENT OF HEALTH AND HUMAN SERVI(S

PUBLIC HEALTH SERVICE

CENTERS FOR DISEASE CONTROL AND PREVENT)N

Minutes of Meeting

ADVISORY COMMITTEE ON IMMUNIZATION PRAC CES
February 23-24, 1994

Atlanta, Georgia

ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES
Centers for Disease Control and Prevention
February 23-24, 1994
Auditorium A

FEBRUARY 23

8:30 AM	Introduction	Dr. J. Davis Dr. C. Broome
9:00 AM	ACIP's Role in the "Vaccines for Children Program"	Dr. W. Orenstein Mr. D. Mason
9:20 AM	Discussion of Responses to Proposed Federal Register Notice Schedule Recommended for the "Vaccines for Children Program"	Dr. S. Hadler Mr. K. Malone
10:30 AM	**BREAK**	
11:00 AM	Status of Simplification of Vaccine Schedule	Dr. C. Hall Dr. J. Gindler Dr. C. Hardegree FDA
11:30 AM	Update on the National Vaccine Program	Dr. A. Robbins NVP
11:45 PM	Revision of Varicella Statement and and Status of Application for Licensure of Varicella Vaccine	Dr. S. Holmes
12:15 PM	**LUNCH**	
1:15 PM	High Risk of Vaccine-Associated Paralytic Poliomyelitis in Romania	Dr. P. Strebel
1:45 PM	Sequential IPV-OPV Schedule Final Results of Studies of Combined Schedules Issues of OPV Revertants Cost Benefit Estimates for Combined Schedules	Dr. O. Kew Dr. J. Modlin Dartmouth Medical School Dr. A. Murdin Connaught Dr. P. Ogra Children's Hosp. Galveston Dr. R. Sutter
3:15 PM	**BREAK**	

ATTENDEES:

COMMITTEE MEMBERS PRESENT
Dr. Mary Lou Clements
Dr. Jeffrey Davis (phone)
Dr. Kathryn Edwards
Dr. Neal Halsey (Acting Chair)
Dr. Rudolph Jackson
Dr. Carlos Ramirez-Ronda
Dr. Joel Ward

Ex Officio Members
Dr. Carolyn Hardegree (FDA)
Dr. G. Rabinovich (LaMontagne)

Liaison Representatives
Dr. Marvin Amstey (ACOG)
Dr. David Fleming (HIPAC)
Dr. Pierce Gardner (ACP)
Dr. William Glezen (IDSA)
Dr. Caroline B. Hall (AAP)
Dr. Walter Hierholzer (HICPAC)
Dr. Kristin Nichol (VA)
Dr. Georges Peter (AAP)
Dr. Michael Peterson (DOD)
Dr. Gregory Poland, (AHA)
Dr. Anthony Robbins (NVP)
Dr. William Schaffner (AHA)
Dr. David Scheiffle (NACI)
Dr. Richard Zimmerman (AAFP)

Executive Secretary
Dr. Claire Broome

Office of the General Counsel
Mr. Kevin Malone

Epidemiology Program Office
Dr. J. L. Conrad

Office of Program Support
Ms. Kitty Armstrong
Ms. Connie Blalock
Ms. Pollye Koenig
Ms. Renelle Woodall

National Center for Infectious Diseases
Dr. Nancy Arden
Dr. Joseph Bresee
Dr. Paul Cieslak
Dr. Nancy Cox
Dr. Martin S. Favero
Rafael Harpaz
Dr. Gary Sanden
Dr. Craig Shapiro

National Center for P vention Services
Rosamond Dewart

National Immunization rogram
Dr. William Atkinson
Dr. Bob Chen
Dr. Steve Cochi
Dr. Vance Dietz
Dr. Gary Euler
Judy Gantt
Dr. Jacqueline Gindle
Dr. Dayla Guris
Dr. Steve Hadler
Dr. Kimberly Heath
Dr. Sandra Holmes
Muriel Hoyt
Dr. Sonja Hutchins
Hector Lzurieta
Dr. Arthur Manoharan
Dr. W. Orenstein
Dr. Mary Reichler
Dr. Peter Strebel
Dr. Ray Strikas
Dr. Roland Sutter
Dr. F. VanLoon
Dr. Walter Williams
Dr. J. Watson
Melinda Wharton

Office of Public Affa s
Kay Golan

U.S. Public Health Se ice
Mr. Thomas E. Balbier Jr.
Ms. Rosemary Havill

Food and Drug Adminis ation
Sheila Bayne-Lisby
Susan Ellenberg
Karen Goldenthal
Roland Levandowski
Karen Midthun
Dr. Margaret Mitrane

National Institutes o Health
Dr. R. Rabinovich

National Vaccine Prog m
Dr. Joel Breman

Navy Environmental He th Center
Dr. Robert Brawley

Army Surgeon General's Office
incent P. Fonseca

Others Present
Julia Barrett, Merck Vaccine Division
Jill Chamberlin, Vaccine Bulletin
Jean Chow, Lederle Praxis Biologics
Janet Crawford, Merck Vaccine Divivion
Rudi Daems, Smith, Kline, Beecham
Dr. Ruth Ann Dunn, Michigan Department of Public Health
Dr. David C. Epstein, Prudential Insurance
Karen A. Fitzner, University of Hong Kong
Carol Esch, Merck Vaccine Division
Carol Frankel, Evans/Medeva
Dan Granoff, Chiron Corp.
Janet Hardy, Klemm Analysis
Cheryl Pokalo Jones, Infectious Diseases in Children
Dr. Samuel Katz, Duke University Medical Center
Clare Kahn, Smith, Klein, Beecham Pharmacy
Robert Kohberger, Lederle Praxis
Dr. Carlton Meschievitz, Connaught Laboratories
Dr. John Modlin, Dartmouth Medical School
Wayne Morges, Merck & Co., Inc.
Andrew Murdin, Connaught Laboratories
Dr. David Nalin, MRL
Marjorie Nicholls, Forest Labs
Gary Norwith, Wyeth-Ayerst Research
Dr. P.L. Ogra, UTMB
Dr. Stanley A. Plotkin, Pasteur-Merieux-Connaught
Lorraine Radick, Lederle-Praxix Biologicals
R. L. Scott, Lederle
Bob Sharrar, Merck
Judith Shindman, Connaught Laboratories, Ltd.
Dan Soland, Smith, Kline, Beecham
Michael Speidel, Lederle-Praxis Biologicals
Dale R. Spriggs, VRI, Inc.
Barbara Sweeney, NAPNAP
Dr. Joanne Tatem, Lederle-Praxis Biologicals
Miriam E. Tucker, Pediatric News
Dr. Tito R. Ubertini, North American Vaccine
Ted Vigodsky, WGST/WPCH
Robert E. Wervel, DVIC
Dr. Carolyn Weeks-Levy, Lederle-Praxis Biologicals
George Welu, Connaught Laboratories, Inc.
Dr. Jo White, Merck Research Laboratories
Tim Wissman, Merck & Co.

Executive Summary

n Feb. 23-24, 1994, the Advisory Committee on Immunization Pr tices (ACIP) convened at the Centers for Disease Control and Prevention (CD . Dr. Neal Halsey presided in the absence of Dr. Jeffrey Davis, State Epi miologist for Wisconsin and the new ACIP Chairperson.

New liaison members introduced were Dr. Richard Zimmerman, Uni rsity of Pittsburgh, representing the American Academy of Family Physic ns; Dr. William Glezen, Baylor College, representing the Infectious Di ase Society of America; and Dr. David Fleming, representing the Hospital I ection Control Practices Advisory Committee (HICPAC).

Following discussion of the area of conflicts of interest by D Claire Broome and Mr. Kevin Malone, CDC counsel, members introduced t mselves and disclosed their conflicts of interest, if any.

ACIP's Role in the Vaccines for Children (VFC) Program

Dr. Walter Orenstein, Director of the National Immunization Pr ram (NIP), outlined the ACIP's role in the VFC. He reviewed that program patient eligibility requirements, and providers' roles and explained t t the decisions made that day would be the basis for NIP's going for rd in the vaccine contracting process.

Discussion of Responses to Proposed Federal Register (F.R.) No ce Schedule Recommended for the VFC Program

Mr. Malone from CDC's General Counsel's Office briefly went ov the provisions of the Omnibus Budget Reconciliation Act of 1993 (O A) that deal specifically with the ACIP's role in the VFC program.

Dr. Steve Hadler, NIP, then led the discussion and voting. He sked ACIP members to refer to Handout #1 ("Issues for Vote at ACIP Meeti "). He reminded members that they had had a preliminary vote at the l t ACIP meeting. The F.R. notice about this preliminary vote (58 FR 6 25)--which included the ACIP General Recommendations on Immunization--app red December 16, 1993.

He read nine diseases (pertussis, diphtheria, tetanus, Haemoph us influenza type b, measles, mumps, rubella, poliomyelitis, and hepatitis and brought up the following proposal for vote:

> The ACIP reaffirms that vaccines which are currently used o prevent the 9 diseases listed above should be included in the Vaccine for Children (VFC) program. Specific vaccines to prevent these diseas will be determined in subsequent votes.
>
> This vote does not exclude consideration of vaccines to p vent additional diseases such as influenza and pneumococcal di ases.

Except for two absentee members, the vote was unanimous.

He then read the list of vaccines for diphtheria, tetanus and rtussis (p. 2 of Handout #1) and proposed the following for vote:

> The ACIP recommends that the vaccines listed above, inclu ng the recently licensed vaccine "Pasteur Merieux Haemophilus in uenza b conjugate vaccine (PRP-T) which may be reconstituted with TP vaccine (produced by Connaught Laboratories, Inc.)" be included i the Vaccines for Children program.

The vote carried: 7-0, with 3 abstentions.

Dr. Hadler proposed the third issue for vote:

> The recommended schedule for children includes 5 doses of TP vaccine (or DT or DTaP or combined DTP-Hib vaccines where appropr te) by school entry, and 1 dose of Td vaccine given at 14-16 years of a .
>
> "The schedule shown in Table 1 of the Notice shows that d es should be given at the following ages:
>
> 2 months - DTP
> 4 months - DTP
> 6 months - DTP
> 15 months - DTaP (DTP)
> 4-6 years - DTaP (DTP)
> 14-16 years - Td."

However, after discussion, Dr. Halsey changed it, as follows:

> The ACIP recommends the number of doses, schedule, and qu ifications noted above and in the text of the Dec. 16, 1993 notice. he additions we have made are insertion of the word routine for the se ence that now reads, "The routine schedule shown in Table 1," and Dr. W ter Orenstein's suggestion regarding the ACIP's endorsing the AP [American Academy of Pediatrics] recommendations for the timing of e fourth dose.

The vote passed: 6-0, with 4 abstentions.

The next item for vote was:

> The ACIP recommends that text be included in the final No ce and in the schedule which states preference for the use of DTaP for e 4th and 5th doses of the DTP series.

This vote did not carry. The vote was: 2-5, with 3 abstention and 2 absentees.

The next vote was on the vaccines to prevent Haemophilus influ za type b disease. The vote was on the following:

> The ACIP recommends that the vaccines listed above, inclu ng the newly licensed vaccine "Pasteur Merieux Haemophilus influenza b onjugate

vaccine (PRP-T) which may be reconstituted with DTP vacci (produced by Connaught Laboratories, Inc.)" be included in the Vaccine for Children program.

The vote carried, 5-0, with 4 abstentions.

The next vote was on the schedule for H. flu vaccines. The sc dule for children included 3 or 4 doses of a H. flu b (Hib)-containing ccine by age 2 years, depending on the specific vaccine used. The vote was n the following:

> The ACIP recommends the number of doses, schedule, and qu ifications noted above and in the text of the Dec. 16, 1993, Notice, ith the addition of the Hib conjugate vaccine, which may be recon ituted with DTP as an acceptable alternative for schedule A.

This vote carried, 4-0, with 4 abstentions.

The next vote was on the consistency in the Hib primary series The vote was on the following:

> The ACIP recommends language on interchangeability of Hib accines for the primary series, as cited in the current General Recom ndations on Immunization, be incorporated into the final Notice for V cines for Children.

This vote carried 3-0, with 5 abstentions and 5 absentees.

The next several votes dealt with the use of combination versu single-antigen vaccines. The first proposal for vote was:

> The ACIP should strongly endorse--or endorse--the prefere ial use of the combined vaccines, particularly in the first year of fe, but should not restrict the use of or reimbursements for sing -antigen Hib vaccines during these visits, and the Department should c plete contracts for both single-antigen and multiple-antigen pr lucts.

This wording generated a lot of discussion. One change, agree upon by consensus, was to use the word encourage rather than strongly dorse or endorse. Dr. Halsey asked Drs. Rabinovich and Ward to meet wit Mr. Malone at lunch and work out specific wording on which to vote.

The next vote dealt with the interchangeability of vaccines ot r than Hib. Dr. Hadler first read this background:

> When at least one dose of a hepatitis B vaccine produced one manufacturer is followed by subsequent doses from a diffe nt manufacturer, the immune response has been shown to be cc arable with that resulting from a full course of vaccination with a s gle vaccine.
>
> When administered according to licensed indications, diff ent DTP vaccines as single antigens or various combinations, as w l as live and

inactivated polio vaccines, can also be used interchangeal y. However, published data supporting this recommendation are general limited.

