United Nations Development Programme

Republic of Korea/Global

ESTABLISHMENT OF AN INTERNATIONAL VACCINE INSTITUTE

GLO/94/003B/11/31 and RAS/96/003B/01/31

Report of the Mid-Term Evaluation Mission

Evaluation Team:
Kees Lucas
Violaine Mitchell
Tikki Pang

FINAL **REPORT**
March 1, 2000

Table of Contents

List of Acronyms

BDP Bureau of Development Policy (UNDP)
CVI Children'sVaccine Initiative
DOMI Diseases of the Most Impoverished
GAVI Global Alliance for Vaccines and Immunization
GMP Good Manufacturing Practices

HibHaemophilus influenzae type B
IPR Intellectual Property Rights
ISC Institute Support Council
IVI International Vaccine Institute
ROK Republic of Korea
UNDP United Nations Development Programme
UNICEF United Nations Children's Fund
WHO World Health Organisation

I. EXECUTIVE SUMMARY

This report is a mid-term evaluation of UNDP's on-going project: Establishment of an International Vaccine Institute in Seoul, Korea.

A. **Findings**

Over 13 million deaths worldwide and one half of all deaths in developing countries are caused by infectious diseases.' Six diseases-pneumonia, tuberculosis, diarrhoeal diseases, malaria, measles, and HIV/AIDS-account for almost 90% of deaths from infectious diseases globally. In addition to the overwhelming toll of infectious diseases on the mortality of children and young adults worldwide, infectious disease-related disability has a major and direct bearing on income and poverty worldwide.

Vaccines are the most cost-effective means to prevent and curtail the spread of infectious diseases. As "global public goods," however, vaccines are vastly under-utilised. Existing vaccines are not as widely introduced globally as they could be. And no effective vaccines are available for the vast majority of infectious diseases.

The private pharmaceutical industry has demonstrated an ability to develop and produce vaccines that are technically feasible and that have remunerative markets. The challenges to the development and introduction of vaccines of importance to developing countries are complex however, and extend beyond market considerations. alone. In some cases, the science itself is not sufficiently developed to encourage private sector investment in research and development.

With the increased concentration of the pharmaceutical industry, resource capacity, both human and financial, for vaccine development has been strained, and vaccine development research priorities have narrowed to the most commercially attractive. Under these conditions, the private sector is unlikely to invest in the development of vaccines of questionable market value, and the public sector will have to shoulder many of the risks and costs associated with the development of vaccines for indigent populations.

Against the backdrop of consolidation within the pharmaceutical sector in industrialised countries is the trend for developing countries to produce more of their **own vaccines. In fact, the** majority of vaccines administered to children in developing countries today are now produced locally. Over the past few years, there has been mounting concern about the quality of locally produced vaccines including outdated facilities, staff training, lack of established production standards, and inadequate regulation by national control authorities.

Recognising that new vaccines for developing world populations are needed urgently, and building upon its unique strengths in institution and capacity building, the UNDP created the International Vaccine Institute (IVI) to address the gaps that exist in targeted vaccine research, product development, and technical support in production and quality assurance for vaccines needed in developing countries. Today, the IVI is an independent and autonomous international organisation established in May 1997 under the Vienna Convention.

[1] World Health Organization. 1999. Report on Infectious Diseases: Removing Obstacles to Healthy Development.

The IVI is based in Asia-home to over half of the world's children who suffer from infectious diseases. Although IVI's vaccine research and development projects are currently within the Asia region, most are of global importance and significance. For example, shigella, typhoid, and cholera are all important causes of morbidity and mortality among indigent populations not only in Asia, but also in Africa, the Middle East, and Latin America. Furthermore, IVI is fulfilling a critical need through its technical assistance and cooperation program to vaccine manufacturers and regulatory authorities seeking to meet internationally accepted vaccine production standards.

In the IVI's start-up phase, there was some concern among some members of private industry, international organisations, and national governments related to IVI's mandate, scope, and respect for intellectual property rights. As the mission and scope of the IVI have been clarified and communicated effectively, and as the need for an IVI grows ever greater, the IVI has received widespread support for its activities from many quarters, including developing countries, multilaterals, international organisations, private industry, public sector organisations and institutes in a number of countries, and other key players in the vaccine arena. In the opinion of the Evaluation Team, there is no justification whatsoever for concern that the IVI is less than totally committed to maintaining intellectual property rights. In addition, it is clear and evident that the IVI will never be involved in the manufacture and sale of vaccines at any time, now or in the future.

With the dynamic changes occurring in all aspects of vaccine delivery, including

research, development, management, and production, introduction, and utilisation, the IVI has a clear and unique niche-perhaps even more now than at its conceptualisation eight years ago. The IVI is uniquely positioned to operate at the intersect of public and private sectors. With its strategic location in Asia, within reach of 50 percent of the world's population, the IVI is the most important new institution in vaccine research and development, working in partnership with WHO, UNICEF, and other institutions to accelerate the development and introduction of new vaccines.

The IVI is a unique institution in the global science and technology infrastructure-it is the only international organisation exclusively dedicated to vaccine research and technical cooperation for developing countries. It has emerged as an important centre of vaccine-related activities, capable of working in novel partnerships with public and private sectors and national and international collaborators. The IVI has attracted an exceptionally talented and highly committed staff, and is directed by a world-renowned scientist. The IVI has also received substantial external project support in addition to funds provided by UNDP and the ROK.

