RF Bd. of Trustees 12/13/94 RF 96019

Children's Vaccine Initiative

RF 94051

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GUIDELINE: Population-Based Health Care

GRANTEE: For allocation by the officers

OBJECTIVE: To support vaccine research programs and other activities related to the development and distribution of developing-country children's vaccines.

AMOUNT: $1,200,000 (to be charged to the 1995 HS budget) in addition to RF 93-86 RF 93059

DURATION: Period ending December 31, 1995

STRATEGY: Vaccines are among the most cost-effective tools of population-based health care. The current vaccine supply used in the World Health Organization's Expanded Programme on Immunization (EPI) prevents an estimated three million childhood deaths each year but requires a cumbersome regimen of multiple visits to deliver all the doses of the six vaccines currently in use. An estimated eight million childhood deaths each year could be prevented by the development of new vaccines against diseases for which no immunizations are now available or by the more effective distribution of existing vaccines. To develop and introduce additional vaccines and simplify the dosage schedule of existing vaccines requires substantial funding by a wide range of private- and public-sector agencies. The Children's Vaccine Initiative (CVI) is the vehicle for mobilization of resources and coordination of the research and product development activities required for new cost-effective vaccine technologies to help reach the goals of population-based health care.

DESCRIPTION: Since 1985, the Foundation has supported research on vaccines for developing-country diseases through appropriations to the World Health Organization (WHO) totaling $8.7 million. A brief review of the history of Foundation involvement in international vaccine research may clarify the resulting, sometimes overlapping efforts. The program components were founded at separate times and are in an active process of consolidation and coordination.

The idea for the Programme for Vaccine Development (PVD) was conceived in 1984 to accelerate and focus research on "second generation" vaccines for developing country diseases. The PVD organizes laboratory research on new vaccines against bacterial and viral causes of childhood respiratory diseases and diarrhea, on tuberculosis, meningitis, hepatitis, Japanese encephalitis, the dengue viruses, and improved polio and measles vaccines, and on fundamental mechanisms of immunization. The initial funding partners were the Pew Charitable Trusts, the Foundation, WHO, the United Nations Development Programme (UNDP), and several bilateral donors. It operates under the direction of a scientific advisory committee and vaccine steering committees composed of experts in specific research fields. Each steering committee of the PVD has designed a five-year strategic research plan. The weaknesses of the PVD that emerged over time are its lack both of the technical and financial capacity to move re-

search products into licensure and large-scale production, and of the ability to raise funds.

Since 1989, the Foundation has contributed to a small research effort organized by the EPI to evaluate technologies related to the effectiveness and delivery of existing vaccines. This program supported studies to improve measurement of disease burden, vaccine availability, and delivery systems, examination of the behavioral aspects of immunization activities, methods of introducing new vaccines, and mechanisms for using the immunization contact for other primary health care interventions. The research program has supported studies of safety issues in vaccination of developing-country children such as injection practices and the risk of transmitting HIV and hepatitis B, the role of diagnostic tests in the control of EPI target diseases, reformulation of oral polio vaccine to improve its immunogenicity when administered in the tropics, the effectiveness of polio and measles vaccines administered in mass campaigns versus routine immunization programs, effectiveness trials of high-dose measles vaccines in several West African countries, and assessment of the effectiveness of EPI hardware such as single-use syringes and solar-powered refrigerators. The EPI research program has an overlapping, but different, donor group and research advisory committee from that of the PVD and shares the same weaknesses.

To address the weaknesses in both the PVD and EPI programs, a group of agencies - WHO, UNICEF, UNDP, the World Bank, and the Foundation - founded the Children's Vaccine Initiative (CVI) in 1990. While CVI's ultimate goal is to develop a single-dose multi-antigen vaccine to protect against multiple diseases, it began its work with a series of practical steps to improve vaccine production and supply. These steps include: the manufacture by developing-country producers of diphtheria-pertussis-tetanus (DPT) combination vaccines; development of a vaccine self-sufficiency initiative designed to help the 20 largest developing countries produce international-quality vaccines; the creation of product development groups to accelerate vaccine development; and the formation of task forces for data-gathering, priority-setting, and strategic planning.