The issue for vote was:

> The ACIP recommends that the final Notice on Vaccines for hildren contain language equivalent to that noted above permittin interchangeable use of different licensed vaccines to pre nt hepatitis B; DTP; and polio disease.

The vote carried unanimously.

The next vote was on polio vaccines. The proposed wording for ote was:

> The ACIP recommends that the vaccines listed above [OPV a IPV] be included in the Vaccines for Children program.

The motion passed, 8-0, with 2 abstentions, and 2 absentees.

Dr. Halsey deferred the vote on the details of the polio shced e to later in the day.

The next vote was on measles, mumps and rubella vaccines. The urrent Notice proposes not only MMR, but also measles and rubella combined v cine (MR), measles vaccine, mumps vaccine, and rubella vaccine. The vote as on this proposal:

> The ACIP recommends that the vaccines listed above be inc ded in the Vaccines for Children Program.

The motion passed, 7-0, with 2 abstentions and 3 absentees.

The next vote concerned the schedule for MMR (2 doses, one at -15 months and one at 4-6 years). The proposal for vote was:

> The ACIP recommends the number of doses, schedules and qu ifications as noted above and in the text of the Dec. 16, 1993 Notice, th the clarification in text and table that single-antigen vacci s may also be used for outbreak control, but that routine vaccination s uld only be completed with MMR.

The vote carried 7-0, with 3 abstentions.

ACIP Statement on Varicella Prevention

Dr. Sandra Holmes outlined the key wording changes in the new aft of the ACIP varicella statement.

Update on the National Vaccine Program (NVP)

Dr. Tony Robbins said that the NVP is putting together a new w king group on the introduction of new vaccines. The NVP has also gotten inv ved in a problem around technology transfer. Third, the NVP is working n what Dr. Robbins termed the long-standing problem between FDA and CDC r garding vaccine labels. Finally, the NVP is working on increasing the umber of sites at which underinsured classes of children can receive fr vaccines.

Vaccine-Associated Paralytic Polio (VAPP)

r. Peter Strebel reported on the high incidence of VAPP in Ro nia. He reported the results of a case-control study, which suggests t t exposure to intramuscular (IM) injections of antibiotics given during the cubation period of OPV is associated with VAPP. This was followed by a ief overview by Dr. Roland Sutter on VAPP in the United States.

Sequential IPV-OPV Schedule

Dr. Sutter then introduced several topics and speakers on reve ion to virulence of polioviruses contained in OPV when given after IP sequential IPV-OPV study; follow-up on the Institute of Medicine (IOM) re rt; and the impact of a sequential IPV-OPV schedule. Dr. Sutter the summa zed answers to the questions raised by the recent IOM report, followed by s report on the potential impact of a sequential schedule on VAPP cases an cost-benefit estimates. He then led the final discussion, pointing out tha the purpose of the previous presentations was for the ACIP to decide wheth or not to change polio vaccination policy and, if so, how. After discus on, it was decided that there was no consensus for a change. The group d ided to delay a vote until licensure for a combined vaccine is in the works.

Postexposure Prophylaxis for Hepatitis C

Dr. Miriam Alter discussed postexposure prophylaxis for hepati s C, targeted mainly at HCWs. The group voted unanimously to rescind wordin about recommending immune globulin G after percutaneous exposures. e also asked the ACIP to decide whether it should recommend a hepatitis C p tocol for the follow-up of HCWs who sustain accidental percutaneous and perm osal exposures. The ACIP withheld its judgement on this matter unt it could view the revised document.

Voting on the VFC--continued

Discussion then return to voting on what to include in the VFC rogram. Dr. Hadler returned to the polio issue and the critical footnote t t "enhanced, inactivated IPV may be substituted for OPV, using a different hedule." This is really not consistent with current ACIP recommendations, he aid. The issue for vote was:

> The ACIP recommends the number of doses, schedule and qua fications as noted above and in the text of the current Notice, with t clarification in text and footnotes that OPV is the recom nded vaccine for routine vaccination of normal infants and children. y changes in recommendations that are endorsed by the ACIP in the June 994 meeting will be incorporated into the final notice.

The vote carried, 6-0, with 2 abstentions and 2 absentees.

Votes on Vaccines for Hepatitis B

Discussion then moved to the next votes, on hepatitis B vaccin Dr. Hadler. noted that the F.R. proposed Hepatitis B vaccine and Hepatitis Immune Globulin (HBIG) (for infants born to HBV-carrier mothers). Th vote was on this proposal:

The ACIP recommends that the vaccines listed above be inc ded in the Vaccines for Children Program.

Dr. Halsey decided to have two separate votes. The first vote as on including the parenthetical phrase, "for infants born to HBV c rier mothers". This vote did not pass (3-3, with 3 abstentions), s the phrase was deleted.

The second issue for vote was the vaccines to include for hepa tis B. The motion carried, 7-0, with 3 abstentions and 2 absentees.

The next vote was on the attendant footnotes in the F.R. notic which were added to note acceptance by the ACIP of the AAP's alternative hedules. These schedules were to reference the AAP by name. This vote w deferred for Dr. Robbins to draft appropriate language.

The next vote was on the schedule for hepatitis B (p. 19 of Ha out #1), with attendant footnotes.

The ACIP recommends the number of doses, schedule and qua fications as noted above and in the text of the Dec. 16, 1993, Notice.

This vote carried, 6-0, with 4 abstentions and 2 absentees.

The ACIP then returned to the following earlier proposal, whic had been revised somewhat:

The ACIP encourages use of DTP-Hib vaccines (combined or censed for combined administration) when receipt of each antigen of e combined vaccine is indicated; however, at this time, the ACIP doe not restrict separate administration of DTP and single-antigen Hib vac nes. The Department should complete contracts for both single-anti n and multiple-antigen products.

The proposal passed, 4-0, with the rest abstaining or absent.

The next votes were on the use of brand names in ACIP OBRA doc ents:

Any use of brand names in ACIP OBRA documents is not inte ed to mandate purchase of particular brands of vaccine, but rather is i ended for identification purposes only.

This passed unanimously. The next proposal for vote was:

Use of the phrase "combined DTP-Hib vaccine" in ACIP OBRA locuments includes any DTP and Hib vaccines which are either combin or are licensed by the FDA for combined administration.

The proposal passed, 5-0, with 5 abstentions.

A proposal that the ACIP request NIP staff to review the curre ACIP recommends to identify any inconsistencies with the ACIP OBRA commendations adopted at this meeting for the purpose of reconciliation of t se recommendations at the next meeting of the ACIP was deferred.

This was deferred until the program compiled inconsistencies i these specific recommendations and mailed them to ACIP members befor the next eeting.

Scope of the F.R. Notice

The last set of issues dealt with the scope of the Notice, whi involved lengthy discussion about universal immunization of adolescents nd high-risk persons. The meeting adjourned for the day with no decisions this matter.

Adolescent Vaccination Against Hepatitis B

The meeting began at 8:08 the next day with an update by Dr. H Margolis on the action plan for eliminating hepatitis B virus transmission After considerable discussion on this matter, the ACIP decided to vo in principle that the Committee is interested in trying to improve delivery f immunizations to all high-risk groups. That includes improved elivery of hepatitis B vaccine to the adolescents, and influenza and pneu coccus vaccines to high-risk groups. There was consensus that this w the long-term desire of the Committee.

Dr. Halsey then summarized discussion by saying that the ACIP d two options: 1) to form working groups and put off the vote until une, and 2) to vote on influenza now and put off pneumococcal vaccine unti later. Option #1 carried unanimously.

IOM Report on Adverse Reactions and Contraindications to Vacci s

Dr. Orenstein announced that the law had changed regarding the accine information materials so they can be simplified and shortened. He requested that the ACIP decide which adverse events not already in these orms be added.

Next, Dr. Rabinovich said that PHS will be conducting a scient ic review of the IOM Report on March 15. The thoughts of the ACIP will be esented.

Then Dr. Tuttle reviewed the recent activities of the working oup, appointed after the October 1993 ACIP meeting to review the im ct of the IOM report on ACIP recommendations. She focused on some of the mo controversial adverse events--OPV and GBS; tetanus-toxoid-cont ning vaccines and GBS; and combined MMR and thrombocytopenia.

GBS and OPV

First, Dr. Tuttle reported on a reanalysis of a Finnish study d an observational study done in the United States, which provided idence against a causal relationship between GBS and OPV. She read a roposed change to that effect. A vote was taken about the acceptabili of this wording to the Committee. The motion carried 6-0, with 3 abst tions.

TT and GBS

Dr. Tuttle then reviewed estimates of risk of GBS following DT The group decided to postpone this vote until later.

MMR Vaccine and Thrombocytopenia

:t was decided in discussion that the Committee did not want t rewrite this section now and would await written comments for a vote.

Incorporating Changes into ACIP Statements

Dr. Tuttle then asked the ACIP to address how these changes wc .d get incorporated into previous ACIP statements. The group conside ed having an official, brief ACIP response to/commentary on the IOM report the MMWR. However, no consensus was reached on this issue, and it will k decided at the next ACIP meeting.

Simplification of the Vaccine Schedule

Dr. Jacqueline Gindler, NIP, summarized work to simplify the c iferences between the ACIP and AAP recommendations. She reviewed five r ltine and two flexible options for schedules. She said the NIP would like a working group to be formed and meet within the next month to agree on a sche le.

It was decided to form such a working group and to have membe and liaison members (as consultants) on it. Dr. Hall was named chair. Ot r members or consultants asked to serve on the group were: Dr. Edwards, Ha ey, Hardegree, Peter, Rabinovich, Thompson, and Zimmerman. The gr p was asked to report recommendations back before the June ACIP meeting sc he decision could be made then.

Formation of Working Group for High-Risk Populations

This group was to deal with hepatitis B, the second dose of MM influenza, and pneumococcal vaccines. Dr. Halsey proposed the following mbers: Drs. DeBuono, Fleming (consultant), Schoenbaum, Ward, Schaffner (as consultant), Davis (as Chair), Jackson and Glezen.

New Language on Vaccines for Children Purchase

Dr. Tony Robbins proposed the following new language to recogr e the value of other schedules:

> The Committee has adopted schedules for administering vac nes. The Committee also finds that vaccine schedules of the Americ Academy of Pediatrics published in the 1994 edition of the Report of he Committee on Infectious Diseases (The Red Book) may be followed by ccines for Children program providers.

It was decided there needed to be a process for the ACIP to fc ally review the AAP recommendations. Dr. Peter agreed to provide members the ACIP with the 1994 Red Book.

Update on the Injury Compensation Program

Dr. Thomas Balbier from the National Vaccine Injury Compensati Program reviewed major accomplishments of the program for 1993.

Update on Large-Linked Database Studies of Adverse Events

)r. Hadler gave a brief update on the large-linked databases t monitor adverse reactions. It was suggested that the ACIP get a 2-3-p ge summary mailing of the plans for this data system and that the topic p :haps be placed on the agenda for the next meeting.

Status of the Development of New Vaccine Information Statement

Ms. J. Gantt said that CDC has contracted with the University : Rochester School of Medicine and Dentistry to rewrite and simplify vacci e information statements for the antigens in the Vaccine Injury Table (DTP, l, MMR, and polio).

Update on Typhoid Recommendations

Dr. P. Cieslak passed out the revised draft statement for ACI)n typhoid immunization.

Status of BCG Guidelines

Dr. Broome summarized the work of three advisory groups that a e working together on such guidelines. A joint working group was formed :o look at the next version of the statement and iron out any problems. Drs. Edwards and Halsey are the two ACIP members on this group. Dr. Halsey is iairperson.

Update on FDA Committee Meeting on BCG

Dr. Hardegree said that last October FDA had a review of the I ; meta-analysis information that had been presented to ACIP. One of ie manufacturers presented new data on BCG for prevention of TB : children. The group felt that the data did support the efficacy of BCG : very narrow indications. FDA is continuing its review.

IOM Report--Continued

DTP and GBS

This topic had been deferred from the morning's discussion of iverse events. Dr. Bob Chen reported his recalculation of the association of 3S following DTP. Review of a study of GBS incidence from Los Angeles sho i that there were fewer cases reported following receipt of DTP vaccine tha expected by chance alone.

The proposed change for vote was:

> [in Side Effects and Adverse Reactions" replace "due to" ith associated with, as follows: "Persons with a prior history of GBS a sociated with a particular vaccine may be at increased risk of recurre GBS. . ."
>
> [in "Precautions and Contraindications" section, add the)llowing underlined phrase: "A previous episode of GBS within 6 w eks following a tetanus-containing vaccine is a contraindication to ad tional doses."

However, the members were not comfortable voting on this, and ıe matter was sent back out for review and rewrite, to emphasize the rarity ᴇ the event. The program was asked to revise this section and mail--perhaps vith additional, separate language for adults and children--to all ᴄIP members.

Vaccination Against Hepatitis A

Dr. Craig Shapiro said that both SmithKline Beecham (SKB) and ɐrck Sharp & Dohme (MSD) have efficacious inactivated hepatitis A vaccines ıose reactogenicity profile is acceptable. Dr. David Nalin then rep ːted on data from the Monroe County efficacy trial with this Merck's vaccir .