Although in the early stages of implementation, the IVI is successfully implementing coordinated multi-disciplinary country studies, enhancing the introduction of new and improved vaccines, providing technical assistance to developing countries in vaccine production standards in conjunction with the World Health Organisation, and strengthening local capacity in vaccine evaluation. The IVI is absolutely unique in its abilities to undertake coordinated multi-country studies and multi-disciplinary programs of research and technical assistance.

The Evaluation Team believes that UNDP demonstrated exceptional vision and leadership in the establishment of the IVI. As host country, the Republic of Korea is to be highly commended for providing substantial and unstinting support, financial and moral, to the IVI.

The IVI is a new organisation, and has really only been operational for one year. As a new and emerging organisation, the IVI needs time and support to ensure that it develops fully and becomes self-sustaining.

Through its support of the IVI, UNDP is facilitating the production of global public goods (vaccines), enhancing capacity-building regionally, and contributing substantially to sustainable human development and poverty alleviation globally. In addition to maintaining IVI's international and impartial status and encouraging additional donors to lend their support to the IVI, continued UNDP involvement will be critical in facilitating the uptake of eventual vaccines at the country level. Addressing the gap between vaccine supply and demand and ensuring sustainable vaccine supply necessitates good governance, decentralised decision-making, and

integrated management, all of which fall uniquely and solely within UNDP's experience and mandate.

B. Recommendations

Based on a mid-term review of on-going IVI activities, the Evaluation Team has the following recommendations for UNDP and the IVI:

UNDP Involvement

1. UNDP should continue its support of the establishment phase of the IVI for an additional 3 years at a minimum of current funding levels. Continued UNDP commitment, both moral and financial, is critical to the sustainability, credibility, and stature of the IVI as an impartial scientific organization dedicated to the research and development of vaccines of importance to developing countries. Should UNDP decrease its level of support for the IVI, the future of this evolving institute and its activities will be in jeopardy. Whether UNDP support is drawn from the Regional or Global programmes is a matter for internal UNDP discussion and resolution. It is important to note that although IVI's current research projects are in Asia, they are of global significance. And IVI's technical cooperation program is currently global in scope.

2. Given UNDP's original commitment to facilitate resource mobilisation, the UNDP should continue to chair and lead the Institute Support Council (ISC) and in so doing, should work closely with the IVI to develop a formal policy for international fundraising. Such a fundraising initiative, "Friends of the IVI" could draw upon international expertise in global fundraising and contribute substantially to the development of an endowment for the IVI. Within the recommended extension period of three years, the ISC could realistically aim to secure $3 million annually.

3. In light of the goodwill and trust between the UNDP and the Republic of Korea, and the role the Republic of Korea wishes to play within the emerging donor community, the importance of a continued partnership and communication between UNDP and the ROK with regard to the IVI cannot be over-emphasised.

4. Cooperation and communication between IVI and the Global Alliance for Vaccines and Immunization (GAVI) should be continued and expanded in well-defined areas. GAVI appears excellently positioned to receive ear-marked donations from bilateral donors for the IVI. In this context, and as also recommended in *UNDP's External Evaluation of the Global Programmes, Health and Development (February 2000),* UNDP should reconsider its decision not to be a participating board member of GAVI. In the current

unprecedented global effort to enhance immunization worldwide, UNDP can and should play a pivotal role in country coordination. In addition, UNDP is uniquely positioned to assist countries in developing appropriate polices and institutions; disseminate knowledge and experience among member countries; mobilize public and private sector resources; and, promote technical cooperation and transfer.

5. Thought should be given to a different kind of future relationship between IVI and UNDP -not one of donor-recipient only, but one based additionally on a strong partnership to achieve IVI's objectives. Such a partnership, building on UNDP's presence in 136 countries, policy expertise, extensive network and outreach capabilities, is, in fact, consistent with UNDP's new direction.

Future Directions for the IVI

1. The IVI should strive to develop itself into a fully international institution. The current network of collaborators should be enlarged to include centres in Africa, Latin America, and former Soviet republics. IVI should consider formalizing the cooperation arrangements established with partners in various countries in order to secure their continued loyalty in the IVI network. Participation in the network should be formally agreed to describing and delineating the area(s) of collaboration. The IVI should define what it means to be "international" and incorporate this view into its strategy and work plan.

2. The future research efforts of the IVI should be closely linked to its ongoing activities in epidemiological field studies of disease burden and vaccine effectiveness. It should utilize its comparative advantage and unique position in having access to patient materials in disease-endemic areas (e.g. strains/ isolates, sera, CSF, tissues, good clinical and epidemiological information) and in having extensive networks of collaborators in place. In this regard, IVI should focus its efforts on strategic and applied research rather than dealing with basic research in vaccine-related areas. Examples of potentially valuable research areas would include study of human immune responses to candidate vaccines, improvement of laboratory diagnostic tests, molecular epidemiology of selected pathogens (and building a repository of isolates and strains), and improvement of vaccine delivery and formulation. Another potentially important 'niche' for IVI is to focus on the implementation and application issues related to novel vaccine technologies, e.g. DNA

vaccines and oral vaccines. The linkage of IVI's research efforts to the established networks will also facilitate training and research

capacity building efforts in the collaborating countries.

3. IVI needs to communicate more effectively its existence, mandate and mission to developing countries. This could be done in cooperation with key stakeholders, especially UNICEF, UNDP, WHO, and the World Bank, all of which have extensive regional and national networks in place.

4. IVI should continue to communicate its mission to private industry and donors. Given early misconstrued information that the IVI might be involved in full-scale vaccine production facility and would have little regard for intellectual property rights, this is a critical step in the process to obtain continued future cooperation and support.

