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The structure, role, and procedures of the U.S. Advisory Committee on Immunization Practices (ACIP)☆

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ABSTRACT

The National Immunization Technical Advisory Group (NITAG) in the United States is the Advisory Committee on Immunization Practices (ACIP). The ACIP was established in 1964 by the US Surgeon General to assist in the prevention and control of communicable diseases, and includes a chair, an executive secretary, 15 voting members, 8 *ex officio* members and liaison representatives from 26 health-related professional organizations. Meetings are regularly convened at the Centers for Disease Control and Prevention (CDC) and are open to the public. Stringent measures and rigorous screening are used to avoid both real and apparent conflicts of interest, and no special interest or lobbying groups provide any material support to ACIP or its members. The committee recommends licensed new vaccines to be incorporated into the routine immunization schedule, recommends vaccine formulations, and reviews older vaccines to consider revising its recommendations.

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1. Introduction

Policy recommendations for the use of vaccines in the United States since 1964 have been developed by the Advisory Committee on Immunization Practices, which advises the U.S. government on the most appropriate selection of vaccines and related agents for effective control of vaccine-preventable diseases in the civilian population. The committee provides advice for the control of diseases for which a vaccine is licensed in the U.S. This report presents an overview of the history, structure, function and legal authority of the ACIP, and reviews the process of recommendation development; the role played by economic analyses; the role of manufacturers, insurers and other interest groups; and problems encountered and future direction of the committee.

2. Description and background

The National Immunization Technical Advisory Group (NITAG) in the United States is the Advisory Committee on Immunization Practices (ACIP), comprising 15 voting members (including a chair), an executive secretary, eight *ex officio* members from other government agencies, and liaison representatives from 26 health-related professional organizations and foundations. Voting members include a consumer representative as well as experts in infectious diseases, pediatrics, internal medicine, family medicine, virology, immunology, public health, preventive medicine, vaccine research and policy, economics and cost-effectiveness.

ACIP was established in 1964 by the Surgeon General of the US Public Health Service. At that time, the routine childhood immunization series included only six vaccines (smallpox, polio, diphtheria, pertussis, tetanus, measles). With the accelerating pace of development of new vaccines during the 1950s and 1960s, it was increasingly recognized by the US Surgeon General and the Director of the Communicable Disease Center (CDC) in Atlanta, GA (now called the Centers for Disease Control and Prevention) that there was a need for national immunization policy recommendations to be developed by an expert group outside the US Federal Government. The passage of two key federal financing program, the Poliomyelitis Vaccination Assistance Act (1955) and the Vaccination Assistance Act (1962), gave added urgency to this need. Prior to 1964 there was no formal mechanism for establishing national immunization policy in the US (Table 1).

Abbreviations: ACIP, Advisory Committee on Immunization Practices; AHIP, America's Health Insurance Plans; CDC, Centers for Disease Control and Prevention; DHHS, Department of Health and Human Services; FACA, Federal Advisory Committee Act; FDA, Food and Drug Administration; HHS, Health and Human Services; MMWR, Morbidity and Mortality Weekly Report; NITAG, National Immunization Technical Advisory Group; NCIRD, National Center for Immunization and Respiratory Diseases.

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Table 1
Members, affiliations and expertise: as of 1 January 2010.

Chair:
Dr. Carol J. Baker, MD, Professor of Pediatrics; Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas

Executive secretary:
Larry K. Pickering, MD, FAAP, Senior Advisor to the Director, National Center for Immunization & Respiratory Diseases, CDC

Members:
Lance Chilton, MD, Professor of Pediatrics; University of New Mexico School of Medicine, Albuquerque
Paul Cieslak, MD, Medical Director, Immunization Program & Program Manager, Acute & Communicable Disease Prevention; Oregon Public Health Division
Kris Ehresmann, RN, MPH, Section Chief; Immunization, Tuberculosis, and International Health Section; Minnesota Department of Health
Janet Englund, MD, Associate Professor of Pediatrics, University of Washington; Clinical Associate, Fred Hutchinson Cancer Research; Center Division of Inf. Disease, Immunology and Rheumatology; Children's Hospital and Regional Medical Center; Seattle, Washington
Franklyn Judson, MD, Professor, Departments of Medicine (Infectious Diseases) & Preventive Medicine and Biometrics; University of Colorado Health Sciences Center
Wendy Keitel, Professor, Molecular Virology and Microbiology, Baylor College of Medicine, Houston, TX
Susan Lett, MD, MPH, Medical Director; Immunization Program Division of Epidemiology and Immunization; Massachusetts Department of Public Health
S. Michael Marcy, MD, UCLA Center for Vaccine Research, Torrance, CA
H. Cody Meissner, MD, Professor of Pediatrics; Tufts Medical Center, Boston, MA
Kathleen Neuzil, MD, MPH Senior Clinical Advisor, PATH; Clinical Associate Professor of Medicine, University of Washington
Sara Rosenbaum, JD, George Washington University School of Public Health and Health Services, Dept of Health Policy, Washington, DC [Consumer Representative]
Mark Sawyer, MD, Professor of Clinical Pediatrics, Division of Pediatric Infectious Disease, UCSD School of Medicine and Rady Children's Hospital San Diego, CA; Medical Director, San Diego Immunization Partnership
Ciro Sumaya, MD, MPH&TM, Founding Dean and Cox Endowed Chair in Medicine School of Rural Public Health; Texas A&M Health Science Center
Jonathan Temte, MD, PhD, Associate Professor, Department of Family Medicine, University of Wisconsin School of Medicine and Public Health