Dr. Shapiro said his section was drafting guidelines on hepati ls A vaccination. Dr. Halsey asked him to come up with a draft. I . Clements volunteered to work with him on preparing this.

Public Comment

Dr. Halsey asked if any members of the audience wanted to make ı public comment. There was none.

U.S./WHO Influenza Vaccine Recommendations for 94/95

Dr. Nancy Cox briefly reviewed worldwide influenza activity ar the vaccine recommendations for the next flu season. The WHO has recommer ɐd that the trivalent influenza vaccine prepared for the 1994-1995 season ıll include: an A/Shangdong/9/93-like (H3N2) strain; an A/Singapore 6/86-l ᴄe (HlNl) ɜtrain; and a B/Panama/45/90-like strain.

Dr. Joe Bresee gave a brief update of U.S. flu activity. Dr. ıncy Arden reviewed the proposed revisions in the ACIP Recommendations fc the Prevention and Control of Influenza. These revisions updated ıe recommendations for use of the vaccine and antiviral agents a\ ılable for controlling flu, including information concerning rimantadine; ıntiviral resistance; and dosage precautions.

Dr. Rabinovich reported that the National Vaccine Advisory Cor ıttee approved a report on adult immunization. She suggested that it be a fı ıre agenda item for an ACIP meeting.

Working Groups--Continued

Concern was raised about whether there should be three workin; ɡroups, instead of the two which were identified. (The high-risk one ɔuld be separated into two groups). Dr. Halsey asked for a one-hour l ɔck of time on the June agenda to deal with adolescent immunization. Dr. Da\ s, as chairperson of the high-risk working group, would have the op\ ɔn of dividing the working group into two. Consensus was agreement with th: suggestion.

The meeting was adjourned.

Summary of Agreed-Upon Actions

Kevin Malone will prepare a cover letter along with the summar of the committee votes on the recommended vaccines and schedule for t Vaccines for Children program. As acting chair of the February ACIP meetin Dr. Halsey, will forward this to the Secretary, HHS.

Any written suggestions or comments on the Varicella statement should be forwarded to Gloria Kovach by March 23rd.

Miriam Alter will mail to ACIP members, information on Hepatit C virus infections in the occupational setting.

Ray Strikas will consult with Miriam Alter to incorporate chan s on Hepatitis C for the health care workers immunization recommend ion.

Steve Hadler, with the assistance of FDA, will compile a list inconsistencies between ACIP statements and package labeling. his will be included in the simplification discussions during the June mee ng.

Paul Cieslak will make the typhoid vaccination recommendation nsistent with the FDA package labeling.

The working group on simplification of vaccine schedules (Edwa s, Hall, Hardegree, Halsey, Peter, Rabinovich, Thompson, Zimmerman) and he working group on high risk issues (Davis, DeBuono, Fleming, Glezen, Ja son, Schaffner, Ward) will lay out key issues before the June meeti . NIP will provide support for both working groups. Comments on the simp fication issues presented by the NIP staff (Gindler) should be provided o Dr. Gindler by March 23rd.

A working group (Arden, DeBuono, Schaffner) will review the wo ing on risk groups and will come up with a plan for any needed changes in e ACIP statement on influenza vaccine by June.

ACIP members will be requested to provide written comments to draft summary of issues raised by the IOM reports on vaccine safety (Will be rovided by Drs. Tuttle and Chen). David Nalin of Merck Sharpe and Dohme ll write a letter to the National Immunization Program on data on MMR and thrombocytopenia.

Bob Chen will draft language for the section on DTP in respons to the IOM's Report on Adverse Events.

Georges Peter will provide the ACIP with copies of the new Red ook.

Bob Chen and John Glasser will provide to ACIP members, a 2- t 3-page summary of the large-linked databases.

Hal Margolis will draft proposed changes for hepatitis B and p vide a draft to all ACIP members in time to review before the next ACIP mee ng.

Craig Shapiro will draft guidelines on hepatitis A risk-groups Mary Lou Clements is to be a consultant.

Nancy Arden will revise the wording for the ACIP antiviral ag ts section of the influenza recommendation by March 6. Caren Hall and the A will review it before the ACIP members are asked for comments. She will so send to the committee additional data on rimantadine and amantadine by Ma h 6.

Nancy Arden is supposed to contact FDA regarding the age cut f for rimantadine.

Hal Margolis along with Bill Schaffner and Barbara Ann DeBuon will consider recommendation for vaccination of adolescents, and consult wi the high risk

working group. A discussion of this topic will be scheduled r the June agenda.

Full Minutes

On Feb. 23-24, 1994, the Advisory Committee on Immunization P ctices (ACIP) convened at the Centers for Disease Control and Prevention (C). Dr. Neal Halsey presided in the absence of Dr. Jeffrey Davis, the new IP Chairperson. Dr. Halsey opened the meeting at 8:35 a.m. on F . 23.

Introduction

Dr. Claire Broome, Executive Secretary, reported that Dr. Dav was hooked up by conference call. Dr. Steve Schoenbaum had also accepted t invitation to join the ACIP but was unable to attend the meeting.

Dr. Broome clarified the issues of potential conflicts of int est. Members, as always, were asked to disclose potential conflicts of inte st and to abstain from voting on--but not from discussing--vaccines mad by companies in which they have direct financial interest within the last months (i.e., grants and other funding sources of vaccine studies, employme , stocks, honoraria). Members were also asked to disclose--but not to stain from voting--if they received travel support for attendance at mee ngs from a vaccine manufacturer.

Mr. Kevin Malone reiterated that federal law does generally p hibit employees from having financial interest in matters in which ey are working; however, the same federal law acknowledges that ther is value in having persons who have expertise, which almost inherently in lves conflicts of interest. Therefore, the law does provide for waivers und certain circumstances. Each ACIP member has been given a waiver lett and should sign and return it to Ms. Gloria Kovach.

Mr. Malone also clarified that one has direct financial inter t if one not only receives funds from a particular manufacturer but also h control over the grant funds. Receiving pooled grant funds is not disclos le if one has no control over the distribution of funds. Travel support to cientific meetings is not considered a direct financial interest; howev , receipt of honoraria is. Nevertheless, Mr. Malone asked members to disc se meetings attended in the last year that had travel support from a manu cturer.

Dr. Halsey introduced new liaison members: Dr. Richard Zimme an, University of Pittsburgh, representing the American Academy of Family Ph icians; Dr. William Glezen, Baylor College, representing the Infectious D ease Society of America; and Dr. David Fleming, representing the Hospital fection Control Practices Advisory Committee (HICPAC).

Members then introduced themselves and disclosed their confli s of interest, if any. Dr. Neal Halsey from Johns Hopkins School of Hygiene nd Public Health reported no direct financial interests in any vaccine nufacturer. He has received grant support in the past 12 months from the stitute Merieux (measles vaccine-related projects); and Connaught (po o vaccine studies). He reported receiving travel support to attend vac ne-related conferences from the American Academy of Pediatrics (AAP), Sm hKline Beecham (SKB), the FDA, NIH, Ross Laboratories, and the the Institute f Medicine

(IOM). He has received small honoraria from SKB and Ross Lab atories. He announced that he would excuse himself from voting on issues lated to SKB and Connaught.

Dr. Kathy Edwards, Professor of Pediatrics at Vanderbilt Univ sity, is not receiving any direct funding, although in the past she receiv funds for acellular pertussis and Haemophilus vaccines. She has receiv honoraria for speeches from Lederle-Praxis and Connaught and thus would ref in from votes on vaccines manufactured by those two firms. She has also re ived travel funds from Lederle-Praxis, Connaught, Institute Merieux, and B.

Dr. Rudolph Jackson, Professor of Pediatrics at Morehouse Sch l of Medicine, reported that his only potential conflict of interest was the eceipt of travel support and an honorarium from Wyeth Laboratories, for rotavirus vaccine meeting.

Dr. Barbara Ann DeBuono, Director of the Health Department in hode Island and Clinical Associate Professor of Medicine at Brown Univers y, also had no known conflicts of interest.

Dr. Gena Rabinovich, NIH, had no conflicts of interest. She ked if the new rules for conflict of interest enjoined members from acceptin grants or moneys in the next 12 months. Dr. Broome said CDC is not try g to discourage members from working with vaccines, only to preser the integrity of the Committee. She only asked that forms be updated and d closures made as new working arrangements with manufacturers occur.

Dr. Carolyn Hardegree, FDA, had no conflicts of interest.

Dr. Joel Ward, UCLA, reported no direct financial interest wi any vaccine manufacturer. But as Director of UCLA's Center for Vaccine R earch he is the principal investigator on one research study on pneumococ l conjugate vaccine funded by Merck Sharpe & Dohme (MSD). He has receive travel reimbursement from SKD for a hepatitis A meeting in the past months. He excluded himself from voting for any MSD issues.

Dr. Carlos Ramirez-Ronda, Professor of Medicine at the Univer ty of Puerto Rico School of Medicine, had no financial interests with any ccine manufacturer. He has received travel reimbursement and an ho rarium from Roche, but it is not a vaccine manufacturer.

Dr. Mary Lou Clements, Director of the Center for Immunizatio Research, Johns Hopkins University, is participating as a principal inv tigator for a study on hepatitis B funded by Merck Research Laboratories. e may have received travel support--but no honoraria--to an AIDS vaccine onference supported by Pasteur Merieux. She excused herself from votin on Merck vaccines.

Dr. Jeffrey Davis, State Epidemiologist with the Wisconsin Di sion of Health and also Adjunct Professor in the Departments of Pediatrics a of Preventive Medicine at the University of Wisconsin, reported no direct o indirect interest in vaccine manufacturers.

Liaison members then introduced themselves. They were not as d to disclose conflicts of interest. The 50-plus members of the audience t n introduced themselves. They included representatives of vaccine manufac rers, academia, state and federal government agencies, and scientif journals.

ACIP's Role in the Vaccines for Children (VFC) Program

Dr. Walter Orenstein, Director of the National Immunization P gram (NIP), outlined the ACIP's role in the VFC program. He reviewed tha program, patient eligibility requirements, and providers' roles and ex ained that the decisions made today would be the basis for NIP's going forwa in the contracting process.

Mr. D. Dean Mason, NIP, summarized the preliminary analysis o the state responses to a VFC survey, undertaken to determine the needs communities to implement this program. Responses were received from all states and from 59 of 63 projects. State estimates of vaccine purchase sts for fiscal year 1995 for eligible children under this program totaled $4 .4 million. State requests for direct assistance through the grant mechan m for providing additional vaccines were for $131.9 million. The s tes' estimates of the proportion of children nationwide that would be covere through this program were: 38% eligible through Medicaid; 1% Native Ameri n and Alaska; 14% covered because they have no health insurance; and 8% cov ed by presentation to federally qualified health centers. This mak a total coverage estimate of 61% of children potentially eligible und the VFC.

Mr. Mason also reported that 12 of the states have universal ccine supply (e.g., the state provides all vaccines to all providers); and 2 more states would like to have this policy.

Dr. Orenstein said the VFC program is to go into effect Oct. 1994, so vaccines will have to be shipped to providers by September. erefore, solicitations for contracts have to go out at the beginning o March.

Discussion of Responses to Proposed Federal Register (F.R.) N ice Schedule Recommended for the VFC Program

Mr. Malone briefly went over the provisions of the Omnibus Bu et Reconciliation Act of 1993 (OBRA) that deal specifically with he ACIP's role in the VFC program. There are two sections that deal with th ACIP's role. The first states that the Secretary of HHS will purchase the ccines from a list established by the ACIP. The other provision states tha providers who participate in this program must follow the recommendations o the ACIP as regards the appropriate periodicity, dosage, and contraindica ons applicable to those vaccines--except in such cases as, in the provider's edical judgment subject to accepted medical practice, such complianc is medically inappropriate. The law also provides for states to provide f variations on the ACIP recommendations.

The law is written in very broad terms. The word routine is t used in describing what vaccines to choose; instead the phrase pediat c vaccines is used. This, in turn, gives the ACIP broad discretion. He th read the following from the OBRA '93 Statement of Managers:

> The Conferees intend that the Advisory Committee on Immu zation Practices be allowed to conduct its work in an objective anner, concerned only with matters of public health and medicin While decisions regarding the listing of recommended vaccines ll, undoubtedly, have some budget implications for the progr and the Secretary, it is the Conferees' intention that the ACIP' work be rigorously separated from such concerns. The Conferees e troubled by past examples of budgetary influence in matters of scien and has [sic] chosen the Advisory Committee on Immunization Practices the Centers for Disease Control and Prevention as a committee less v nerable than some others to such influence. So, for example, if the IP were to decide that one vaccine that produces side effects and r ctions should be replaced with a more expensive vaccine that does not, either the Secretary nor any other public officer should attempt to ffect that judgment. If proposed changes present a budget implicat n so serious as to cause the Secretary to question their validity, th Secretary should present that concern and a proposed legislative c nge to the Congress, but until legislative change is made, the enti ements of States to ACIP-recommended vaccines are to continue in e ect.