Since its creation, CVI has expedited fund-raising and vaccine development. At the 1993 annual meeting in Kyoto, Japan, which was attended by representatives from over 200 funding partners, the wife of the Japanese prime minister became a patron of CVI and a Japanese fund-raising effort was launched. As an example of vaccine development, a CVI Product Development Group has discovered that deuterium oxide, a stable non-radioactive isotope of water, when incorporated into oral polio vaccine, produces remarkable gains in heat-stability. This new product is now under industrial development by Sclavo and by the Institut Merieux (Italian and French vaccine manufacturers, respectively) and promises to increase greatly the odds of success for global polio eradication before the end of the century.

Soon after Hiroshi Nakajima was re-elected WHO director general in 1993, a major reorganization of the agency's vaccine programs was instituted. The EPI, PVD, and the WHO biologics unit were consolidated into the Global Program for Vaccines (GPV) under the leadership of Dr. J. W. Lee, who for ten years was director of the WHO Western Pacific region.

To facilitate coordination between this new vaccine initiative and the CVI, Dr. Lee was also appointed executive secretary of the CVI. Advisory input for all GPV programs has been placed in the hands of a single committee (list attached) to review all WHO vaccine research programs, and to assess global immunization policies and strategies for the development, production, quality control, and supply of vaccines. The GPV reports to a donor group, a self-designated Meeting of Interested Parties.

To accommodate to a stronger, better-staffed, and better-led WHO vaccine program, CVI now serves as an umbrella program - a broadly based partnership of UN agencies, foundations, national governments, and NGOs dedicated to improving global vaccines and immunization programs. The CVI shares the GPV's advisory and donor groups.

What is in store for 1995? No major changes are anticipated in the PVD component, but the EPI portion of GPV is likely to be completely revamped as a result of the restructuring to rely more heavily on developing-country vaccine manufacturers and to emphasize vaccine self-sufficiency and quality-control programs. CVI programs should make substantial progress in 1995, including further development of the micro-encapsulated single-dose tetanus toxoid vaccine, commercial production of the new heat-stabilized oral polio vaccine, and further work on a new measles vaccine.

The described restructuring should improve the sometimes strained relationships between WHO in its role as lead international health agency and the CVI, a multi-agency coalition, which for several years has assumed leadership in designing and implementing international vaccine development programs. As a member of formally composed donor groups that monitor the GPV and the CVI, the Foundation will continue to be a partner in the process of vaccine research and development and in the pursuit of a single-dose, multi-antigen vaccine for the world's children.

RISKS/EVALUATION: The CVI, which from the outset adopted a high-profile advocacy and fund-raising posture, has generated some antipathy in the donor community, particularly among European bilateral donors who do not have much experience appealing to or working with the private sector. The CVI strikes many of them as "too American." Finding a balance to permit a steady infusion of funds into the research arm of the GPV and into the CVI's vaccine self-sufficiency programs will be a severe test of Dr. Lee's leadership. An estimated several billion dollars will be needed by research agencies and vaccine manufacturers over the next 10-20 years to license and produce a multi-component children's vaccine with reduced dosage characteristics. There is, of course, a risk that this particular venture in international cooperation will fail. But the knowledge that many effective vaccines are already available and that money is the only barrier to their deployment should empower our successors to continue to seek ways to improve and make universally available the best possible vaccines for the world's children.

BUDGET: Of the proposed appropriation of $1.2 million, $850,000 would be allocated for the GPV in support of basic and applied vaccine research.

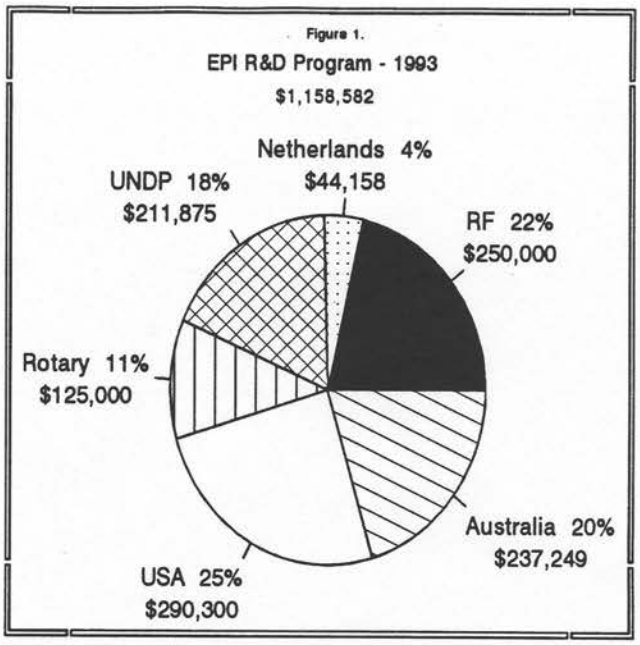
Figure 1.
EPI R&D Program - 1993
$1,158,582
Netherlands 4%
$44,158
UNDP 18%
$211,875
RF 22%
$250,000
Rotary 11%
$125,000
Australia 20%
$237,249
USA 25%
$290,300