Ex officio members:
Centers for Medicare and Medicaid Services (CMS)
Department of Defense (DOD)
Department of Veterans Affairs (DVA)
Food and Drug Administration (FDA)
Health Resources & Services Administration (HRSA)
Indian Health Service (IHS)
National Vaccine Program Office (NVPO)
National Institutes of Health (NIH)

Liaison representatives:
American Academy of Family Physicians (AAFP)
American Academy of Pediatrics (AAP) – two representatives
American College Health Association (ACHA)
American College of Obstetricians & Gynecologists (ACOG)
American College of Physicians (ACP)
American Geriatrics Society (AGS)
America's Health Insurance Plans (AHIP)
American Medical Association (AMA)
American Osteopathic Association (AOA)
American Pharmacists Association (APhA)
Association for Prevention Teaching and Research (APTR)
Biotechnology Industry Organization (BIO)
Council of State and Territorial Epidemiologists (CSTE)
Canadian National Advisory Committee on Immunization (NACI)
Department of Health, United Kingdom
Healthcare Infection Control Practices Advisory Committee (HICPAC)
Infectious Diseases Society of America (IDSA)
National Association of County and City Health Officials (NACCHO)
National Association of Pediatric Nurse Practitioners (NAPNAP)
National Foundation for Infectious Diseases (NFID)
National Immunization Council and Child Health Program, Mexico (NIACCHO)
National Medical Association (NMA)
National Vaccine Advisory Committee (NVAC)
Pharmaceutical Research and Manufacturers of America (PhRMA)
Society for Adolescent Medicine (SAM)
Society for Healthcare Epidemiology of America (SHEA)

3. Terms of reference

The official legal documents establishing the committee and defining its structure and mission are Section 311 and Section 317 of the Public Health Service Act, as amended, 42 USC. 243 and 42 USC. 247, authorizing the Department of Health and Human Services (DHHS) to assist states and their political subdivisions in the prevention and control of communicable diseases; to advise states on matters relating to the preservation and improvement of the public's health; and to make grants to states to assist in meeting the costs of communicable disease control programs. More specifically, 42 USC. 217a, Section 222 of the Public Health Service Act states that the committee is governed by the provisions of Public Law 92-463, as amended, which sets forth standards for the formation and use of advisor committees. The ACIP has likewise been given a statutory role under Section 13631 of the Omnibus Budget Reconciliation Act of 1993, Public Law 103-66.

Authority for the continued functioning of the committee is governed by the charter [1], which is updated by DHHS every 2 years. The ACIP may not meet or deliberate unless and until the charter is updated and approved by HHS. The ACIP Charter dictates the purpose, authority and function; structure, meetings and compensation; and costs, reports and termination of the committee. The official Policies and Procedures of the Advisory Committee on Immunization Practices (last updated 2002) are available to the public upon request to acip@cdc.gov [2].

4. Meeting process and selection of members

Meetings are convened at the Global Communications Center at the Centers for Disease Control and Prevention, Atlanta, GA and are open to the public, except in rare instances, as determined by HHS. Meetings are conducted in accordance with the Federal Advisory Committee Act of 1972 (FACA), which stipulates that meetings be announced in the *Federal Register* at least 15 days before the meeting date (http://www.gpoaccess.gov/fr/), that members of the public be permitted to attend meetings and to speak or file written statements, and that meeting minutes be maintained and made available to the public in a timely fashion. In exceptional circumstances, the CDC director may call an emergency meeting of the ACIP without prior notice. ACIP meeting dates are published and posted on ACIP's website 3 years in advance. Regularly scheduled meetings are held three times per year. In 2008, three regular meetings were held, while in 2009 there were three, along with one emergency meeting that was convened in July at CDC Atlanta, to address the emergence of the new influenza A (H1N1) 2009 and to develop vaccine recommendations for using the new vaccine.

Meeting minutes and recommendations are public and available on the ACIP website [3] within 90 days of every meeting. Meeting minutes are carefully reviewed by the technical staff of concerned ACIP work groups (WGs) and must be certified by the ACIP Chair. Provisional recommendations are posted on the ACIP website http://www.cdc.gov/vaccines/recs/provisional/default.htm within 2 weeks of a meeting where a vote was taken. Final ACIP recommendations are published in the CDC's *Morbidity and Mortality Weekly Report* (*MMWR*) following extensive clearance through CDC and are then posted at http://www.cdc.gov/vaccines/pubs/ACIP-list.htm. Additionally, slide presentations from every meeting are posted on the ACIP website within 2 weeks of the meeting.

Members are selected according to criteria that include expertise in: vaccinology; immunology; pediatrics; internal medicine; infectious disease; preventative medicine; public health; or, in the case of the consumer representative, consumer perspectives and/or the social and community aspects of immunization programs. Suggestions for members are sought annually from a variety of sources, including professional societies, current and former ACIP members, and the general public.