5. IVI's GMP pilot plant facility will fulfil a critical niche worldwide not only for improving access to pilot lot production, but also for training local vaccine producers and national regulatory authorities in GMP standards. Because of the global need for the production of low market value vaccine prototypes, financing of this facility might include options to subsidize the production of such vaccine pilot lots, and discussions should involve key partners including the World Health Organisation (WHO), UNICEF, World Bank, UNDP, and national governments, NGOs.

6. IVI should maintain and enhance its capacity in policy research related to the economics and financing of vaccines. This is a key area which requires minimal capital expenditure but addresses a major need in developing countries. If such a capacity cannot be maintained in-house, this type of study could be out-sourced and results made available through IVI.

7. In recognition of its status as an independent international institute, IVI should ensure continued external review of its future activities (e.g. research programme, vaccine production, conduct of clinical trials) to ensure objectivity and transparency.

8. Given the partners' confusion surrounding the definition of "operational" and "fixed" costs, and the responsibilities of the partners toward contributions to the IVI budget, it is recommended that a given annual contribution be made, since a fixed percentage for a developing institution provides for too many uncertainties.

9. The IVI, as an organization seeking to work with industry, should not hesitate to protect its developed know-how and file international patents whenever possible, not for commercial purposes, but to force a dialogue with organisations and companies eager to apply technologies developed at IVI.

II. GLOBAL COOPERATION FRAMEWORK GUIDELINES AND STRATEGIC OBJECTIVES

UNDP's Bureau of Development Policy (BDP) forwarded four questions to the Evaluation Team as part of *A Forward Looking Assessment of UNDP Global Cooperation.* The Evaluation Team considered these four questions in the specific context of the IVI.

1. Is the IVI doing the right things?

Undoubtedly and unequivocally, yes. The IVI's mission is *"To promote the health or people in the developing world by the development, introduction, and use of new and improved vaccines ... through a dynamic interaction among science, public health and business... "* The IVI is facilitating the production and enhancing the quality and use of global public goods (vaccines). Through its projects, the IVI will have a direct and major impact on infectious-disease related morbidity and mortality, and thereby contribute to global efforts to promote sustainable human development.

2. Is the IVI doing the right thing in areas where UNDP has a clear comparative advantage?

Yes. UNDP has extensive expertise globally in institution and capacity-building, has extensive country-level policy and project experience and respect, and shares information and knowledge across member countries. Continued UNDP involvement in the IVI and immunization efforts in general is essential to assist national governments in planning for sustainable vaccine supply, facilitating the uptake of vaccines at the country-level, and by contributing to national and global policy dialogue on governance, and infrastructure issues that affect the introduction and delivery of vaccines.

3. Is the IVI doing the right things well?

It is too early in the implementation phase of the IVI to judge whether it is dong the right things well. However, all indications are that the IVI is on the right track. The IVI is a young and evolving institution. Research projects and activities are currently underway, and results are not expected for another 2 years. The IVI has a committed and highcalibre staff, has an extraordinary network of research collaborators, is actively engaged at the country level in enhancing the quality of locally produced vaccines, and has demonstrated early success in securing external support for its projects. In extensive discussions with key players in the health and development arena, and in particular with the World Bank and WHO, it is clear that UNDP's role and contribution to the field is highly commended and valued. The Evaluation Team strongly recommends that a review of the IVI project be undertaken in 2003-4 at the conclusion of the anticipated funding cycle.

4. Is the IVI and its projects having desirable effects on poverty elimination?

At this point in time, it is too early in the implementation of the IVI to document actual impact on poverty elimination. Improved vaccination coverage improves health and reduce poverty. The IVI will initially contribute to improved vaccination coverage through its technology transfer projects, country level support and training in established

vaccine production standards, development of a shigella vaccine, and accelerated introduction of cholera and typhoid vaccines. Through its programs, the IVI will have a long-term impact on infectious disease morbidity and mortality, health outcomes, and poverty alleviation not only in Asia, but globally as well.

The BDP also forwarded additional questions to the Evaluation Team specifically concerning the linkages, partnership, and cooperation between the Regional and Global Programmes within UNDP. The Evaluation Team considers the IVI to be an excellent example of cooperation between UNDP's Regional and Global Programmes in the implementation of a complex, forward-looking project.

III. PROJECT CONCEPT AND DESIGN

A. Context of Project

Over 13 million deaths worldwide and one half of all deaths in developing countries are caused by infectious diseases.[2] Six diseases-pneumonia, tuberculosis, diarrhoeal diseases, malaria, measles, and HIV/AIDS-account for almost 90% of deaths from infectious diseases globally. In addition to the overwhelming toll of infectious diseases on the mortality of children and young adults worldwide, infectious disease-related disability has a major and direct bearing on income and poverty worldwide.

Health and poverty are not mutually exclusive-the link between poverty and health is strong and bi-directional. Poverty fosters social, economic, and physical conditions that often contribute to the spread of disease. And poor health results in days lost to school or work. Simply, good health is an essential component of sustainable human development.

Vaccines are potentially the most cost-effective means to prevent and curtail the spread of infectious diseases. But as "global public goods," they are not as widely introduced globally as they could be. And for the vast majority of infectious diseases, no effective vaccines are available.

The entire process of global vaccine research and development is fragmented, complex, and changing. Private sector vaccine manufacturers, a shrinking breed worldwide, have demonstrated their ability to develop vaccines that are

scientifically and technically feasible when the anticipated market return is sufficient. Unfortunately, market returns on vaccines targeted mainly to indigent populations in the developing world are insufficient to attract private industry to invest in the extensive costs and risks of development.