Mr. Malone said that CDC's General Counsel's Office is interp ting this statement to mean that the "budget shall not drive the scienc " He said the ACIP needed to provide enough information on childhood vaccin today so that contracts could be issued. He said that the chair of the ACI would write a cover letter to the Secretary of HHS with the Committee's dec ions and a notice would be published in the F.R. Mr. Malone also sugges d the Committee consider developing a specific document for physici s dealing with the vaccines and issues covered under this law. Finally, he commended that the ACIP instruct the CDC staff to examine the current ACIP r ommendations to make sure that there are no contradictions with today's re mmendations so that the documents can be reconciled soon, if necessary.

Dr. Steve Hadler, NIP, then led the discussion and voting. H asked ACIP members to refer to Handout #1 ("Issues for Vote at ACIP meet g"). He reminded members that they had had a preliminary vote at the st ACIP meeting. At that time, members proposed that the vaccines ta eted at the following diseases be included: pertussis, diphtheria, tetan , Haemophilus influenzae type b, measles, mumps, rubella, poliomyelitis, an hepatitis B. The schedule was that currently recommended by ACIP. The F.R notice about this preliminary vote (58 FR 65725)--which included the ACIP neral Recommendations--appeared December 16, 1993.

He said that footnoted changes to each antigen appeared on Ha out #1. He said that CDC had strived to make the proposed wording for re mmendations fully compatible with the current AAP recommendations. Diffe nces are acknowledged in footnotes.

Eleven substantive responses were received as a result of the '.R. notice. One was from a state health department; 8 from practitioners; . from the merican Academy of Family Practioners; and 2 from manufactur 's. Several issues about scheduling, combined vaccines, and scope were ra ed during the discussion with states about the vaccines for the VFC program Dr. Hadler reiterated that a self-contained document for physicians woul be the ideal complete guideline. He also asked the ACIP whether preparing he final document should be overseen by a working group or delegated t CDC staff. Dr. Hadler also said that the ACIP will determine the number doses that are recommended as part of the routine schedule.

An ACIP member asked for reassurance that there would be an e ort made by the program, when there are products that are considered equi lent by more than one manufacturer, to purchase vaccine in a reasonably eq table fashion.

Dean Mason, NIP, responded that the legislation gives CDC the ption, for the first time, of providing awards to more than one manufacturer or similar products. CDC can encourage vaccine manufacturer participati by awarding not only to the low bidder but a certain portion to the high dder as well, so long as that bid is within the price caps established. In hat way, manufacturers from year to year would remain in the market. e contract solicitations, to be published soon, would guarantee a market hare for more than one provider.

Regarding pending vaccines, such as varicella, Mr. Malone sai that the formal ACIP vote would be needed to add any vaccines to the s edule or, for that matter, to change the schedule itself.
Dr. Halsey announced that Ms. Kovach was recording all votes d would announce them after each vote.

Dr. Hadler brought up the first issue for vote, which was whi vaccines should be included in the program. The current notice propos the vaccines to prevent the nine diseases listed here (Handout #1; [pertus s, diphtheria, tetanus, H. flu, measles, mumps, rubella, poliomyelitis, and patitis B]). The proposed language for a vote was:

> The ACIP reaffirms that vaccines which are currently use to prevent the 9 diseases listed above should be included in the Vaccin for Children (VFC) program. Specific vaccines to prevent these disea s will be determined in subsequent votes.
>
> This vote does not exclude consideration of vaccines to event additional diseases such as influenza and pneumococcal d eases.

Mr. Malone ruled that since this matter didn't reference spec ic vaccines, it was essentially a de minimus effort and therefore everyone ould vote on this particular matter. He also said that members who were e using themselves because of a financial interest, should abstain.

Only members of the ACIP voted on this. The vote carried una mously, though Drs. Stephen Schoenbaum and Fred Thompson were absent.

Vaccines to Prevent Diphtheria, Tetanus, and Pertussis

ıe next several issues dealt with vaccines to prevent pertuss ;, diphtheria and tetanus. The current F.R. notice proposes that the follow ıg vaccines may be used for prevention of these diseases:

-- Diphtheria and tetanus toxoids and whole cell pertus .s vaccine (DTP)
-- Diphtheria and tetanus toxoids and acellular pertuss ; vaccine (DTaP)
-- Diphtheria and tetanus toxoids (pediatrics) (DT)
-- Tetanus and diphtheria toxoids (for children 7 years ınd older and adults) (Td)
-- Diphtheria and tetanus toxoids with whole cell pertu ;is combined with Haemophilus influenza b conjugate vaccine.

Dr. Hadler proposed the following for vote:

> The ACIP recommends that the vaccines listed above, inclu .ng the recently licensed vaccine "Pasteur Merieux Haemophilus in .uenza b conjugate vaccine (PRP-T) which may be reconstituted with)TP vaccine (produced by Connaught Laboratories, Inc.)" be included i the Vaccines for Children program.

Dr. Hadler noted that the following manufacturers were involve in production or distribution of such vaccines: Connaught Labs, Lederle Lak Massachusetts Public Health Biologic Labs, the Michigan Depart ent of Public 'ealth, Wyeth-Ayerst, and Pasteur Connaught.

Dr. Carolyn Hardegree of the FDA clarified, for the record, th : the DT acellular pertussis, like the Td, is recommended for specific :oups. Secondly, she requested that the record should show that the I ? vaccine produced by Connaught is Connaught Incorporated, specifically. And thus, that's the approval that was made--not for any other vaccine t be used to reconstitute PRP-T.

At Mr. Malone's suggestion, Dr. Halsey re-read the proposal fc vote. Mr. Malone also clarified that Dr. Davis (not physically present, ıt connected by conference call), could vote.

The vote was taken and the motion passed--7 for (Drs. Clements Davis, DeBuono, Ramirez-Ronda, Ward, Rabinovich, and Hardegree); zerc ıays; 3 abstentions (Drs. Edwards, Halsey, and Jackson); and 2 absente ; (Drs. Schoenbaum and Thompson).

Dr. Hadler said that the next proposal dealt with the schedule ınd the footnotes that go along with the DPT schedule:

> The recommended schedule for children includes 5 doses of)TP vaccine (or DT or DTaP or combined DTP-Hib vaccines where appropı ıte) by school entry, and 1 dose of Td vaccine given at 14-16 years of a e.

The schedule is as shown--this is verbatim from Table 1 of the .R. notice--
and the following footnotes clarify these recommendations. Th first is a
eneric one--that "the recommended immunization schedule may v y for infants
and children who do not begin their series on time" and refers o the table
for accelerated immunization in the General Recommendations on mmunization.

The second footnote stated that this series could begin at 6 w ks of age.
The third footnote stated that DT may be used in place of DTP en pertussis
vaccine is contraindicated. The fourth footnote was, "the fou h dose of DTP
can be given as early as 12 months of age provided that the in rval since
the previous dose of DTP is at least 6 months. DTaP preparati s are
currently recommended only for use as the 4th and/or 5th doses f the DTP
series among children ages 15 months through 6 years." And, f ally, a
footnote stated that these vaccines may be given at 18 months.

Dr. Hardegree noted her concern that this approach to voting d not address
the issue of simultaneous administration of other vaccines. D Halsey said
that a later presentation by Dr. Hadler and Dr. Caroline Hall er attempts
to modify the presentation of the schedule and perhaps simplif the
presentation would address this.

A representative from a manufacturer said that some manufactur s disagree
with package inserts and asked if FDA would let manufacturers ange their
package inserts. Dr. Hardegree said that differences between e ACIP
recommendations and labels was a major concern at the FDA, whi was working
on how this could be resolved. She also stated that in many o the issues
that were going to be discussed, there might be such differenc and, for
hat reason, as an ex officio member, she would often abstain om voting.

Dr. Halsey then read the proposal for vote, which follows:

> The ACIP recommends the number of doses, schedule, and qu ifications
> noted above and in the text of the Dec. 16, 1993 notice. he additions
> we have made are insertion of the word routine for the se ence that now
> reads, "The routine schedule shown in Table 1," and Dr. C nstein's
> suggestion regarding the ACIP's endorsing the AAP recomme lations for
> the timing of the fourth dose.

The proposal passed (6 for [Drs. Clements, Davis, DeBuono, Ram ez-Ronda,
Ward, and Rabinovich]; 4 abstentions [Drs. Edwards, Halsey, Ja son and
Hardegree]; and 2 absentees [Drs. Schoenbaum and Thompson]).

Dr. Hadler then read the following proposal for vote:

> The ACIP recommends that text be included in the final No ce and in the
> schedule which states preference for the use of DTaP for e 4th and 5th
> doses of the DTP series.

He pointed out that the AAP does not state a preference at thi time, and
that the use of DTaP--about 3-1/2 million doses were sold last ear--makes up
about 15%-20% of the DTP market so it has seen much wider use ring the last
year. He added that the managers' language in OBRA states tha the ACIP be

allowed to conduct its work in an objective manner, concerned ıly with issues of public health and medicine. If the ACIP were to de ıe that one accine that produces side effects and reactions should be re aced with a more expensive one that does not, neither the Secretary nor a other public health officer should attempt to affect that judgment.

Dr. Peter did not have the AAP wording with him, but said he ın't think the Red Book meant to discourage the use of DTaP.

In discussion, ACIP and liaison members expressed concern abo giving specific preference.

Dr. Halsey then read the suggested wording for vote:

> The ACIP recommends that text be included in the final N ice and in the immunization schedule which states preference for the us of DTaP for the 4th and 5th doses of the DTP series.

The proposal failed. The vote was 2 for (Drs. DeBuono and Ra ıovich); 5 against (Drs. Clements, Davis, Ramirez-Ronda, Ward, and Harde ee); 3 abstaining([Drs. Edwards, Halsey, and Jackson); and 2 absente (Schoenbaum and Thompson).

Vaccines to Prevent H. influenza type b Disease

The next issues dealt with H. influenza type b (Hib) vaccines again, first with which vaccines, then with the schedule, and then with cl ification ssues. The current notice proposes the following vaccines m be used to prevent Hib disease: Hib conjugate vaccines; Diphtheria and tanus toxoids with whole cell pertussis combined with Haemophilus influenza conjugate vaccine. Dr. Hadler said that the following newly licensed v cine should be added to this list: Pasteur Merieux Haemophilus influenza b ıjugate vaccine (PRP-T) which may be reconstituted with DTP vaccine (oduced by Connaught Laboratories, Inc.). The latter is a new product; ere are no other new products.

Dr. Hadler pointed out that the manufacturers of Hib vaccines nclude Connaught Labs, Inc., which is a subsidiary of Pasteur-Merieu Lederle-Praxis; and MSD. Since one of the PRP-Ts is being distribute by SKB, Mr. Malone was asked whether SKB was a conflict of interest. He id that, to be cautious, persons with such conflicts should refrain from vot g, but that he'd clarify whether this stance is overly cautious at a futu meeting.

Dr. Hardegree added, for the record, that the license on the P-T is issued to Pasteur Merieux, so there are in fact four companies that e licensed for conjugate vaccines: Connaught, Pasteur Merieux, Lederle Prax and MSD.

Dr. Halsey read the following proposal for vote:

> The ACIP recommends that the vaccines listed above, incl ing the newly licensed vaccine "Pasteur Merieux Haemophilus influenza conjugate vaccine (PRP-T) which may be reconstituted with DTP vacc e (produced by

Connaught Laboratories, Inc.)" be included in the Vaccine for Children program.

The vote carried (5 in favor [Drs. Davis, Jackson, Ramirez-Ror ı, Rabinovich, and Hardegree]; none opposed; 4 abstaining [Drs. Clements, Edw :ds, Halsey, and Ward], and 3 absent [Drs. DeBuono, Schoenbaum, and Thompsc).

Dr. Hadler next dealt with the schedule for Hib vaccines. The ?ording was: "The schedule includes 3 or 4 doses of a Hib-containing vaccir by age 2 years, depending on the specific vaccine (see Table 1)." It s)ws Schedule A (2, 4 and 6 months and 12-15 months) and Schedule B (2 and 4 n ıths and 12-15 months). The footnotes clarify which products are schedule A [bOC, PRP-T or DTP-HbOC) and Schedule B (PRP-OMP). It has the same footnote ıat the DTP one had on children beginning late. It also has the same foot)te that this series can begin at 6 weeks of age. As a footnote, any licens l conjugate vaccine may be used as a booster dose at age 12-15 months.

Dr. Hadler then read the following for vote:

> The ACIP recommends the number of doses, schedule, and qu .ifications noted above and in the text of the Dec. 16, 1993, Notice, ?ith the addition of the Hib conjugate vaccine PRP-T, which may be :econstituted with DTP as an acceptable alternative for schedule A.

The vote carried (4 in favor [Drs. Davis, Jackson, Ramirez-Ror ı, and Hardegree]; none opposed; 4 abstaining [Drs. Clements, Edwards Halsey and Ward]; and 4 absent [Drs. DeBuono, Schoenbaum, Thompson, and F)inovich]).

Dr. Hadler next dealt with two specific issues that were raise in the comments. The first one dealt with consistency in the Hib pri ıry series. The comment received said, "The preference for completion of t ? primary [Hib] series with a single Hib conjugate should be expressly a l clearly stated in the schedule."