When openings for membership occur, nominations are solicited on the ACIP website and in the *Federal Register*. Solicitation of new members is widely advertised, and application for membership has purposely been made open, transparent and uncomplicated. Individuals and organizations submit applications to the committee for a formal review by the ACIP Steering Committee, which forwards the names of two nominees for each vacant position to the Centers for Disease Control and Prevention (CDC) director for review. The Secretary of the US Department of Health and Human Services (HHS) makes the final selection.

Members must be US citizens and must not be employed by the US government. Additionally, efforts are made to ensure that the voting membership is balanced according to geography, race and ethnicity, sex, disability and expertise. Members are appointed to overlapping terms of 4 years (i.e., each member serves a 4-year term, such that in any given year approximately 1/3 of the committee turns over and new members are appointed for 4-year terms). The chair is appointed for a 3-year term from among members who have had at least 1 year's experience as a voting member.

Eight non-voting *ex officio* members represent other federal agencies. They can participate in discussions and, in the event that fewer than eight voting committee members are present and eligible to vote, may be designated temporarily as voting members. There are also 26 non-voting liaison members representing organizations with broad responsibility for administration of vaccines to various segments of the population, operation of immunization programs and vaccine development. Although they do not vote on policy recommendations, these representatives bring the perspective of vaccine program implementation, and thus provide important insights into the daily administration of immunization programs. They are required to bring the perspective of their organizations to the ACIP and to disseminate ACIP's recommendations back to their membership.

No payment is given to non-voting members, although travel expenses are covered. Voting members, who are deemed to be Special Government Employees during their tenure on the committee, receive an honorarium of a maximum of US$250 per meeting day (usually 6 days per year), plus reimbursement of travel expenses.

5. Conflicts of interest

Candidates for membership undergo careful screening for potential conflicts of interest before their names are submitted for final consideration. Stringent measures are taken not only to assure technical compliance with ethics statutes and regulations regarding financial conflicts but also to address more general concerns regarding any potential appearance of conflict of interest. Screening is rigorous, and balances the possibility of bias caused by a conflict with the need for vaccine and immunization expertise.

People with specific vaccine-related interests at the time of application are not considered for appointment by the committee. Examples of such interests include direct employment of the candidate or an immediate family member by a vaccine manufacturer or someone holding a patent on a vaccine or related product. In addition, before their names are submitted for final consideration, potential members are asked to resign for their term of membership from any activities that are, or could be construed as, conflicts of interest. These activities include provision of advisory or consulting services to a vaccine manufacturer or acceptance of honoraria or travel reimbursement from a vaccine manufacturer.

Members are required to file confidential financial reports every year with the Office of Government Ethics and to disclose publicly all vaccine-related interests and work, including participation in clinical trials, at each meeting. They must also declare conflicts at each meeting of a WG. Any single conflict, real or apparent, may serve to disqualify a participant from participating in a WG. WG members may receive confidential and proprietary information from the FDA or others to assist them in their discussions. When appropriate, they are therefore required to fulfill confidentiality requirements and, when required, sign non-disclosure forms prior to receiving such information.

If, despite all these safeguards, a conflict exists, limited waivers allow members to participate in committee discussions on condition that they are prohibited from voting on matters involving the specific or competing vaccine manufacturers. A member who develops an important conflict of interest during the 4-year term is required to resign from the ACIP. External consultants may participate despite conflicts of interest if they bring specific expertise, as long as their conflicts are declared and recorded at the beginning of each meeting. No special interest or lobbying groups provide any funding or any other material support to ACIP or its members.

6. Meeting preparation and agenda

Preparatory work for the in-person committee meetings involves two areas of ongoing activity. The ACIP WGs (currently numbering 14) meet regularly – at least once a month – to undertake an extensive, in-depth review of all relevant data and to prepare draft policy recommendations for consideration by the full ACIP in open meetings (see Section 8.1, below).

The ACIP Secretariat is responsible for meeting preparations, which involves facilitation of WG proceedings; compilation of in-depth background technical background material that is published in a bound document distributed at least 2 weeks in advance of the meeting; and compilation of a Briefing Book, comprising concise (1–2 page) summaries of the key issues coming up for consideration or vote, which is distributed to the CDC Director, the ACIP membership and key Center/Division Directors at CDC. The Secretariat also is responsible for logistical preparations for each meeting, i.e. meeting hall arrangements, hard-copy handouts for the public, and audio-visual arrangements (including web-casting meetings in full, since July 2009).

The Executive Secretary of ACIP, the Assistant to the Director for Immunization Policy and the ACIP Committee Management Specialist comprise the Secretariat, which was established in 2004 (prior to 2004 the work of ACIP was managed by the Executive Secretary alone). All three positions reside within CDC at the National Center for Immunization and Respiratory Diseases (NCIRD). Responsibility for reviewing and replying to inquiries from practitioners, members of the public, academics and others regarding the overall functioning of ACIP or about specific vaccine recommendations resides in the Secretariat as well. Inquiries are handled by telephone, e-mail, mail and occasionally by fax. The Secretariat maintains the technical content of the ACIP website, including updating ACIP recommendations, meeting minutes, current immunization schedules for children and adults [4,5] and other key information. The Secretariat (primarily the Assistant to the Director for Immunization Policy) is responsible for the overall guidance of ACIP WGs, particularly the CDC Lead and the ACIP WG Chair for each WG. This ensures a cohesive, standardized approach on the part of each WG in terms of policies and procedures.