Much hope was placed on the emergence of biotechnology firms in the 1990s to meet the research and development needs of "orphan" vaccines. That optimism has been dashed by the reality that such nascent organizations could not manage or sustain vaccine research and development on their own. Indeed, in recent years many larger biotechnology firms have shed their vaccine business altogether.

The challenges to the development and introduction of vaccines of importance to developing countries are complex however, and extend beyond market considerations. In some cases, the science itself is not sufficiently developed to encourage private sector investment in research and development. Furthermore, the involvement of public sector vaccine institutes in vaccine development is decreasing, and where it does exist, is limited largely to isolated individual initiatives.

In the last decade, the pharmaceutical industry has seen a series of mergers and acquisitions, with the end result that there are now just 4 multinational vaccine companies in existence worldwide-down from a dozen just a decade ago. The amalgamation of private vaccine companies has had two important repercussions for the development of vaccines. First,

[2] World Health Organization. 1999. Report on Infectious Diseases: Removing Obstacles to Healthy Development.

within companies themselves, the incentive to advance the development of drugs outweighs that to produce vaccines of uncertain market value with possible patent and liability complications. Second, with fewer firms and more focused competition, there is less capacity, in terms of financial and human resources, for these companies to manage a diversified research portfolio. Simply, with limited capacity resources, private vaccine manufacturers have fewer and more stringent research priorities. Private firms are unlikely to invest in extensive research and development of high-risk, high-volume, low-market value vaccines, such as those for the developing world.

Against the backdrop of consolidation within the pharmaceutical industry is the worldwide trend for countries to produce their own vaccines. The majority of vaccines (most particularly diphtheria, tetanus, pertussis vaccine (DTP)) administered to children in developing countries are produced locally. Over the past few years, there has been mounting concern about the quality of locally produced vaccines including: concerns about outdated facilities; inadequately

trained staff; lack of GMP production; and inadequate regulation by national control authorities. WHO has been working extensively to strengthen local vaccine production entities and national regulatory authorities, and the IVI has a critical collaborative role to play with WHO in training.

The International Vaccine Institute

The International Vaccine Institute was inspired by the Children's Vaccine Initiative, launched at the World Summit for Children in 1990. The Children's Vaccine Initiative was a broad coalition of multilaterals, public sector, non-governmental organizations, and private industry, brought together to accelerate the research and development of safe, effective, easyto-deliver and widely available vaccines.

As one of the founders of CVI, the UNDP sponsored a study in 1992 to assess the feasibility of establishing an international institute for vaccine research against diseases prevalent in developing countries. The feasibility study concluded that an international institute could be effective in vaccine research and development for developing countries, that such an institute could strengthen the capacity of developing country vaccine research and development, and that the most suitable location for such an institute would be in the Asia/Pacific Region.

Drawing on its comparative advantage in institution and capacity building, the UNDP in 1994 with substantial backing from the Republic of Korea, initiated the process to establish an International Vaccine Institute (IVI) in Seoul, Korea. The central mission of the IVI is:

> *To accelerate the introduction of vaccines into developing country public health programs by undertaking research and providing research-based technical assistance that effectively address issues of vaccine development, disease burden, safety and efficacy, delivery feasibility and effectiveness, and sustained supply.*

For a variety of reasons, the Children's Vaccine Initiative was disbanded in 1999; and the Global Alliance for Vaccines and Immunization (GAVI), a broad alliance of interested agencies, partners, and multilaterals established in its place. GAVI, launched at Davos, Switzerland in January 2000 is charged with accelerating the introduction of new vaccines

into immunization programs. GAVI operates through a small Executive Secretariat and three Task Forces on Country Coordination, Advocacy, and Financing. A fourth Task Force on Research and development will be launched in June 2000.

The IVI is currently the only international organization established under the auspices of the United Nations dedicated to research and development of

vaccines against infectious diseases.

Many of the impediments identified in the continuum of vaccine research and development that led to the establishment of the IVI remain unchanged. The evaluation team considers the establishment and support of the IVI to be visionary, with great potential to contribute to a greater understanding of disease burden, and the development and introduction of new and improved vaccines. Investment in vaccines and immunization is an investment in poverty alleviation and sustainable human development.

With the dynamic changes occurring in all aspects of vaccine delivery, from research, development, management, and production, introduction, and utilisation, the IVI has a clear and unique niche-perhaps more so now than at its inception eight years ago. The IVI is uniquely positioned to operate at the intersect of public and private sectors. With its strategic location in Asia, within a short distance of 50 percent of the world's population, the IVI is the most important new institution in vaccine RESEARCH AND DEVELOPMENT, working in partnership with WHO, UNICEF, and other institutions to accelerate the development and introduction of new vaccines.

B. Project Document

The UNDP Project Document for the Establishment of an International Vaccine InstitutePhase I sets out the direction for the IVI for the years 1997-2000 and builds on earlier projects GLO/94/003 (Establishment of the International Vaccine Institute) and RAS/96/003 (Regional Activities of the International Vaccine Institute).

1. Concept and Design Although major changes have occurred in the vaccine world since the inception of the IVI, the project document outlining Phase II of the IVI establishment continues to be highly relevant. The project document includes both long-term and immediate development objectives.

A. Long-Term Development Objectives

The IVI intends to achieve long-term objectives within two main domains: (1) Strategic Research and Product Development and (2) Technical Support and Capacity Building.