Dr. Hadler pointed out that the Hib vaccine recommendations sa : "The primary series should <u>preferably</u> be completed with the same Hib conjuc :e. If, however, different vaccines are administered, a total of 3 dos ; of Hib conjugate vaccines is adequate. Any combination of Hib conjuc :e vaccines that is licensed for use among infants may be used to complete :he series."

The General Recommendations have essentially the same text, al ıough the leading sentence is, "The primary vaccine series should be cor leted with the same Hib vaccine, <u>if feasible.</u>"

For vote was the following:

> The ACIP recommends language on interchangeability of Hil ?accines for the primary series as cited in the current General Recom ıdations on Immunization be incorporated into the final Notice for Va :ine for Children.

The vote carried (3 in favor [Drs. Davis, Jackson and Ramirez onda]; none, opposed; 5 abstaining [Drs. Clements, Edwards, Halsey, Ward, d Hardegree]; nd 5 absent [Drs. DeBuono, Schoenbaum, Thompson, Ward, and R inovich]).

For the next issue, there were a series of overheads that dea with the use of combinations versus single-antigen vaccines. The current tice is silent on the issue of preferential use of DTP-Hib as opposed to the ndividual DTP and Hib vaccines.

One response to the F.R. notice stated that the lack of prefe nce "will foster a two-tiered immunization system which denies children n the public sector access to the latest and best vaccine technology." Dr Hadler pointed out that the language in the law [OBRA 93] basically denies f eral financial participation for inappropriate administration of single-anti n vaccines. It says the federal government would not reimburse for the in propriate use of single-antigen vaccines in "any case in which the administ tion of a combined-antigen vaccine was medically appropriate (as determ ed by the Secretary)."

Dr. Hadler said that the single-antigen clauses cited in Medi id and OBRA were intended to discourage a known practice of administering easles, mumps, and rubella vaccines as separate antigens at separate visits, practice which increased both the cost of vaccine and of reimbursement or vaccine administration, and decreased the chance children would be up o-date. This practice persisted in some areas despite recommendations to t contrary for over a decade.

The combined DTP-Hib vaccines have only recently become avail le, but they are a welcome addition to the vaccine armamentarium and permi fewer injections. However, right now these vaccines account for on a modest proportion of Hib and DTP vaccination. We currently have fou manufacturers producing DTP and three producing Hib. Two produce a license DTP-Hib formulation, while at least one other is working on a combina on that includes five inactivated antigens.

He concluded that, to optimally assure competition in develop nt of combined vaccines, development and use of combined vaccines should be couraged. To assure participation of maximum numbers of manufacturers and providers, the use of individual DTP and Hib vaccines should not be limi d until the new combined vaccines are more widely used and others become ailable.

The proposal for vote was:

> The ACIP should strongly endorse--or endorse--the prefer tial use of the combined vaccines, particularly in the first year of ife, but should not restrict the use of reimbursements for single ntigen Hib vaccines during these visits, and the Department should mplete contracts for both single-antigen and multiple-antigen p ducts.

Dr. Sam Katz, speaking from the floor, addressed Dr. Hadler's tatement that "The use of these vaccines accounts for only a modest proport n." The reason for that, Dr. Katz said, was that many places have lar backlogs of

the single products and would not buy the combined product unt l they used up the old single antigens. An unidentified Lederle-Praxis repre entative greed, saying their estimates were that 75%-80% of private pe latricians have converted to the use of Tetramune.

In subsequent discussion, members expressed concern but the wo is preferential and strongly in the proposal. Dr. Orenstein stat l that concerns over children getting all of the antigens separately lght be leading to lower coverage rates and that, from a program stanc oint, NIP was in favor of encouraging the combination products, whenever pos lble, as it may improve overall immunization coverage rates. Another ACII nember stated that he liked the term preferential.

Dr. Rabinovich of NIH expressed concern about reactogenicity c the individual components and the safety of coadministration. Spe lfically, with the combination product, she said, if you recommend only the c nbination for the 4th dose of Hib-DTP (the focus of the discussion now being Hib) then you're saying not to use the acellular pertussis for the 4th c se, where there is a stated Public Health Service priority for the devel oment of less-reactogenic acellular pertussis vaccines that has been the sou se of the legislation for the National Vaccine Program and the National ccine Injury Compensation Program.

Dr. Broome reiterated that there are specific instances in whi n single-antigen Hib might be preferred.

Dr. Halsey read the handout wording this proposal, as it was n lified omewhat from that on Dr. Hadler's overhead:

> The ACIP encourages the use of DTP-Hib vaccines (combinec or licensed for combined administration), particularly in the first y ar of life, but should not restrict the use of or reimbursement for s ngle-antigen Hib vaccines during these visits, and the Department shou l complete contracts for both single-antigen and multiple-antigen pr lucts.

It was decided that Drs. Rabinovich, Ward, and Hadler should n et with Mr. Malone over lunch and hammer out some specific wording to fina lze this proposal.

Interchangeability of Vaccines other than Hib

The next issue dealt with interchangeability of vaccines othe: than Hib ones. This was not addressed in the F.R. notice directly. However, : is addressed in the General Recommendations, which are cited in the current notice. The language in the General Recommendations reads:

> When at least one dose of a hepatitis B vaccine produced / one manufacturer is followed by subsequent doses from a diffe ent manufacturer, the immune response has been shown to be cc parable with that resulting from a full course of vaccination with a s ngle vaccine.

When administered according to licensed indications, diff :ent DTP vaccines as single antigens or various combinations, as v .l as live and inactivated polio vaccines, can also be used interchange: .y. However, published data supporting this recommendation are genera] r limited.

Then the issue for vote was:

The ACIP recommends that the final Notice on Vaccines fo: :hildren contain language equivalent to that noted above permitti: interchangeable use of different licensed vaccines to pre :nt hepatitis B; DTP; and polio disease.

Although this one dealt with hepatitis B, DTP, and polio, Mr. :lone said this was a generic issue so all could vote. The vote was una: :ous for the proposal (with 2 absentees, Drs. Schoenbaum and Thompson.)

Polio Vaccines

Dr. Hadler said that the F.R. Notice proposes that either ora])olio vaccine (OPV) or enhanced inactivated polio vaccine (IPV) may be used. The vote would be:

The ACIP recommends that the vaccines listed above be inc :ded in the Vaccines for Children Program.

The measure passed (7 for [Drs. Clements, Davis, DeBuono, Jac])n, Ward, Rabinovich and Hardegree]; none opposed; 2 abstainers [Drs. Ec :rds and Halsey]; and 2 absentees [Drs. Schoenbaum and Thompson]).

A vote on details of the polio schedule was deferred to later :n the day.

Vaccines to Prevent Measles, Mumps, and Rubella

Dr. Hadler said that the next vote would be on vaccines to pu: :ase for measles, mumps and rubella. The current Notice proposes not c :ly MMR, but also measles and rubella combined vaccine (MR), measles vacci: , mumps vaccine, and rubella vaccine. The vote would be:

The ACIP recommends that the vaccines listed above be inc :ded in the Vaccines for Children Program.

Persons who had received funds from MSD were the only ones ex(:ded from voting. The vote carried (7 in favor [Drs. Davis, Edwards, H: :sey, Jackson, Ramirez-Ronda, Rabinovich, and Hardegree]; zero noes; 2 abste: :ions [Drs. Clements and Ward]; and 3 absentees [Drs. DeBuono, Schoenbaum, :nd Thompson]).

The next issue dealt with the specifics of the MMR schedule. :e current Notice is as follows: "The recommended schedule for children :ncludes 2 doses of MMR vaccine." The schedule is 12-15 months and 4-6 : :ars. The clarifying footnotes are the one on late schedules and one sp(:ific to this notice that is not in the General Recommendations, saying "Si: :le-antigen measles, mumps or rubella vaccines should be used only if the: is a specific

contraindication to one component of MMR vaccine, or the child .s known to be immune or adequately vaccinated for one or more of these disea es, or measles accine is indicated for a child prior to one year of age (e.g during outbreaks among preschool-age children)." There's also a foot ote saying, "The second dose of MMR vaccine may be given at entry to middl or junior high school."

Dr. Hadler said there had been two comments on the Notice. Or was that single-antigen mumps vaccine should only be used for outbreak ontrol. The second comment was a question, "Is the use of single-antigen m asles vaccine for the second dose of the MMR series compliant with the Notic "

Dr. Hadler noted that the current ACIP statements do not expli .tly recommend two doses of either mumps or rubella vaccine. The mumps state ent predates the 2-dose recommendation, while the rubella statement acknowl lged that "many persons will receive two doses of rubella vaccine as a r sult of the new two-dose schedule for MMR vaccination, which is recommende to improve control of measles."

The proposal for a vote was:

> The ACIP recommends the number of doses, schedules and qu lifications as noted above and in the text of the Dec. 16, 1993 Notice, lth the clarification in text and table that single-antigen vacci es may also be used for outbreak control, but that routine vaccination s ould only be completed with MMR.

In answer to a question, Dr. Hadler clarified that the law cov ed children through 18 years of age. Dr. Orenstein suggested that a state ent be included acknowledging the differences in the recommendations etween the AAP and the ACIP. He offered to write the specific wording and di tribute it that afternoon.

Noting that Dr. Orenstein's phrase to that effect would be ad d, members voted on the proposal. The motion carried (7 in favor [Drs. I vis, DeBuono, Edwards, Halsey, Jackson, Ramirez-Ronda, and Rabinovich]; 0 op osed; 3 abstaining [Drs. Clements, Ward and Hardegree]).

ACIP Statement on Varicella Prevention

Dr. Sandra Holmes outlined three key issues. First was some w wording on the issue of simultaneous administration of varicella vaccine with other recommended vaccines. Upon the suggestion of a liaison membe the wording about 6-week intervals--if varicella vaccine and MMR will be g ven separately--was changed to a 4-week or greater interval. Sec d, was the addition of a more specific statement on the immunization of a olescents over 13 years of age and adults; and 3) the addition of a more de iled statement on the immunization of health care workers (HCWs). An append on the prophylactic use of Acyclovir was also added.

Following this presentation and a brief discussion, the group minus those members who had affiliations with MSD) voted to accept the fo owing:

> Certain risk groups should be targeted for varicella imm ization programs (see below); however, all persons 13 years of a and older with a history of varicella should be offered vaccinatio at the time of any routine health care visit.

The motion carried, but three members abstained.

Regarding the HCW section, members suggested that a couple of entences about infectivity of break-through cases be added. Dr. Tony Robb s asked if this section had been shared with OSHA and NIOSH. It was als suggested that the following sentence, on p. 30, be deleted from the "Pregna y" section because there are no data to support it:

> Because the virulence of the attenuated virus used in th vaccine is less than that of the wild-type virus, the risk to the f is, if any, may be even lower.

It was also pointed out that the use of acyclovir for women w get varicella in pregnancy is never addressed and should be. Finally, it wa suggested that the paragraph on "Children with Conditions Requiring Steroid erapy" could be clearer regarding inhaled steroids; could possibly be comb ed with that on altered immunity (p. 29); and that the draft wording for t AAP statement, which is much more specific, be shared with Dr. Ho es. Comments were to be submitted in writing to Dr. Holmes by March 23.

Dr. Hardegree was then asked to comment on the discussion of cicella vaccine at the January meeting of FDA's Vaccine Products Advi cy Meeting. She said that the advisory group was asked to address several uestions on safety and efficacy of this product in children 1-12 years of ge and to comment on the adequacy of the single dose in that age-group. The advisory group was also asked to address whether or not the safety and fficacy data supported the use of 2 doses in persons over 12 years of age d to address comments related to the adequacy of the data regarding simult eous administration. Her recall was that the group recommended th the data supported the use of one dose in children but that the postma eting studies would need to keep close tabs on whether or not a second dose ould be needed. The group wanted to see additional data on simultaneo administration. There was also discussion about whether addi onal modeling was needed to predict the changes in the epidemiology of the sease (regarding herpes zoster, for example) once a vaccine was int duced. The group emphasized the need for long-term surveillance data. T FDA continues to review the application and to work with the manufacturer o this application, she concluded.

Update on the National Vaccine Program (NVP)

Following a break for lunch, Dr. Tony Robbins of the NVP said t is putting together a new working group on the introduction of new vacci s. NVP recognizes that every time this subject is discussed, the ACI FDA, NIH, and

HCFA are involved. He said there needs to be developed for th United States a strategy of what we go through, what we look at when we're c nsidering the introduction of a new vaccine.

He then reported that the NVP had also gotten involved recentl in a problem around technology transfer. He said the NVP discovered that t new federal law and rules may not be properly suited to vaccines. When a mall firm wanted to get some measles strains to study and to work on imp oving measles vaccines, the upfront price was very high, with much less conc n about what would be charged down the road. The NVP recognized that that ght be a very useful approach at recouping costs for pharmaceutical products nd things that were evidently going to produce a high profit in the end t it was probably not a great strategy for getting more researchers and ore companies working on vaccine problems--that one should really lower the rriers on the front end and simply make sure the government understands what ts purposes were in the long run. And the NVP found that NIH and CDC had ver had a separate set of policy guidance for vaccines and they were eag to have this. So the NVP is setting up a working group on technology ransfer and vaccines.