The ACIP Steering Committee, which has responsibility for general operating policy, procedures, and related matters affecting the ACIP as a whole, comprises 15 members who represent the three CDC Centers that have activities related to vaccines and immunization, as well as the current ACIP Chair and a representative from FDA. Four meetings of the ACIP Steering Committee are organized annually by the Secretariat: three for the development of ACIP meeting agendas and one for the selection of new members. The Secretariat provides comprehensive orientation and training to new ACIP members once they are selected and also fields requests for the appointment of new liaison organizations, preparing justification for their inclusion (or exclusion) to present to the ACIP Steering Committee. These requests are then submitted to the Secretary of HHS if the organization is deemed appropriate for official designation as a liaison; final selection and appointment of liaison organizations is made by the Secretary of HHS.

ACIP meeting agendas are prepared by the ACIP Secretariat following deliberation by the ACIP Steering Committee. Approximately 10 weeks prior to an upcoming meeting, suggestions for meeting topics are solicited from the ACIP WGs, ACIP members, *ex officio* members and liaison representatives, and academic consultants. Meeting topics may include items that do not require a vote but are presented for informational purposes, such as data on vaccine-preventable disease epidemiology, vaccine efficacy, and updates on outbreaks of vaccine-preventable diseases. Presentation of data on new vaccines typically occurs at ACIP meetings starting at least 2 years in advance of vaccine licensure by the FDA; this allows committee members to be fully informed about all aspects of the vaccine at the time a vote is taken following licensure. Agenda items are reviewed by the ACIP Secretariat and discussed in depth at a meeting of the ACIP Steering Committee held 7 weeks before the ACIP meeting, with finalization and distribution of the meeting agenda 6 weeks before each meeting.

The Secretariat prepares material concerning new initiatives (e.g., standardization of the approach to presentation of economic analyses, development of an explicit evidence-based format to be used for ACIP recommendations) to present to the ACIP Steering Committee and CDC leadership. The Secretariat facilitates and guides submission of full ACIP statements for publication in CDC's *Morbidity and Mortality Weekly Report* (*MMWR*), which is the official public health publication of the US Department of HHS. Publication of ACIP statements in the *MMWR* is the final step providing them status as official recommendations of the US Government.

The estimated annual running costs of operating the committee, including compensation and travel expenses for members but excluding staff support, was US$122,138 in 2008. The estimated annual number of person-years of staff support required is 3.9, at an estimated annual cost of US$477,068.

7. Scope of work

The scope of the ACIP's work focuses on development of national policy for the use of vaccines and other biologics and antimicrobials targeting vaccine-preventable diseases. The committee votes on whether to include a new vaccine in the routine immunization schedule, vaccine use in high risk groups, and use of vaccines outside the routine schedules (e.g. rabies, Japanese encephalitis). ACIP also makes recommendations on vaccine formulations (e.g., multivalent vs. monovalent presentations) as well as recommendations on different vaccines targeting the same disease (e.g., rotavirus and human papillomavirus vaccines). ACIP may recommend that additional studies be conducted to aid decision making (e.g., to provide local disease burden or cost-effectiveness analyses) when necessary. For each recommended vaccine, the committee develops written guidance, subject to the approval of the CDC Director, for administration of FDA-licensed vaccines to children and adults in the US civilian population, including age for vaccine administration, dose and frequency of administration, and precautions and contraindications of vaccine use and information on adverse events. In addition, as provided by Section 1928 of the Social Security Act, the ACIP designates those vaccines to be included in the Vaccines for Children (VFC) Program.[1] Apart from the VFC Program, reimbursement for vaccine administration is usually covered by private insurance companies. Although ACIP recommendations do not carry any legal mandate, they are generally regarded as national policy and are respected and adopted by most private insurers; the inclusion on ACIP of a liaison representative from America's Health Insurance Plans (AHIP) facilitates communications with private insurers. The committee may alter or withdraw its recommendation(s) regarding a particular vaccine when new information becomes available or the risk of disease changes. A recent initiative has been undertaken by the ACIP Secretariat to ensure that every ACIP Recommendation is reviewed every 3–5 years and revised, renewed, or retired as needed.