1. Strategic Research and Product Development:

(a) Through laboratory research, to make significant contributions to developing new vaccines;
(b) Through collaboration with production centres and others to help bring promising candidates from the laboratory into clinical and field

study;

(c) Through the conduct of epidemiological studies, and clinical and field trials, to play an essential role in the introduction of new vaccines for respiratory diarrheal and other priority diseases;
(d) Through the professional execution of collaborative projects, to be recognized by industry as a highly valued partner in the development and introduction of new and improved vaccines.

2. <u>Technical Support and Capacity Building:</u>

(a) To become a leading institution for the training of epidemiologists, clinical investigators, field researchers, and national regulatory personnel;
(b) To be a leading source of up-to-date, authoritative information about immunization, vaccination, regulation, etc. through the distribution of a newsletter and the maintenance of internet resources.
(c) To become recognized by governments, international agencies, and the private sector as a leading source of technical expertise in the vaccine-related sciences and in education, training and information dissemination.

B. Immediate Objectives

The immediate objectives as stated in the project document are:

1. Strategic Research and Product Development
"Undertake programs that will contribute significantly to the accelerated introduction of new and improved vaccines into national immunization programs. "

2. Technical Support and Capacity Building
"Provide services that will enhance the impact of the research and development program and provide support to collaborating partner institutions in developing countries. "

3. Governance and Management
"Ensure the establishment of the Institute as an autonomous, international centre of excellence in vaccine research and development. "

4. Building Staff Capability
"Build a core of high quality international and national staff, and associates who can effectively develop and implement the Institute's programs. "

5. Resource Mobilization
"Secure diversified funding that will permit the Institute to meet its operational and programmatic needs. "

C. Beneficiaries

Although there is no specific statement as to the intended beneficiaries or target group in the project document itself, ultimately children and adults in all

developing countries at risk of infectious diseases are the intended beneficiaries of this project. The IVI is now working on diseases important in Asia (e.g. Japanese Encephalitis) and of global

significance (meningitis, shigella, cholera, typhoid fever). The more immediate beneficiaries of the project include research institutions in Asia and abroad, local vaccine production centres, and national regulatory authorities.

D. Work Plan

The project document does not include a detailed work plan or schedule. The project document does, however, organise the IVI's activities into four phases with associated time frames: Feasibility Phase (October 1992-December 1994); Establishment Phase I (January 1995-October 1997), Establishment Phase II (October 1997-December 2000), and Operations Phase: 2001 onwards. The Project Document under consideration covers Establishment Phase II.

Although the work schedule as outlined in the project document is tentative, there have been delays specifically related to the construction of the physical facilities, hiring of the first IVI Director, and the burden of disease studies, all of which are discussed under Section IV, Project Implementation.

IV. PROJECT IMPLEMENTATION

A. Funding

The UNDP provided seed money ($232,000) for the feasibility study and committed $2.5 million as core funds to the initial establishment of the institute.

The Republic of Korea has demonstrated extraordinary commitment to the IVI through its contribution of 100 percent of the operating expenses for the years 1995-1997 amounting to $2.79 million; subsequent funding of $2. 4 million in 1998 and 1999; and additionally its commitment to finance the construction and equipment of the physical facilities (offices, laboratories, and pilot plant), estimated to be approximately $40 million.

The IVI has been successful in securing project support from an unprecedented mix of private and public sector institutions for its projects, including three private pharmaceutical companies (Wyeth-Lederle, Merck, and SmithKline Beecham) who have provided $1.635 million (1997-present) towards the burden of Hib disease studies in conjunction with PATH/ Children's Vaccine Program. In December 1999, the Gates Foundation pledged $40 million over 5 years for the IVI's Diseases of the Most Impoverished (DOMI) Program. Additional funds have been provided by the

Rockefeller Foundation (1997), and the Government of The Netherlands (1998). (See Annex X for Financial Statement)

B. Activities

Feasibility Phase: October 1992-December 1994

A feasibility study confirmed the need for an international institute dedicated to research and development of vaccines for the developing world. In 1994, following the feasibility study, an international and multidisciplinary group of experts recommended that the Republic of Korea be selected to host the IVI. UNDP initially appointed an advisory board of trustees.

Establishment Phase I: January 1995-September 1997

From 1995 - 1997, a project team went to Korea and laid the groundwork for the Institute. The IVI was officially launched on May 29, 1997, and now has 33 official signatories to the agreement including WHO. During this period, IVI staff also organized four international conferences on vaccine research and development, published papers on vaccine policy, and initiated technical consultations to vaccine manufacturers in Asia.

Establishment Phase II: October 1997-December 2000

This phase is on-going but the following milestones have been achieved:

- Board of Trustees: A 17-member Board of Trustees with membership from WHO, ROK, and eminent scientists and public health experts from both developed and developing countries was formed and met in October 1997 and December 1998. The next Board meeting is scheduled for March 2000.

- Institute Support Council (ISC): The UNDP-chaired ISC is intended to *' provide a means by which supporters can help to mobilize funding and to make recommendations to the Board of Trustees on programs and policy of the Institute."* Unfortunately, the ISC has met only once (in conjunction with the first Board of Trustees meeting in October 1997). To date, the ISC has not been effective as an advocate of the IVI or in the mobilization of resources.
- Scientific and Technical Advisory Council (STAG): The STAC was formed reviews IVI's research programme and directions.
- Headquarters Agreement with ROK: In January 1999, the Institute Headquarters Agreement with the Republic of Korea went into full effect thereby empowering the Institute to operate as a fully autonomous and independent institution.
- IVI's First Director: In July 1999, the Board of Trustees recruited a highly-regarded Director to lead the IVI. The recruitment of the first IVI Director proved to be a lengthier process than initially anticipated. Prior

to the recruitment of the Director, the IVI was ably managed by three UNDP-sponsored staff.