Third, the NVP is working on what Dr. Robbins termed the long- anding problem between FDA and CDC regarding labels. Finally, the NV is working on increasing the number of sites at which underinsured class of ildren can receive free vaccines.

High Risk of Vaccine-Associated Paralytic Polio (VAPP) in Roma a

Dr. Peter Strebel reported that since 1970, Romania has report l exceptionally high rates of VAPP. The leading hypothesis for is was that Romanian-produced OPV had increased neurovirulence. According , in 1990, WHO recommended that the Romanian OPV be replaced with importe vaccine. Yet, even with imported OPV, the relative risk of acquiring VA remained more than 15 times the rate of VAPP in the United States. A c se-control study suggests that exposure to intramuscular (IM) injections y be associated with VAPP. He reported that 27 VAPP patients had r eived a mean number of 17 IM injections versus 3 injections among 77 contr . Ninety-five percent of the injections were antibiotics. There was a rong association between receipt of one or more IM injections duri the 30 days prior to paralysis onset and vaccine-associated disease. Among ecipient VAPP cases, the bulk of risk was with injections received after rec pt of OPV. He concluded that IM injections of antibiotics given during the i ubation period of OPV may provoke paralytic illness.

U.S. Experience with VAPP

Dr. Roland Sutter briefly summarized the current experience wi injections (during the last 30 days prior to onset of paralysis) and VAPI etween 1988-12992 in the United States. His presentation focused on VAPP immunologically normal persons, including recipients and conta s. All recipient cases did receive OPV with Hib vaccine and/or DTP; h ever, the interval between IM vaccination and onset of paralysis for nea y all recipient VAPP cases was outside the "high-risk window" for pr rocation

poliomyelitis (i.e., 7-21 days). Only one contact case had a IM injection prior to onset. The low prevalence of IM injections in conta cases, and he fact that most IM injections (with vaccines) fell outside he high-risk window, both weigh against the initiation of a case-control s dy in the United States. Nevertheless, CDC will continue to collect an summarize data on injections and VAPP.

Sequential IPV-OPV Schedule

Dr. Sutter then introduced several topics and speakers--rever on of poliovirus contained in OPV when given after IPV; sequential V-OPV study; follow-up on the IOM report; the impact of a sequential IPV-O schedule on VAPP; and option for vaccination policies.

Dr. Olen Kew spoke first, his main point was that reversion f lowing OPV was similar regardless of the prior administration of IPV, and wa not a serious issue for concern. Dr. Andrew Murdin reported on shedding an reversion studies. He concluded that a combined vaccination schedule r uces excretion and does not increase the proportion of isolates that contain evertant virus. He then examined the Canadian experience with a combi d schedule. He concluded that vaccine-associated disease in Canada had on been reported from provinces that used OPV exclusively.

Dr. P. Ogra, Children's Hospital, Galveston, reported on his trospective studies and congratulated Dr. Murdin on his prospective studi . He felt that Dr. Kew was probably right that too much is being read i o Ogra's reversion data. Nevertheless, his data do show reversions wi both IPV and OPV, and IPV does not change the pattern.

Dr. J. Modlin presented data from a study on the immunogenici and relative gastrointestinal immunity conferred by three different sequen al IPV-OPV polio schedules and compared these to the standard schedule. he data showed that two doses of this particular IPV were somewhat less immu genic for all 3 types of polio than other IPV preparations studied before a after this study. The IPV used in this study is no longer in production nd is not available in the United States. Researchers did rule out a l oratory method artifact; further, there is no indication that the potency of his vaccine had declined.

A second finding was that, regardless of when OPV was introdu d into the schedule, it produced a substantial boost in antibody titer. hird, it appears that a sequential schedule is quite reasonable from a immunogenicity point of view. If we went to this schedule, however, Dr. Mod n predicted that an optimal sequential schedule would require two or thre doses of IPV in the first 6 months of life, followed by two or three doses f OPV, and that the first dose of OPV might be administrered as early as months of age.

Dr. Sutter then summarized answers to the questions raised by he last IOM report:

- **Is wild virus circulating in the country?** It is ve unlikely.

- **What are the levels of immunity in young adults?** Th[ey] seem to be very high for polio type 1 and 2, but somewhat lowe[r] for type 3.
- **What are the levels of immunity in preschool-age ch[il]dren, particularly those in the inner city?** For most gro[up]s, they were about 90%.
- **To what extent, in the United States, does OPV vacc[ine] virus spread from vaccinees to contacts?** Serotype 2 appears to [be] the most efficient in spreading; serotypes 1 and 3 are less [ef]ficient.

Dr. Sutter then discussed the potential impact of a sequentia[l] schedule on VAPP cases and cost-benefit estimates. He said that three VA[PP] cases would be prevented annually by going to the sequential schedule, an[d] that the direct costs per case prevented was estimated at $10.5 millio[n] for a 4-dose sequential schedule, $34.2 million for a 5-dose schedule, and $8.6 million for a 6-dose schedule.

He summarized by saying that he hoped the presentations had a[l]leviated concerns about reversion, and that a sequential schedule mode[l] tely reduces VAPP cases (43%-51%), but at a very high cost per case prevent[ed].

He pointed out that the purpose of the previous presentations [was] for the ACIP to decide whether or not to change polio vaccination poli[cy] and, if so, how. The Committee's choices were a decision for no change; a [de]cision to change to a permissive recommendation allowing either OPV only [or] a sequential schedule; or choosing a sequential IPV-OPV recommen[d]ation.

After discussion, it was decided that there was no consensus [for] a change. The group decided to delay a vote until licensure for a combi[ned] vaccine is in the works, at which point the item should be put back on t[he] agenda. Meanwhile, it was suggested that an ACIP member be added to a[n] NVAC subcommittee on new vaccines.

<u>Postexposure prophylaxis for Hepatitis C</u>

Dr. Miriam Alter discussed postexposure prophylaxis for hepat[itis] C, targeted mainly at HCWs. She explained that the current ACIP recommen[da]tions (published in 1990) state:

> For persons with percutaneous exposure to blood from a pa[tient] with PT-NANB hepatitis, it may be reasonable to administer IG (0.[06] ml/kg) as soon as possible after exposure. In other circumstances, no specific recommendations can be made.

She asked the Committee to consider whether the ACIP should no[t] longer recommend immune globulin G (IG) after percutaneous exposures [be]cause recent studies indicate that IG does not protect against infection w[ith] HCV. The group voted unanimously to rescind the previous wording and a[c]ept her new wording, which was:

> Recent studies indicate that immune globulin does not pro[tect] against infection with HCV. Thus, available data do not support [the] use of IG for postexposure prophylaxis of hepatitis C. There are [no] data on the

efficacy of IG for postexposure prophylaxis of other (nor ICV) parenterally transmitted non-A, non-B hepatitis.

She also asked the Committee to decide whether it should recor end a "hepatitis C protocol" for the follow-up of HCWs who sustain a cidental percutaneous (and permucosal) exposures. These would include esting of the source for anti-HCV, baseline and follow-up testing of the exp sed employee for anti-HCV, and counseling of the exposed employee regarding risk of infection and transmission to others. She said data are limite on the risk of transmission after percutaneous exposure and on the types c exposures that do result in transmission. The total cost of such a scre ling program would be $2.1-$4.2 million for an estimated 245-490 cases a ye , 12-25 of whom would respond to therapy-- for a cost per patient of $167 000.

In follow-up discussion, members asked about the status of the ACIP document on HCWs; they were told it awaits only the sections on hepatit s, varicella and BCG. It was suggested that that document could include a ood description of the HCW problem and make a case for screening. Another member suggested that the ACIP withhold its judgment on this matter u cil the Committee can view that revised document and then come to a sc olarly decision. Dr. Alter was asked to mail some alternative wordir s regarding universal screening to members.

Discussion of Responses to Proposed F.R. Notice on the Schedu Recommended for the VFC Program--continued

Polio Vaccines--continued

Discussion then returned to voting on what to include in the V program. Dr. Hadler returned to the polio issue and the critical footnc e that "enhanced, inactivated IPV may be substituted for OPV, using a different schedule." This is really not consistent with current ACIP re ommendations, he said. The issue for vote was:

> The ACIP recommends the number of doses, schedule and qua lfications as noted above and in the text of the current Notice, with e clarification in text and footnotes that OPV is the recor ended vaccine for routine vaccination of normal infants and children. ay changes in recommendations that are endorsed by the ACIP in the Jun 1994 meeting will be incorporated into the final notice.

Dr. Orenstein recommended using the same language as used in e AAP recommendations. Mr. Malone said he had that and would prese it later. Persons with support from Lederle Laboratories, Pasteur-Merie -Connaught were to abstain. The vote carried (6 in favor [Drs. Davis, C ments, DeBuono, Jackson, Ramirez-Ronda, and Ward]; none opposed; 2 al tentions [Drs. Edwards and Halsey], and 2 absentees [Drs. Schoenbaum and Thor son]).

Dr. Rabinovich was concerned that manufacturers' labels might ot be consistent. Dr. Halsey said this would not be the first time at recommendations were inconsistent with labels. Dr. Orenstein eminded the

group that the ground rules for the meeting were "no changes i the ACIP schedule," and this would require a change. It was decided tc ıove on.

However, Dr. Hardegree suggested it would be helpful for the A :P, in the future, to provide manufacturers with all the data that led tc ıaking changes in recommendations so that the manufacturers could adjust thei labels, if necessary.

Votes on Vaccines for Hepatitis B

Discussion then moved to the next votes, on hepatitis B vaccir Dr. Hadler said that the current notice proposes the followinç ʼaccines be used for prevention of these diseases: Hepatitis B vaccine ar Hepatitis B Immune Globulin (HBIG) (for infants born to HBV-carrier mothei

The vote read:

> The ACIP recommends that the vaccines listed above be inc ıded in the Vaccines for Children Program.

In response to a question, Dr. Orenstein said the NIP has purc ısed HBIG--even though it's not technically a vaccine--and included it as ı fundamental part of its hepatitis prevention program.

An ACIP member said that HBIG was not provided in her state ur ːr universal purchase of vaccine and perhaps other states as well.

˜t was suggested that the parenthetical phrase ("for infants k ːn to HB-ɔarrier mothers") be deleted since the ACIP hasn't gotten intc ʂuch specifics on the other votes. However, state health personnel seemed tc ːeel it should stay in. Dr. Halsey decided to have two separate votes.

The first vote was on including the parenthetical phrase, "foı .nfants born to HBV carrier mothers". MSD, Cutter and Abbott support calle for abstentions. This vote did not pass, so the phrase was delete from p. 18 of Handout #1. [Vote tally was 3 in favor (Drs. DeBuono, Jackson, ınd Ramirez-Ronda); 3 noes (Drs. Davis, Edwards, and Halsey); 3 abstentioı (Drs. Clements, Ward, and Hardegree); and 2 absentees (Drs. Schoenbɑ ı and Thompson)].

Receivers of support from MSD and SKB could not vote on the ne : issue, which was the vaccines to include for hepatitis B (p. 18 of the Hanc ıt #1). The vote was 7 in favor [Drs. Davis, DeBuono, Edwards, Jackson, Rɑ .rez-Ronda, Dr. Hardegree, and Dr. Rabinovich]; none opposed; 3 abstentioı [Drs. Clements, Halsey and Ward]; and 2 absentees [Drs. Schoenbaum ɑ l Thompson].

The next vote was on the schedule for hepatitis B (p. 19 of Hɑ lout #1), with attendant footnotes. Drs. Hall and Orenstein addressed the wc ling of the generic, permissive footnote tying ACIP and AAP recommendatioı together. Dr. Hadler then read the following:

These are the footnotes in the Dec. 16 F.R. notice, whic[h] [were added to] note acceptance by the ACIP of the American Academy of Pe[diatrics'] alternative schedules, and which will be revised in the f[inal notice to] reference the AAP by name.

Mr. Malone said that there was a problem with the ACIP just e[ndorsing,] generically, AAP recommendations--because of a delegation of g[overnmental] function problem. Therefore, each issue for which the ACIP wi[shes to accept] AAP as an acceptable alternative needs to be addressed direct[ly]. There was no problem with referencing the AAP as long as it's the ACIP deci[ding that it's] OK to have that as an alternative schedule.

What this language would do is change what's already out in th[e Dec. 16 F.R.] as footnotes and mention specifically by name that AAP was be[lieved that] particular recommendation.

Dr. Halsey asked Mr. Malone to draft acceptable wording for a [vote on the] AAP/ACIP matter before 6:00 p.m.

Dr. Hardegree asked that the record show that several of the l[abels do not] necessarily meet the options that were listed here.

Dr. Halsey then proposed the following for vote (from pp. 19-2[0 of Handout] #1):

> The ACIP recommends the number of doses, schedule and qua[lifications as] noted above and in the text of the Dec. 16, 1993, Notice.

[P]ersons receiving support from MSD and SKB were excluded from [voting. The] vote carried (6 in favor [Drs. Davis, DeBuono, Edwards, Jacks[on, Ramirez-] Ronda, and Rabinovich]; no nay's; 4 abstentions [Drs. Clement[s, Halsey, Ward,] and Hardegree]; and 2 absentees [Drs. Schoenbaum and Thompson]

Dr. Hadler then read the following proposal:

> The ACIP encourages use of DTP-Hib vaccines (combined or [uncensed for] combined administration) when receipt of each antigen of [the combined] vaccine is indicated; however, at this time, the ACIP doe[s not restrict] separate administration of DTP and single-antigen Hib vac[cines. The] Department should complete contracts for both single-anti[gen and] multiple-antigen products.