As new vaccines are licensed and subsequently recommended by the ACIP, they are incorporated into the childhood and adult immunization schedules [4,5]. Changes in recommendations are made when new data and FDA licensing regulations become available for specific vaccines – for example, an expansion in the target age range or new safety data that would lead to a change in a recommendation, such as the recognition in 1999 of a possible link between rotavirus vaccine (RotaShield®, licensed and recom-

[1] The Vaccines for Children Program, established in 1993, is a federal entitlement program with a current annual cost of ~US$3 billion. A unique statutory authority was established by the Omnibus Budget Reconciliation Act of 1993, giving ACIP the authority to determine the vaccines that will be provided in the VFC Program. Eligible recipients include children under the age of 19 years who are Medicaid eligible, uninsured, American Indian/Alaska Native, and underinsured. Currently the VFC Program pays for vaccine administration to almost 50% of American children <6 years of age.

mended in 1998) and intussusception, leading to withdrawal of the recommendation for use of the vaccine [6,7]. Newly licensed vaccines in the past 2 years include herpes zoster [shingles], human papillomavirus, and rotavirus vaccines. New recommendations have been issued for several older vaccines, including influenza, mumps, pneumococcal, rotavirus, anthrax, and rabies vaccine and others. In the coming years, additional new, safe, and effective vaccines may become available that would be considered for inclusion in the childhood and adult schedules. ACIP guidance routinely is sought whenever a new vaccine is licensed, or when there is a change in licensure specifications (e.g., age of administration, indications); in matters affecting vaccines that do not involve a change in licensure – e.g., a temporary interruption in supply, an update on adverse events reported in connection with a vaccine – the CDC may issue written notices in the *MMWR* without seeking guidance from the ACIP.

8. Development of recommendations and the basis for decision making

Sources of technical data and expertise for the committee include ACIP voting members, *ex officio* members and liaison representatives, along with CDC subject matter experts working within the various National Centers (e.g., the National Center for Immunization and Respiratory Diseases; the National Center for HIV/AIDS, Hepatitis, STD and TB Prevention, etc.) and recognized experts from within and outside the United States.

Recommendations of the ACIP may be developed and issued jointly with nongovernmental professional organizations or other public health service advisory committees. Examples include the Adult Immunization Schedule (issued jointly by the American College of Physicians, the American Academy of Family Physicians, the American College of Obstetricians and Gynecologists and the CDC) and Immunization of Health Care Personnel (issued jointly by the ACIP and the Healthcare Infection Control Practices Advisory Committee). Other sources include invited *ad hoc* experts from throughout the US and abroad, particularly academic experts at medical colleges, WHO members invited on an *ad hoc* basis, WHO position statements (reviewed by WGs as part of data review) and other national position statements, especially from Canada (National Advisory Committee on Immunization of Canada), which borders the United States and whose immunization policies are fairly similar to those in the United States.

8.1. ACIP work groups

ACIP work groups (WGs) are formed as a resource for gathering, analyzing, and preparing information for presentation to the full committee in open, public meetings. They meet throughout the year to conduct in-depth reviews of vaccine-related data and to develop options for policy recommendations for presentation to the full committee. Four ACIP WGs are permanent and the remaining ones, which typically focus on one vaccine or group of vaccines, are established and then disbanded as needed. Their purpose and functioning are addressed in the 2002 ACIP Policies and Procedures Document.

ACIP WGs conduct extensive background preparation for development of recommendations. They conduct in-depth reviews of vaccine-related data and develop options for policy recommendations. WG members collect and review data on disease epidemiology; vaccine efficacy, effectiveness, safety; feasibility of program implementation; and economic aspects of immunization policy to include in written policy statements. Following rigorous review of available data, the WG formulates suggested policy options for presentation to the full ACIP. The WG maintains a written record of each meeting for internal use by WG members.

Four ACIP WGs are permanent: (1) Adult Immunization Schedule; (2) Influenza Vaccines; General Recommendations on Immunization; and (4) Harmonized Schedule for Children and Adolescents, which works to ensure that vaccine schedules for children and adolescents are harmonized among ACIP, the American Academy of Pediatrics and the American Academy of Family Physicians, all of whom participate together in this WG. Separate task-oriented WGs are established as required to address a specific vaccine or topic. The current roster, as of January 2010, includes WGs on evidence-based recommendations, human papillomavirus vaccines, meningococcal vaccines, pneumococcal vaccines, yellow fever vaccine, hepatitis vaccines, rabies vaccine, pertussis-containing vaccines, respiratory syncitial virus immunoprophylaxis and measles vaccines.

Each WG operates under specific terms of reference (TOR) determined upon formation of the WG and re-evaluated periodically, when major tasks are completed, when the chair or lead CDC staff change, if new issues arise and when events result in shifts in public health priorities. WGs customarily meet via monthly teleconferences; in-person meetings may be scheduled in association with ACIP meetings. Each WG includes at least two voting ACIP members (one of whom functions as WG Chair) and a CDC subject matter expert. Other WG members may include ACIP *ex officio* members and liaison representatives, members of academia, other CDC staff and invited consultants as required. Vaccine manufacturers may be invited to present results of clinical trials and other relevant data at meetings of ACIP WGs, but are not permitted to serve as full-time WG members or to participate in WG deliberations. Insurance companies are represented on ACIP through participation as a liaison organization of America's Health Insurance Plans (AHIP). The AHIP representative may serve on ACIP WGs, and attends all ACIP meetings. AHIP does not provide any funding or other resources (except for expenses for travel to ACIP meetings of their representative).