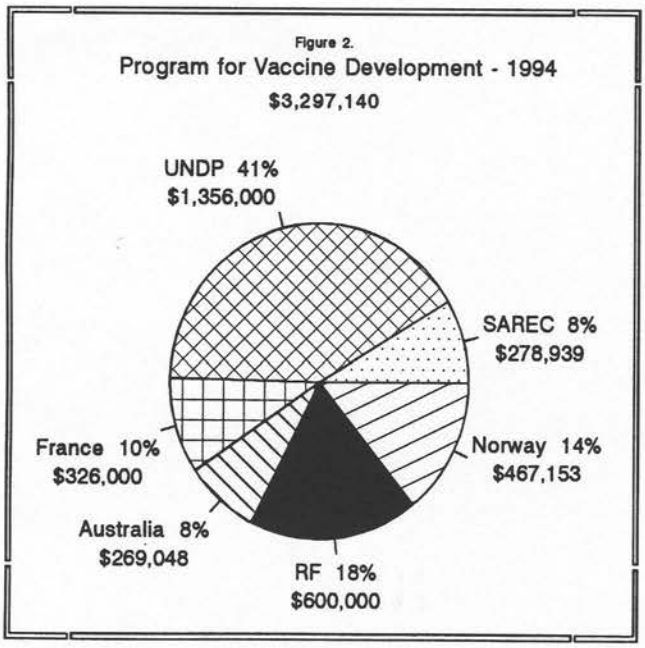
Figure 2.
Program for Vaccine Development - 1994
$3,297,140
UNDP 41%
$1,356,000
SAREC 8%
$278,939
France 10%
$326,000
Norway 14%
$467,153
Australia 8%
$269,048
RF 18%
$600,000

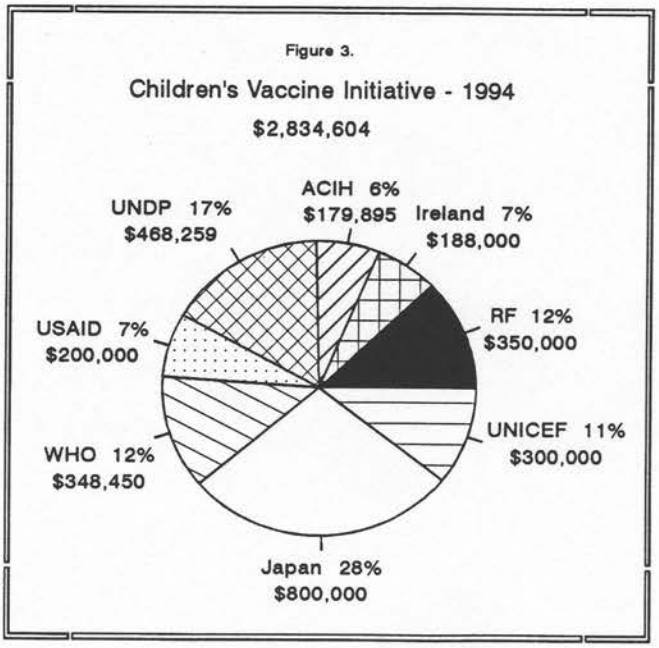
Figure 3.
Children's Vaccine Initiative - 1994
$2,834,604
ACIH 6%
$179,895
UNDP 17%
$468,259
Ireland 7%
$188,000
RF 12%
$350,000
USAID 7%
$200,000
UNICEF 11%
$300,000
WHO 12%
$348,450
Japan 28%
$800,000

Figure 1 shows the 1993 budget for EPI Research and Development (latest total amounts available), of which the Foundation's $250,000 constituted 22 percent. Figure 2 shows the 1994 PVD budget, of which the Foundation's $600,000 constituted 18 percent. The remaining $350,000 in the appropriation would support core activities of the CVI and provide 12 percent of its total budget (Figure 3).

FURTHER SUPPORT: The officers expect to continue support for the development and delivery of new vaccines for the world's children until there is evidence that the Foundation can no longer contribute usefully to this process.

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