Dr. Halsey announced that support from the following companie[s required] abstention from the vote: for DTP--Connaught, Lederle, Massac[husetts Dept.] of Public Health, Michigan Dept. of Public Health, Wyeth-Ayer[s for DTP-Hib-] -Lederle Praxis, Pasteur-Merieux-Connaught, and MSD.

The vote carried (4 in favor [Drs. Davis, DeBuono, Rabinovich, [and Ramirez-] Ronda]; 0 opposed; rest abstained).

Dr. Hadler then asked members to vote on the following:

Any use of brand names in ACIP OBRA documents is not inte ied to mandate purchase of particular brands of vaccine, but rather is i :ended for identification purposes only.

This is already in a footnote on a table, but was voted on to et it on the record. The vote, when taken, was unanimous for this proposal

Dr. Hadler then asked for a vote on the following clarificatic of terms:

Use of the phrase "combined DTP-Hib vaccine" in ACIP OBRA documents includes any DTP and Hib vaccines which are either combi i or are licensed by the FDA for combined administration.

Anyone who was excluded from the previous combined statement v ; also excluded from this vote. The vote carried (5 for: Drs. DeBuor Ramiriz-Ronda, Davis, Hardegree, and Rabinovich; 0 opposed; 5 abstaine [Drs. Clements, Edwards, Halsey, Jackson, and Ward]).

Dr. Hadler then read the following "reconciliation of ACIP rec mmendations with ACIP OBRA recommendations":

The ACIP requests NIP staff to review the current ACIP re ommendations to identify any inconsistencies with the ACIP OBRA recomm idations adopted at this meeting for the purpose of reconciliatior of those recommendations at the next meeting of the ACIP.

Rather than vote, Dr. Halsey asked if there was a consensus tc isk the NIP to compile inconsistencies in AAP, ACIP and ACIP OBRA recommendat ons, bring them back to the ACIP in the form of a mailing well in advance of the next meeting, and provide the ACIP with some opportunity for adding some issues to the agenda for the next meeting. All were in agreement.

Dr. Hadler asked the FDA to help NIP with this project. Dr. F :degree agreed.

<u>Scope of the Notice</u>

Dr. Hadler said that the last set of issues dealt with scope c the notice (pp. 21-22 of Handout #1). Basically, there are three issues iat have been raised--Should the hepatitis B risk-groups for which the vacci e is recommended be included? Should any clarification be provided i measles second-dose cohorts? Should pneumococcal and influenza vacci :ion of high-risk groups be included?

The law does not give specific guidance on this. CDC has atte oted to estimate the numbers of children to which these recommendatior would apply (see p. 21 of handout)

Dr. Orenstein clarified that, under universal purchase, a stat will take what is covered in this program, and then add funds--either fe eral grant funds or their own funds--to purchase all vaccines for all pe ons. There are currently 12 such states; another 12 suggested that they were iterested in

it. As the ACIP considers all of these recommendations, the ɔre that is added on to the program, the more any state considering unive: al purchase ill have to also add. Dr. Orenstein also said that, in term: ɔf the general recommendations, the ACIP might wish to consider universal re(mmendations for any of these.

Dr. Hadler said that, when NIP started examining OBRA, NIP's : itial reaction was that universal routine vaccines would be included and the ɔtice was drafted accordingly. It wasn't until staff looked at the lan(age that they saw it didn't say universal and it didn't say routine. NIP i: now trying to clarify these issues.

Many ACIP and liaison members expressed their opinion that hi(-risk adolescents be included for hepatitis B. Accordingly, Dr. Ha: ey asked Dr. Hal Margolis to briefly summarize his presentation from the n(t day on this subject. Dr. Margolis said that his presentation would deal v th a catch-up immunization for high-risk Asian populations and adolescents. e noted that the AAP does basically take a stand supporting catch-up immun: ation and says "all adolescents." But there are some programmatic issues of : plementing that. He said that adolescent immunization is obtainable, at east in certain program settings. He said his program hoped to see t] Committee make a strong, catch-up adolescent immunization recommendatio: ɔy the end of the year.

One ACIP member expressed concern about moving too quickly th: ugh some of these more troublesome areas without having the necessary rev: w time. She asked if this decision could be delayed until June.

ɔr. Orenstein said that the more that could be done at this m(ting, the easier it would be for NIP. The same ACIP member said that t] funding and implementation issues are important concerns, when states mov(toward universal coverage. She noted that the infrastructure to sup] rt infant and child immunization differed in most states from the infrastru(ure for adolescents and adults. The importance of combining as many ccines as possible during the adolescent period in one visit was very c: tical since getting adolescents into care is difficult. She wanted time think this matter through.

Dr. Halsey asked for 2 or 3 alternatives regarding adolescent nd other high-risk groups be drafted and placed in front of members for vot(Drs. Edwards, Schaffner, and DeBuono volunteered to work with Dr.] rgolis and Frank Mahoney on these.

Returning to the catch-up, second dose of MMR, Dr. Hadler sai(the question was, can it purchased for all cohorts of children 6-18? The nguage in the current ACIP recommendation is permissive. Currently, 36 sta s require it for at least one cohort of children; 4 states require this fo: all school attendees (K-12), and 16 others for 2 or more cohorts. So th(e's already movement toward this. He said that an estimated 20-30 millio: doses had been distributed already.

Dr. Halsey said that he was concerned, from discussion thus fa , that the wording of some of ACIP's votes and recommendations might car obligations o states. And that's not what most of members had intended. The ACIP had been trying to make it possible, but not necessarily obligato . He asked those drafting the wording of the 2-3 alternatives for high-r groups to see if they could find some language that would allow this to e done where it is possible and practical without mandating it.

Mr. Malone cautioned that NIP would be putting out bids for c tracts, where minimum purchases would be guaranteed. So if the ACIP increa purchases, then later rolled it back, CDC would be buying a lot of vacci . He said if members thought there was a chance of that, he would recommen putting this issue on the table for now.

Dr. Orenstein said it would be useful to set up some working g oups to discuss this between now and June to come to the Committee in ine with some firmer recommendations that have been thought through--as opp ed to trying to force it.

The meeting adjourned for the day at 6:35 p.m.

The meeting reconvened the next day at 8:08 a.m.

<u>Adolescent Vaccination against Hepatitis B</u>

Dr. Margolis updated the Committee on the action plan for eli inating hepatitis B virus transmission. The plan has three phases: 1) universal screening of pregnant women for HBsAg; 2) universal immunizat n of infants; and 3) catch-up immunization of adolescents and high-risk chi cen and of selected high-risk adults.

Next, Dr. Mahoney reported on the current status of the infan program. He said that the prenatal program has been well integrated into p enatal care; screening is increasing; but universal screening has not occu ed. State laws and hospital policies both improve program effectiveness. Regarding the infant vaccination program, data clearly indicate that attitu s of providers are changing. A high percentage of infants are being vaccina d at birth--mainly determined by the standards set by hospitals. In fact, hepatitis B vaccination in the public sector may be approaching the cover e levels of other vaccines.

Dr. Margolis then introduced adolescent issues (what he terme phase 3 of the strategy). Dr. Brad Woodruff updated the ACIP on the effecti ness and feasibility of adolescent hepatitis B immunization. He descr ed five projects throughout the United States to vaccinate this group. He concluded that hepatitis vaccination is feasible in a variety of setti , including schools, detention facilities and residential institutions. A olescent vaccination, however, requires flexible programs and flexible chedules, especially school-based vaccinations. Education about hepati s B and vaccination against it <u>does</u> motivate adolescents to seek vacc ation. Consent is obtained more often among white students than blac and among younger students than older ones. Further evaluation is need on the best

age to vaccinate in schools; the best motivators to maximize c verage; and the most-efficient way to vaccinate in schools.

Dr. David Scheifele reported that the province of British Col ɔia started a program for hepatitis B immunization of sixth-graders in the l1 of 1992 (population: 45,000). The uptake for first doses averages 94 The completion rate the first year was 92%. The program is conti ing this year.

Votes on Hepatitis B

Dr. Halsey said that the ACIP would like to come up with a st tegy for buying the vaccines for all the high-risk groups.

Dr. Joel Ward proposed a strategy for the high-risk vaccines, ıich comprised hepatitis B, influenza, and pneumococcal vaccine. He sketche some questions that he hoped a working group or the program people might be a le to address for each of these three vaccines [Handout #3]. In this way t ACIP could assess how big these high-risk groups are; what the morbidity ıd mortality is for each group; what health care costs would be prevented l this strategy; a cost assessment; how many doses; and implementati problems and issues.

Dr. Halsey noted that a careful laying out of options, their i ɔact, and programmatic issues was necessary.

Dr. Orenstein asked that two things be added to the charge to ıe working roups: 1) second dose of MMR and the whole issue of catch-u ınd 2) ıdolescent immunization for hepatitis B.

Dr. Halsey asked the Committee for a sense of how to go--whet r to come up with a specific recommendation today to purchase vaccines or v ether to form a working group to come up with a recommendation that will in rporate some of the planning for the implementation for the June meeting. Since there was clearly a division among the ACIP and the liaison members, ıe asked for a vote on whether to move ahead with a vote about purchase of p ımococcal and influenza vaccine under the purchase program, today. He aske those in favor of forming a working group to come up with a specific program tic plan to present to this meeting in June to raise their right hand.

A member asked what the intent of the law, as written, was. . Broome said that CDC has looked into this in detail, and the law is not c ar. These groups weren't even considered when the law was framed--they v re only looking at childhood immunization. She said she thought a ca for coverage could be made, but that having a well-reasoned program, imple ıtation strategy and a sense of what this will involve would be helpf in moving forward into areas that she believed were not considered when ıe law was passed.

There was considerable discussion about whether to have worki groups come up with a plan and present it for a vote in June or whether t take a eparate vote on influenza, right now, and one on pneumococca vaccine in June.

Dr. Halsey asked that the group deal with the issue on which ere appeared to be agreement, namely, a vote in principle that the ACIP is nterested in trying to improve delivery of immunizations to high-risk grou , including adolescent hepatitis, influenza, and pneumococcus. There was onsensus that that is the long-term desire of the Committee.

Dr. Halsey then reiterated the two options: 1) to form workin groups and put off the vote until June; 2) to vote on influenza now and put f pneumococcus until later. The vote for option #1 was unanimous.

Dr. Broome announced that people with potential conflicts of terest could be on working groups but should not chair them.

IOM Report on Adverse Reactions and Contraindications to Vacc es

Dr. Bob Chen referred the ACIP to a memo that had been mailed them from Jessica Tuttle, which updated the current ACIP statements in cordance with the IOM report.

Dr. Orenstein announced that the law had changed regarding th vaccine information materials so they can be simplified and shortened One criterion is that the risks have to be clearly mentioned. The NIP want these vaccine nformation forms revised by the end of April. Therefore, h requested that he Committee decide which adverse events not already in the rm be added.

Next, Dr. Rabinovich said that PHS will be conducting a scien fic review of the IOM report on March 15. The thoughts of the ACIP will be resented.

Then Dr. Tuttle reviewed the recent activities of the working roup, appointed after the October 1993 ACIP meeting to review the i act of the IOM report on ACIP recommendations. The group consisted of Mr. M one, and Drs. Clements, Jackson, Halsey, Orenstein, and Ward. The Annex to andout #4 details the adverse events identified in the IOM report and p posed language to make the corresponding ACIP statements consistent. She th focused on some of the more controversial adverse events--OPV and Guilla - Barre syndrome (GBS); tetanus-toxoid-containing vaccines and GBS; a combined MMR and thrombocytopenia--and asked that comments about ones not scussed be mailed in.

GBS and OPV

First, Dr. Tuttle reported on a reanalysis of a Finnish study nd an observational study done in the United States, which provided vidence against a causal relationship between GBS and OPV. She read proposed change to that effect (see p. 5 of Annex to Handout #4). Dr. roome said it would be useful for the ACIP to suggest to the authors that a e-analysis be published.

A vote was taken about the acceptability of this wording to tl Committee. Those with Lederle conflicts of interest abstained. The vote as 6-0-3, with absent.

TT and GBS

Dr. Tuttle then reviewed estimates of risk of GBS following D . The group decided to postpone a vote on this until later.

MMR Vaccine and Thrombocytopenia

Dr. Tuttle then referred members to pp. 6-7 of the Annex. The group changed one line in paragraph one (p. 7) to read as follows:

> "In prospective studies, the reported incidence of clinic lly apparent thrombocytopenia following MMR ranged from 1 per 30,000 t 40,000. . ."

Dr. Halsey asked Dr. David Nalin of MSD to write a letter for ne record on Merck's data on thrombocytopenia and MMR. Basically, there's ever been a fatal case and MSD does not believe the data warrant physician checking platelet counts. It was decided that Dr. Tuttle would combine these comments with any written ones submitted after the meeting into propose wording, which could then be voted upon.