To formulate policy recommendations, the ACIP reviews data on morbidity and mortality associated with the disease in the general US population and in specific risk groups along with available scientific literature (both published and unpublished) on the safety, efficacy, effectiveness, cost-effectiveness, and acceptability of the immunizing agent, with consideration of the relevant quality and quantity of data. When data permit, specific rules of evidence – such as those followed by the US Preventive Services Task Force – are used to judge the quality of data and to make decisions regarding the nature and strength of recommendations. In the absence of data or when data are inadequate, expert opinions of voting members and other experts are used to make recommendations.

Other considerations and inputs used in formulating policy recommendations include clinical trial results and information provided in the manufacturer's labeling or package insert; equity in access to the vaccine and responsible management of public funds; recommendations of other professional liaison organizations; and the feasibility of incorporating the vaccine into existing immunization programs. ACIP WGs often review WHO recommendations as a secondary source of information in their deliberations. In the U.S. setting WHO recommendations (vaccine position papers) may not be as relevant as they are in the WHO Regions and countries. In general, differences between ACIP's recommendations and WHO recommendations are relatively minor and reflect differences in epidemiology and clinical presentations between the US and the developing country setting.

Draft recommendations are subjected to extensive review by scientific staff of the CDC, other relevant federal agencies, ACIP members, liaison representatives and external expert consultants. WG members or ACIP members may identify a need for additional data, corrections in data content and modifications of the

interpretation of the data and may critique or challenge expert opinions. Occasionally surveys are considered, e.g. surveys of parents concerning acceptance/knowledge of a vaccine or surveys of immunization providers. Public comments are solicited during each ACIP meeting and are considered in the decision-making process. These inputs are synthesized by the WG in an iterative process, and options are presented to the ACIP for final consideration and vote.

WG meeting minutes are not available to the public, as WGs are not governed by the laws and procedures of the US Federal Advisory Committee Act. WG meetings are closed, internal meetings for the purpose of fact-finding and data review; neither involve deliberation nor voting on specific policy recommendations; nor do they include the entire membership of the ACIP.

Recommendations are accepted by majority voting, with a quorum present of at least eight eligible committee members or *ex officio* members, if a quorum of regular voting members is not present; in the history of ACIP, absence of a quorum of voting members has occurred very rarely, as membership in the ACIP is viewed as a great honor and members are highly dedicated to their tasks. Votes are taken in meetings of the full ACIP, which are open to the public. Votes are recorded and the vote tally is captured in the ACIP meeting minutes, which are open to the public and posted on the ACIP website. ACIP members may never undertake full committee deliberations or voting in a closed meeting, with very rare exceptions (noted above).

Depending on the relative importance of the issue, either formal (for example, Delphi, nominal group techniques) or informal methods for soliciting expert opinions are used. Published statements of the ACIP explicitly describe the methods used for developing recommendations and providing the evidence used to develop the recommendations (for example, results of controlled trials, case–control studies, case series, expert opinion, meta-analyses, Delphi surveys, focus groups, cost-effectiveness analyses and other inputs). For an ACIP recommendation to be adopted during voting, a simple majority of voting members is sufficient for the recommendation to be passed by the ACIP.

Following adoption in open meetings of the ACIP, recommendation statements are refined by members of the concerned ACIP WG and then forwarded through CDC's clearance hierarchy, ultimately to the Office of the CDC Director. Statements must be cleared for technical accuracy, clarity, and acceptance of policy through all administrative layers of CDC: Branch, Division, Center, Office of the Chief Science Officer, Officer of the Director of CDC. Most recommendations are cleared at the level of the Director of CDC, who is delegated to adopt immunization policy on behalf of HHS. On rare occasions, the Secretary of HHS may be contacted by the CDC Director for input on clearance, e.g. in the case of a particularly sensitive vaccine or topic. Because ACIP serves in an advisory role to the U.S. Government, CDC/HHS may take the prerogative to revise or reject the recommendations in whole or in part, or to return the topic to ACIP for additional deliberation. In practice, due to the lengthy process of data presentation and review that typically goes on over several months and years before an ACIP vote is ever taken, and because of the extensive input by concerned stakeholders, virtually all ACIP recommendations are adopted by CDC/HHS. In the history of ACIP there has been only one instance when the government did not accept the recommendations voted on by ACIP (2003, recommendations for use of smallpox vaccine in a pre-event vaccination program [8]). In this case, HHS overrode the recommendations of the ACIP.

Once the recommendations have been cleared at the level of the CDC Director, recommendation statements are forwarded to the office of CDC's *Morbidity and Mortality Weekly Report*, where they undergo careful editing by a designated technical writer-editor. Recommendations published in the *MMWR* (with on-line access as well), are final policy of CDC/HHS and become official CDC recommendations for immunization of the US civilian population.

8.2. Role played by economic evaluations

Formal economic evaluations (cost-effectiveness, cost-benefit, cost-utility) play a role in ACIP decision making. Published and unpublished economic analyses relevant to vaccine recommendations are reviewed and presented routinely to the ACIP. ACIP also may use economic evaluations undertaken by international organizations or experts. All economic analyses must be peer-reviewed by a CDC health economist or other qualified economist before presentation to the ACIP to ensure that key methods are followed and if necessary to review underlying assumptions.