- Facilities Construction: The construction of the IVI headquarters building and pilot facility began in December 1998 on the campus of Seoul National University. Ground-breaking and construction had been delayed a year due to the Asian financial crisis. The estimated date of completion for the building is the end of 2001. Work is currently proceeding on schedule.
- WHO Global Training Network: IVI became a designated centre in WHO's Global Training Network to strengthen local vaccine production and national regulatory authorities in developing countries.
- GAVI Task Force on Research and development: IVI has been invited to participate in the Task Force on Research and Development.
- Resource Mobilization: IVI secured a $40 million grant from the Bill and Melinda Gates Foundation for a five-year Diseases of the Most Impoverished Program to define the need for, obstacles to, and cost-effective use of new-generation vaccines against cholera, typhoid, and shigellosis in developing countries of Asia; to introduce successfully existing, new generation vaccines against cholera and typhoid fever; and to evaluate new candidates against shigellosis.

In addition, the IVI initiated its first activities in four broad areas: research including epidemiology; policy and economic analysis; technical assistance and training; and information dissemination.

- *Epidemiologic Research:* A multi-country epidemiologic burden of disease study on *Haemophilus influenzae type B (Hib)* began in 1999 in China, Korea, and Vietnam. Shortly after project start-up in China, it became apparent that a vaccine manufacturer was selling Hib vaccine in the area, thereby rendering the study site non-informative. A new site and collaborating institution in China have since been found and work is expected to begin mid-2000. The Korea and Vietnam sites are up-and-running after completion of a rigorous pilot phase during which patient referral, data collection procedures, laboratory protocols and methods were tested and revised where necessary.
- *Policy and Economic Analysis: IVI* Staff have written and published several papers on vaccine financing and policy.

- *Technical Assistance and Training:* The IVI is particularly fortunate to have on staff a world expert on GMP vaccine production. In 1998, IVI staff gave training workshops in GMP production in Korea, Singapore, China, Thailand, Bulgaria, Vietnam, and Iran. In addition, the IVI has assisted in WHO inspections of vaccine production facilities in Korea, Brazil, Denmark, and Bulgaria. The IVI has also embarked on a technical

assistance project with the Korean Food and Drug Administration to enhance their in-house capability with regard to vaccine evaluation, research and regulation. And in a recent development, the IVI is providing technical assistance to the Socialist Republic of Vietnam in the design and of GMP manufacturing facilities to produce recombinant Hepatitis B, Japanese Encephalitis B, cholera, typhoid, and rabies vaccines.

- *Information Dissemination:* The IVI continues to convene conferences, publish and widely distribute its strategic plan, and has an internet web site (www.ivi.org) with information on IVI's on-going activities.

Operations Phase: 2001 and onwards,

Given the delays in the facilities construction, full operations are expected to begin in 2002 at which time the IVI plans full implementation of its scientific and technical programs. In addition to continuing its multi-disciplainary program of epidemiologic studies, Phase 1-3 and effectiveness trials, social, economic, and policy research and technical assistance and training in vaccine production, the IVI proposes to focus its vaccine research in the following areas:

- Vaccines against enteric infections (rotavirus, ETEC, shigella, cholera, typhoid)
- Vaccines against respiratory infections (Hib, Pneumococcus, Meningococcus)
- Vaccines against vector-borne infections (JE)
- Cross-cutting research (Vaccine safety, social, economic, and policy research, volunteer unit for Phase 1-2 trials)

C. Quality of Monitoring

According to the project document, the project shall be subject to review once every 12 months with the expectation that the Institute Director will prepare and submit to each review a Project Performance Evaluation Report. During the reporting period, IVI staff prepared extensive compilations of IVI activities on an annual basis and reported on-going activities to UNDP staff on a regular but informal basis. The Institute Director began his term of office on July 1, 1999.

PROJECT RESULTS

A. **Relevance**

The International Vaccine Institute, its projects, programs, and future directions, is integral to international efforts to increase the introduction of new vaccines through the enhancement of research and development of vaccines of importance for diseases of special importance to developing countries, and especially to the most vulnerable segments of society.

B.Efficiency

As part of this mid-term review, the evaluation team gave a cursory review to the policies and procedures established for the IVI. The following areas-human resources, financial authorization, budgeting, managerial policies-appear to well organized and professional. The procurement policy, while adequate for the current size and operations of the IVI, will need to be updated as the Institute evolves. The Evaluation Team does have some concerns related to budgeting, which are discussed further under D. Immediate Objectives/Resource Mobilization.

C. Outputs

The Institute has established an important network of partners and collaborators in Asia, Europe, and South Africa. Multi-country research projects were launched in 1999, although first scientific results will not be available until late 2001. The IVI has also convened international conferences, published policy papers, and is disseminating information on its activities through its website *http://www.ivi.org*. A recent technical paper[3] by IVI staff and an outside vaccine expert presents a novel financial analysis and approach for the introduction of new vaccines into developing countries. The approach outlined in this paper is being reviewed by GAVI as it develops a global strategy for the GAVI Global Fund for Children's Vaccines.