Incorporating Changes into ACIP Statements

Dr. Tuttle then asked the ACIP to address how these changes wo ld get incorporated into previous ACIP statements. The group decided o have an official, brief ACIP response and commentary on the IOM report in the MMWR and perhaps insertions about changes, upon request, in the ind ridual ACIP statements. As no consensus was reached regarding this, option for incorporating changes will be brought up for discussion again the next ACIP meeting.

Simplification of the Vaccine Schedule

Dr. Jacqueline Gindler summarized the work of Drs. Hadler, St oel, Watson, Hall, Halsey, and herself to simplify and unify the ACIP and ? immunization schedules. She proposed five routine and two flexible option for schedules. She said the NIP would like a working group to be formed and et within the next month to agree on a schedule.

It was decided to form such a working group and to have membe and liaison members (as consultants) on it. Drs. Hall and Halsey were nan i co-chairs. Other members or consultants asked to serve on the group were Dr. Edwards, Hardegree, Peter, Rabinovich, Thompson, and Zimmerman. The g up was asked to report recommendations back before the June ACIP meeting s the decision could be made then. Dr. Broome emphasized that the full grou would make the decision.

Dr. Rabinovich announced that on March 4 an inter-agency meet g would be held to discuss changes in schedule in detail.

An MSD representative offered to be a consultant to the worki group. Dr. Rabinovich said she thought it was appropriate to have a mech ism for manufacturers to have input. Dr. Halsey agreed and said that he chairperson could arrange that.

Formation of Working Group for High-Risk Populations

This group will deal with hepatitis B, the second dose of MMR influenza, and pneumococcal vaccines. Dr. Halsey proposed the following mem rs: De. DeBuono, Dr. Fleming (consultant), Dr. Schoebaum, Dr. Ward, D: Bill Schaffner (as consultant), Dr. Jeff Davis (as Chair), Dr. Jac on and Dr. Glezen.

New Language on VFC Program Purchases

Dr. Robbins proposed the following new language to recognize e value of other schedules:

> The Committee has adopted schedules for administering va ines. The Committee also finds that vaccine schedules of the Ameri n Academy of Pediatrics published in the 1994 edition of the Report o: the Committee on Infectious Diseases (The Red Book) may be followed b Vaccines for Children program providers.

It was decided there needed to be a process for the ACIP to f nally review the AAP recommendations. Dr. Peter agreed to provide members f the ACIP with the 1994 Red Book.

Update on the Injury Compensation Program

Dr. Thomas Balbier from the National Vaccine Injury Compensat n Program reviewed major accomplishments of the program for 1993 and re rred members to a nice article about the program in the Journal of Infecti s Diseases, written by Dr. Sam Katz.

Update on Large-Linked Database Studies of Adverse Events

Dr. Hadler then gave a brief update on the large-linked datab es to monitor adverse reactions. It was suggested that the ACIP get a 2-3- ge summary mailing of the plans for this data system and that the topic rhaps be placed on the agenda for the next meeting.

Status of the Development of New Vaccine Information Statemen

Ms. J. Gantt said that CDC has contracted with the University f Rochester School of Medicine and Dentistry to rewrite and simplify (to h-grade reading level) vaccine information statements (VIMs) for the tigens in the Vaccine Injury Table (DTP, Td, MMR, and polio). It will be t ted on parents and physicians. Full implementation of the new VIMs is expec d by October

1, 1994. Dr. Edwards asked if hepatitis B and Hib VIMs will] generated as well; Dr. Gantt said yes, but not immediately.

Update on Typhoid Recommendations

Dr. P. Cieslak passed out the revised draft statement for ACI] on typhoid immunization. All suggestions from previous meetings were in(rporated. A table of common adverse reactions was added, as was a section ı "Choice of Vaccine." A footnote will be added to the table noting gastr(ıtestinal side effects.

Status of BCG Guidelines

Dr. Broome summarized the work of three advisory groups that ; e working together on such guidelines. The Advisory Council for the El: ination of Tuberculosis raised several relevant issues, specifically, sul equent program implications for maintaining skin-test surveillance in such p(ılations where BCG has been used; interpretation of the possible booster eff(: of skin testing in those who received BCG vaccination; and what shoul(ɔe recommended for prophylaxis in vaccinees who were exposed to a drug-sensi: ve case. That committee thought these issues should be addressed in the sta: ment, so additions are being made.

A joint working group to look at the next version of the stat(ent and iron out any problems was also appointed. It has 2 members from A(? (Drs. Edwards and Halsey), 2 from ACET [Drs. Schecter and Nolan], a: 2 from HICPAC. Dr. Halsey will be the chairperson.

Update on FDA Committee Meeting on BCG

Dr. Hardegree said that last October FDA had a review of the] ; meta-analysis information that had been presented to ACIP. One of ıe manufacturers presented new data on BCG for prevention of TB : children. The group felt that the data did support the efficacy of BCG : very narrow indications. FDA is continuing its review. Dr. Halsey said] hoped to have something on BCG available for final approval in June.

DTP and GBS

This topic had been deferred from the morning's discussion of ıe IOM Report on adverse events. Dr. Chen reported his recalculation of th(ıssociation of GBS following DTP, as assessed in a recent study in Los Angel(. Among children 2 years old or older, the expected number would be 1 -3.5. Among children 5 or older, the expected number of cases would be 0.(to 2.2. The numbers of observed cases were lower than those expected by c] ıce.

Dr. Halsey read the proposed change there to be voted on. Th(following changes were made:

> [in Side Effects and Adverse Reactions" replace "due to" ith associated with, as follows: "Persons with a prior history of GBS ; sociated with a particular vaccine may be at increased risk of recurre: GBS. . ."

[in "Precautions and Contraindications" section, add the ollowing underlined phrase: "A previous episode of GBS <u>within 6 </u>eks following a tetanus-containing vaccine is a contraindication to ad tional doses. . ."

However, the members were not comfortable voting on this, and he matter was sent back out for review--to emphasize the rarity of the even The program was asked to revise this section and mail--perhaps with addit nal, separate language for adults and children--to all ACIP members.

<u>Vaccination against Hepatitis A</u>

Dr. Craig Shapiro said that both SKB and MSD have efficacious nactivated hepatitis A vaccines. MSD's data have been previously presen d to the ACIP and subsequently published. Data from the unpublished study SKB's vaccine were presented by Dr. Bruce Innis from the Walter Reed Army I titute of Research.

Dr. Innis said that a double-blind, randomized, controlled, c munity-based study in 148 communities in Thailand, completed about a year , showed that the SKB vaccine's efficacy after 2 doses was 94%.

Dr. Shapiro summarized by saying that both the SKB and MSD va ines have been studied in numerous trials and schedules. Findings are that ese vaccines are highly immunogenic; after 2 or 3 doses, generally 100% of eople have antibodies. In general, the reactogenicity profile is accept le. Data on infants are much more limited.

e then reviewed the epidemiology of this disease in the Unit States, where periodic large epidemics occur about every 10 years. In 1992, some 23,112 cases were reported to CDC. In a study in Washington state i 1990, on average, case-patients with hepatitis lost 27 days from work; 1% were hospitalized; and they had an average of four health-care pro ler visits. The total cost of illness was related to age: for those older an 15: $2,500; for those under 15, $400. Estimates of the total ann l cost of hepatitis A in the United States are about $200 million. The ase-fatality rate is 0.4%. Cases in children account for about 30% of cas , but because their infections are often asymptomatic, this is probably an derreport. He said disease among recognized risk groups such as travelers r resent a limited percentage of cases. Children play an important role disease transmission in many settings. Therefore, to really have a s nificant public health impact, hepatitis A vaccination would have to b sed on a widespread basis.

Dr. David Nalin then reported on data from the Monroe County ficacy trial with this Merck vaccine. It is so efficacious that the trial as stopped and all controls given vaccinations. No subsequent cases of hepa tis A have occurred in the community, which had an on-going problem with his disease. The vaccine gives 100% protection after a single dose. After 500 doses, no serious vaccine-adverse events have been reported.

Dr. Shapiro said his section was drafting guidelines on hepat: is A vaccination. Dr. Halsey asked him to come up with a draft. I . Clements olunteered to work with him on preparing this.

Public Comment

Dr. Halsey asked if any members of the audience wanted to mak a public comment. Ms. Kovach said no one had requested one, but if su a request was made, she would inform Dr. Halsey.

U.S./WHO Influenza Vaccine Recommendations for 94/95

Dr. Nancy Cox briefly reviewed worldwide influenza activity a the vaccine recommendations for the next flu season. Flu activity starte early, with local outbreaks of influenza A(H3N2) in Louisiana, Scotland, a the United Kingdom. Quite severe epidemics were reported in November an December in western and northern Europe. Epidemic activity is on-going i the Russian federation and eastern Europe.

The WHO has recommended that the trivalent influenza vaccine p epared for the 1994-1995 season include: an A/Shangdong/9/93-like (H3N2) st in; an A/Singapore 6/86-like (H1N1) strain; and a B/Panama/45/90-lik strain.

Dr. Joe Bresee then gave a brief update of U.S. flu activity. Following late summer outbreaks of flu, this season's activity increased ste lly in the fall and peaked around the beginning of the year. It was dec ed steadily since then. This season has been associated with high excess ortality.

Dr. Nancy Arden then reviewed the boldface proposed revisions the ACIP Recommendations for the Prevention and Control of Influenza. ese revisions updated the recommendations for use of the vaccine and antivi agents available for controlling flu, including information concerni rimantadine (which was approved for marketing last fall); antiviral resis ce; and dosage precautions.

There is now a substantial difference between the Red Book an the ACIP recommendations about vaccinating children who demonstrate se e, anaphylactic reactions to eggs. (ACIP recommends consulting a physician; AAP recommends not receiving vaccine.) Dr. Arden asked about e rationale for the Red Book changes; Dr. Halsey said he believes the rat ale was that such children would require yearly vaccination; with the poss lity of increasing sensitization, it was best not to recommend vaccin lon.

Several members suggested leaving the ACIP wording because the wo are not really inconsistent and a great deal of thought went into the rding. By consensus (no vote), the group decided to leave the ACIP stat ent regarding anaphylactic language as is.

It was suggested that children under 1 year be added as a hig risk group for influenza vaccine. It was decided that that was premature fo the day's discussion, but that the program should be asked to generate a on

reassessing the risk-groups for influenza and present them at future meeting.

The ACIP then was asked to approve the following language whi differs from the Red Book:

> Children at high risk for influenza-related complication may receive influenza vaccine at the same they the receive other rou ne vaccinations, including pertussis vaccine (DTP or DTaP). Since influenza vaccine in young children can cause fever, DTa may be preferable in those children 15 months or older who are ceiving the fourth or fifth dose of pertussis vaccine. DTaP is not censed for the initial three-dose series of pertussis vaccine.

A vote was taken about whether to accept this wording as is, to accept it without the last two sentences. Excluded from voting were th e with support or affiliation with Connaught Labs, Lederle, Park Davis and W th. By vote, this wording was left as is. The vote count was: 3 in favor Drs. Ramirez-Ronda, Ward and Rabinovich]; 1 opposed [Dr. Clements]; and 3 stentions [Drs. Jackson, Edwards, and Thompson].

Next to be discussed was the section on antiviral agents. Th paragraph was discussed:

> In otherwise healthy adults, amantadine and rimantadine ve been shown to reduce the severity and duration of signs and symptom of influenza A infection when administered with 48 hours of illness ons . Studies evaluating the efficacy of treatment with either amantad e or rimantadine in children are limited, **but the studies tha have been conducted indicate that either drug can also reduce the verity and duration of influenza A illness in children.** Amantadine as been approved by the Food and Drug Administration (FDA) for t atment and prophylaxis of all influenza type A virus infections sin 1976, while rimantadine was approved for marketing in September 1993 By present FDA standards, there are insufficient data to assess the fficacy of rimantadine treatment in children. Thus, rimantadine is urrently approved for prophylaxis in children, but not for treatm t.

The group questioned the use of the word marketing and voted delete the boldface sentence [above]. It was finally decided that Dr. A en should prepare two alternative rewrites of this paragraph and show i to Dr. Caroline Hall, then FDA, and finally the ACIP for comment and ote. Dr. Arden was also asked to contact Donna Freeman at FDA about ag cutoff data for rimantadine.

ACIP members were asked to return any written comments to Ms. rden with copies to Ms. Kovach or Dr. Broome within 10 days (March 6) s that she can get it published in May in the MMWR.

Dr. Rabinovich then reported that the National Vaccine Adviso Committee approved a report on adult immunization. She suggested that be a future agenda item for an ACIP meeting.

Concern was then raised about having just two working groups. It was
uggested that the high-risk one be separated into two groups for a total of
aree working groups. Another alternative suggested was that he CDC program
address and make a proposal for adolescent immunizations and t the working
group focus on high-risk immunizations. Dr. Halsey asked for one-hour
block of time on the June agenda to deal with adolescent immu zation. Dr.
Davis, as chairperson of the high-risk working group, would h e the option
of dividing the working group into two. Consensus was agree nt with this
suggestion.

The meeting adjourned.

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

Neal A. Halsey, M.D.
Acting Chairperson, ACIP

Date: _____