Procedures for this process may be found on the ACIP website [9]. Economic analyses undertaken by the pharmaceutical industry can be used as well, subject to the same standards and procedures.

The ACIP does not use a threshold value to determine whether a vaccine is considered to be cost-effective. Cost-effectiveness is only one factor considered in the development of immunization recommendations. Currently, although cost-effectiveness and similar analyses are presented and discussed for the introduction of every new vaccine, there is no clear consensus on the weight that should be given to economic data. In practice, vaccine recommendations are made primarily on the basis of the burden of disease, vaccine effectiveness and safety. CDC and ACIP will take steps in the coming months and years to enhance ACIP's ability to factor economic data into decision making.

If no economic analyses relevant to the vaccine issues have been done, the ACIP may request that they be undertaken, either before or after issuing a recommendation. Currently it is held by CDC and ACIP that economic analyses should be undertaken for all new vaccines being considered by the committee. In these times, economic analyses are routinely conducted for all new vaccines by any combination of CDC staff, academic researchers, and vaccine manufacturers.

Following adoption of ACIP recommendations by CDC/HHS, decisions about sources of funds to pay for vaccine purchase and administration are made at the level of other federal agencies, state health departments, and private insurers; ACIP has no direct role in vaccine financing.

8.3. Role of the ACIP in the ultimate decision-making process

Implementation and evaluation of the impact of the recommendations is the responsibility of the relevant CDC program and not the ACIP. However, CDC programs develop an implementation and evaluation plan for each set of recommendations and periodically report information relevant to these activities to the ACIP. As mentioned earlier, most of the responsibility for implementation of ACIP recommendations lies with the state-level governments. Recommendations are subject to approval by the CDC Director and generally come to serve as standards of practice but do not serve as mandates that require vaccination of members of the civilian population.

8.4. Example of recommendation development: rotavirus vaccine review and approval

The case of recommendations made for the use of rotavirus vaccines (2004–2009) offers a typical example of and timeline for the recommendation process. The WG was established in December 2004, just before Merck applied for a biologics license from the FDA for their vaccine, RotaTeq®, in April 2005. Shortly after the FDA approved the license on 3 February 2006, ACIP voted on the vaccine on 21 February 2006. On 11 August 2006 the *MMWR* published a

statement entitled Prevention of Rotavirus Gastroenteritis among Infants and Children, which constituted formal approval of the vaccine and its inclusion in the vaccination schedule [10]. Beginning in June 2007, the WG expanded it focus to include consideration of a new rotavirus vaccine, Rotarix® (Glaxo-Smith-Kline), which was ultimately licensed by FDA in April 2008. From June 2007 until February 2009, the WG met at least once monthly, and often bimonthly in preparation for data presentations at ACIP meetings. The WG, comprising 25 members, included CDC subject matter experts; immunization safety experts; ACIP members, *ex officio* members and liaison representatives, and invited academic consultants. At every ACIP meeting from June 2007 until June 2008 (four meetings), the WG presented information on efficacy and safety of Rotarix®, RotaTeq® vaccine coverage and adherence with age recommendations, draft proposed recommendations for use of Rotarix®, post-licensure safety monitoring of RotaTeq®, and final recommendations for use of Rotarix® following licensure by FDA. The ACIP voted in June 2008 to add Rotarix® to the routine infant immunization schedule, and provided guidance on use of Rotarix® vs. RotaTeq®, since there were now two licensed vaccines on the market. The WG finalized the full ACIP statement, which was published in the *MMWR* in February 2009 [11]. The WG has been disbanded for now, but CDC program staff continue to monitor rotavirus vaccine coverage rates, rotavirus disease rates, vaccine coverage, and vaccine safety. The WG can be reassembled at any time, if necessary.

For all newly licensed and recommended vaccines, ACIP members are briefed during meetings on changes in disease epidemiology that occur following introduction of a vaccine, and this has been the case with rotavirus vaccines. At meetings following the 2006 and 2009 recommendations for the use of RotaTeq® and Rotarix®, ACIP members were informed about the reduction in rotavirus disease burden in the US from 2000 through 2009—the 2007–2008 and 2008–2009 rotavirus seasons were shorter, later, and characterized by substantially fewer positive rotavirus test results reported to the national surveillance system compared to the pre-vaccine era (overall number of positive test results decreased by 64% from 2000–2006 to 2007–2008) [12,13]. With presentations on the surveillance and epidemiology of vaccine-preventable diseases following changes in national immunization policy, the ACIP is kept informed about the impact of vaccination on the target population. In addition to data on disease epidemiology, ACIP members are also kept informed about adverse event surveillance through meeting presentations that are regularly made following introduction of any new vaccine.

9. Communication activities and training practices

ACIP disseminates information and data concerning its activities in a variety of ways. Since July 2009, live webcasts of all ACIP meetings have been made available on the internet, with an archive maintained on the committee's website for viewing at any time after a meeting (http://www.cdc.gov/vaccines/recs/acip/livemeeting-archive.htm).