D. Immediate Objectives

The IVI is well on its way to meeting the immediate objectives set out in the Project Document.

a. Strategic Research and Product Development

"Undertake programs that will contribute significantly to the accelerated introduction of new and improved vaccines into national immunization programs. "

The IVI is conducting a multi-country *Haemophilus influenzae type b* burden of disease study, and has embarked on a $40 million Diseases of the Most Impoverished (DOMI) project to accelerate the introduction of vaccines against shigella, typhoid, and cholera. The IVI is also developing a project related to the development and introduction of an improved Japanese Encephalitis vaccine.

[3] Richard T. Mahoney, S. Ramachandran, and Zhi-Xi Xu. Introduction of New Vaccines into Developing Countries. International Vaccine Institute, Seoul, Korea. 1999.

b. Technical Support and Capacity Building

"Provide services that will enhance the impact of the research and development program and provide support to collaborating partner institutions in developing countries. "

Through its technical cooperation and assistance program, the IVI is providing workshops on GMP production, and is assisting various countries through the WHO and governments with on-site inspections, facilities design, vaccine production inspections, and technical assistance to national regulatory authorities. The IVI is a member of WHO's Global Training Network.

The IVI's GMP Pilot Production facility which is expected to be completed in 2003-4 will be an important, and indeed unique, training centre for developing country nationals to receive hands-on experience in GMP production, quality control, and quality assurance.

c. Governance and Management

"Ensure the establishment of the Institute as an autonomous, international centre of excellence in vaccine research and development. "

Established in May 1997 under the auspices of the UN, the IVI became an autonomous international centre on January 1, 1999, reporting to an independent Board of Trustees. The IVI's Institute Support Council, which is chaired by the UNDP, only met once in October 1997. It is scheduled to meet again in March 2000 in conjunction with the Board of Trustees meeting. In addition, a Scientific and Technical Advisory Council was formed.

d. Building Staff Capability

"Build a core of high quality international and national staff, and associates who can effectively develop and implement the Institute's programs. "

The IVI has a core group of highly skilled and committed international and national personnel with expertise in clinical field trials, project management, vaccine production and policy. The IVI is directed by a world-class scientist with expertise in diarrhoeal diseases and clinical trials. There are currently eight international professional staff members and eight national staff members. IVI continues to add to its core group in other key areas including clinical/field epidemiology. Despite the relative youth of the organisation, the IVI has an impressive recruitment record.

e. Resource Mobilization

"Secure diversified funding that will permit the Institute to meet its operational and programmatic needs. "

The IVI has sought and received substantial project funds from multiple private and public sector sources. However, IVI's access to unrestricted core funds is uncertain while the need for such funds is increasing. Unfortunately, there has been a misunderstanding, which does not appear to be fully resolved, between the Republic of Korea and the UNDP regarding future support of the IVI.

At project start-up, the Republic of Korea committed to providing 30 percent of the operating budget, on the expectation that UNDP and other donors would make up, or be instrumental in raising, the remaining 70 percent. There has been some confusion with regard to the responsibility UNDP would play in securing the remaining 70% of operating funds.

Although the evaluation team found no UNDP documentation guaranteeing long-term financial commitments, official letters convey UNDP's enthusiasm for the IVI and could well have been construed to ensure long-term support. For example, a letter from James Gustave Speth, UNDP Administrator to H. E. Mr. Lee Hong-Koo, Prime Minister Republic of Korea, 4 September 1995 reads, *"Let me assure you that UNDP is fully committed to the success of the Institute. I want to pledge to you my highest level of commitment to the Institute, and I will work with member countries to encourage their support for the Institute. "* In a letter from Frank Hartvelt, Deputy Director, Science, Technology, and Private Sector Division to Mr. Sung Ho Kum, Director General Ministry of Education, Korea, Mr. Hartvelt writes, *"In order to assure you of UNDP's continued commitment to the financial stability and long-term success of the Institute, I would like to inform you that UNDP will favorably consider an arrangement by which Korean contributions in excess of 30% during the initial years would be off-set by corresponding reduction after the Institute goes into full operation. "*

E. Long-Term Development Objectives

Despite not yet having a research and development facility that is operational, the IVI is working toward two long-term development objectives as articulated in the UNDP project document: (1) Strategic Research and Product Development and (2) Technical Support and Capacity Building.

Strategic Research and Product Development: The IVI has established partnership/collaboration agreements with academic institutes, private industry, and public sector organizations in 15 countries, many of them developing countries. The Hib epidemiological studies currently underway in Korea and Vietnam and soon to be started in China are ground-breaking studies, with unprecedented private sector support and collaboration, designed to assess the burden of Hib, meningoccal and pneumoccal disease in Asia. The DOMI project will, over the course of the next five years, define the need for, impediments to and cost-effective use of new-generation vaccines against cholera, typhoid, and shigellosis in Asia. It will spur the development and introduction of existing new-generation vaccines against cholera and typhoid fever, while at the same time evaluate new candidate vaccines against shigellosis. Several other promising projects involving

public-private partnerships in targeted research are currently under development.

Technical Support and Capacity Building: The IVI has a core staff of highly skilled and committed staff and is actively participating in a variety of technical support and capacity building initiatives worldwide.

(a) Technical Cooperation and Training: In 1998, IVI staff gave training workshops in Good Manufacturing Practices (GMP) production in Korea, Singapore, China,

Thailand, Bulgaria, Vietnam, and Iran. In addition, the IVI has assisted in WHO inspections of vaccine production facilities in Korea, Brazil, Denmark, and Bulgaria. The IVI is providing technical assistance project with the Korean Food and Drug Administration to enhance their in-house capability with regard to vaccine evaluation, research and regulation. And in a recent development, the IVI is providing technical assistance to the Socialist Republic of Vietnam in the design of GMP manufacturing facilities to produce recombinant Hepatitis B, Japanese Encephalitis B, cholera, typhoid, and rabies vaccines.