The ACIP website (http://www.cdc.gov/vaccines/recs/acip/default.htm) provides ongoing, detailed information concerning the committee's activities that is supplemented by letters from CDC to public health officials and physicians and by CDC's flagship publication, *MMWR*. CDC media relations and press releases are handled by CDC communications staff. Publications (e.g., Epidemiology and Prevention of Vaccine-Preventable Diseases [14]) and guides (e.g., Vaccine Information Statements [15]) provide useful information for clinicians and patients.

Information is also disseminated at professional medical meetings via concerned ACIP Liaison Organizations, e.g. American Academy of Pediatrics, American Academy of Family Practice, American College of Physicians, American College of Obstetricians–Gynecologists.

Members of ACIP communicate via meetings, e-mail and conference calls. ACIP shares information formally with ITAGs in Canada, Mexico and the UK and informally with nascent ITAGs in other countries who have contacted the committee and/or have attended ACIP meetings.

Committee members are trained specifically about ACIP's responsibilities and activities by the ACIP Secretariat using face-to-face training and distance learning techniques. It is not uncommon for a person serving as a liaison representative (e.g., from the American Academy of Pediatrics) to be appointed at a later time as a voting ACIP member; in this case, the experience brought by service as a liaison representative – attending meetings as well as serving on WGs – provides valuable background to a new voting committee member.

10. Problems encountered, limitations and future developments

There are no serious constraints or issues concerning ACIP's activities. Due to its long history ACIP has worked through any structural challenges in years gone by and is now entering an era featuring issues presented by an ever-increasing number of vaccines being developed, increased cost of the total expenditure on vaccines, and societal concerns regarding the number of vaccines.

In terms of the operation of the ACIP, especially concerning its appropriate composition, efforts to avoid conflicts of interest and implementation of its vaccine recommendations, we would say that the organization operates very smoothly and is highly respected by all branches of Government, professional organizations and the public. This is due to steady work on the part of CDC staff members and the ACIP Secretariat to bring improvements.

Regarding improvements, the ACIP Evidence Based Recommendations WG (EBRWG) is in the process of developing a standardized and more explicit process for characterizing quality of evidence in the development of immunization recommendations. In general, ACIP recommendations have always been evidence based, due to careful scrutiny and evaluation of data by WGs prior to formulating policy options. However, ACIP recommendations have not generally been presented in an explicit evidence-based format. The WG plans to finalize a complete methods paper by June 2010. They will then apply these methods to a vaccine recommendation ("pilot test"), most likely an existing ACIP recommendation (e.g., rotavirus vaccine) in order to gain experience and to fine-tune the methods if necessary. To develop the methods paper, the WG has been reviewing approaches taken by the U.S. Preventive Services Task Force, the Task Force on Community Preventive Services, the Oxford Centre for Evidence-Based Medicine, the Canadian Task Force on Preventive Health and others. Once the methods are finalized, all future ACIP recommendations would be prepared and presented in an explicit evidence-based format. The methods paper will provide ACIP WG staff with detailed guidance on steps taken toward developing explicit evidence-based recommendations. These include developing the analytic framework; searching for and collecting evidence; evaluating the quality of the studies; summarizing the evidence; and converting the evidence into an overall recommendation.

Moreover, it has been observed that ACIP statements (published in *MMWR*) have become much longer over the years and that users frequently have difficulty pulling out key recommendations from the text. Some critics have said that ACIP statements have begun to resemble book chapters. The ACIP secretariat is in the process of reviewing statements and is discussing whether a more simplified, standardized approach to written statements should be taken. Cur-

rently, statement content and length is entirely at the discretion of each individual WG.

Finally, ACIP membership composition has traditionally favored pediatricians, internists, and state public health officers. With the introduction of Family Medicine as a clinical specialty in 1969, the role of family physicians has become increasingly important in the US. Similarly, obstetricians–gynecologists have never been represented on ACIP (i.e., not as voting members). The ACIP Secretariat will review the committee's composition to decide whether there should be some updates/modifications made.

11. Conclusion

The 45 years of ACIP's progress parallels the steady increase in the number of vaccines recommended for the US civilian population: from 6 routine childhood vaccines in 1964, to today's 16 separate antigens that are recommended for routine use in childhood as well as the routine vaccines recommended for the adult population. As the number of vaccines has increased, the workload of the ACIP has kept pace: it is widely acknowledged that the work of the ACIP has escalated dramatically in recent years. ACIP's decisions about the inclusion of new vaccines in the routine childhood immunization schedule have become much more difficult, as some parents and care-givers question the need for, and safety of, so many vaccines. The ACIP today struggles to ensure that inclusion of a new vaccine in the routine immunization schedule is genuinely in the public health interest.

New challenges face the ACIP and so changes to the committee's functioning are always being considered. Although the ACIP has been in existence for 45 years, its approach to making vaccine recommendations has not been stagnant. The ACIP Secretariat and ACIP overall is considering several areas for possible modification or enhancement, some of which have been described above. As the vaccine context evolves, new activities will be required to deal with changes in the health environment. ACIP is remarkably well-placed to respond to the challenges now present as well as those that will arise.

Conflict of interest statement

The authors state that they have no conflict of interest.

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This document can be found on the CDC website at:
http://www.cdc.gov/vaccines/recs/acip/downloads/article-2010-role-procedures-ACIP-508.pdf