(b) Capacity Building in Epidemiology for Asian Scientists: IVI scientific staff have initiated capacity building efforts in Asia as part of a long-term goal of developing scientists skilled in the evaluation of vaccines important to developing countries in conjunction with the London School of Tropical Medicine and Hygiene, Seoul National University and Tokyo National University. Training will occur in all of the aforementioned institutions, and doctoral and post-doctoral scientists will actively collaborate on IVI studies.

(c) Information Dissemination: The IVI has established an internet website, convened conferences, and published papers in vaccine sciences and policy. The GAVI Global Fund for Children's Vaccines (GFCV) recently adopted a financing mechanism for the introduction of new vaccines into developing countries that was outlined in an IVI policy paper.

F. Effectiveness

The IVI is the only international centre devoted to the research and development of vaccines against diseases in developing countries. During the early 1990s, some critics of the IVI argued that resources could have been directed to strengthening public sector vaccine institutes to perform some of the functions of an IVI. Today, some of these public sector vaccine institutes that have played an essential role in vaccine development have closed (e.g. State Serum Lab in Denmark, State Bacteriological Laboratories in Sweden),

and others such as the RIVM in The Netherlands are faced with possible privatization. Only a handful of public sector vaccine institutes remain and their future role in vaccine development is far from certain.

Some individuals within multilateral organizations expressed concerns that the IVI had too broad a mandate that appeared to trespass on the mandate of other organizations, namely WHO. It is important to note, however, that WHO is not an operational organization, and is unable to undertake vaccine research and development activities. These concerns have diminished in the last year, and WHO considers the IVI to be a valuable part of its global efforts. Indeed, IVI's research and technical work is designed to support fully WHO priorities. Multiple levels of interactions between IVI and WHO including through the IVI Board of Trustees, WHO Steering Committees, WHO Collaborating Centres, WHO Global Training Network, and direct participation of WHO staff in IVI projects are on-going.

At the outset, certain members of private industry had concerns related to IVI's broad mission, including IVI's possible role in large-scale vaccine production and intellectual property concerns. The IVI has made concerted efforts to clarify and communicate its areas of focus in research and development, and there appears to be less skepticism and more support for IVI future activities from private industry. Indeed, private sector support of the Hib burden of disease studies is indicative of the value private industry places on the IVI to conduct such clinical evaluations. In addition, private vaccine manufacturers in the United States wrote letters of support to the U. S. State Department endorsing the nomination of the first IVI director.

One of the major problems faced by the IVI is the refusal of the United States to ratify IVI's establishment agreement largely due to concerns over governance and respect for intellectual property. The IVI has proposed an addendum to its constitution explicitly ensuring that intellectual property rights will be fully respected, and furthermore, that any disputes arising will be settled in a court of law in the UK, Switzerland, or the United States. The issue of United States support of the IVI's establishment remains unresolved at this time.

G. **Capacity Building:**

Although in the early stages of implementation, the burden of disease studies currently underway in Vietnam, Korea, and China are contributing to long-term capacity building in all three countries. An extensive network of clinicians, nurses, laboratory personnel, and others have been trained. Hospital personnel are following rigourous quality control and quality

assurance procedures, and have even applied these to activities outside of the burden of disease studies. Prior to the study, pediatricians in Vietnam never included lumbar punctures as part of their diagnosis of meningitis. Today, all physicians involved are convinced that for a reliable diagnosis and rational therapy, such an intervention is necessary.

The IVI contributes significantly to human resource development and capacity building, in collaboration with WHO, through the training of personnel in national regulatory authorities and developing country vaccine manufacturers in quality control and Good Manufacturing Practices (GMP).

IVI's program currently under development to train doctoral and post-doctoral scientists from developing countries in vaccine sciences and evaluation will have a major impact on building capacity to manage and monitor vaccine evaluations in developing countries.

H. Impact

It is too early in the implementation of the IVI to begin to assess its full impact on vaccine development and introduction. The IVI will play an instrumental role in the introduction of new vaccines through determination of the burden of disease, the potential impact of a given vaccine on disease burden, and assistance in the development of plans to finance and introduce vaccines.

The IVI has already demonstrated its ability to design and implement the first ever population-based studies on the incidence of Hib disease in both Korea and Vietnam with China anticipated to begin in spring 2000. The evaluation team was impressed with the commitment and enthusiasm of the principal investigators in Vietnam and Korea, and their positive assessment of the working relationship with IVI.

Through the DOMI (Diseases of the Most Impoverished) project, the IVI has established an impressive and diverse network of global partners in research and development and vaccine introduction related to shigella, typhoid, and cholera. With these and upcoming projects, including a proposed trilateral technology transfer agreement among RIVM, Bio Farma and IVI, and a comprehensive study of Japanese Encephalitis burden of disease, characterization of sequelae, and effectiveness of vaccine, the IVI is fulfilling a critical niche in vaccine research and development.

I. Sustainability

Financial Sustainability

The Republic of Korea (ROK) has given the IVI unparalleled support from and has committed itself to funding 30% of IVI's operating expenses into the future. There appears to be some confusion, however, among the partners as to what is actually included in "operational expenses." As the IVI is growing, and as project grants and funds are often unknown at the beginning of the financial year, it has been impossible to calculate ROK's percentage contribution of the operating expenses at the outset. At this stage of the IVI's development, there are too many uncertainties in the budgeting process to continue with the current percentage formula.

The Bill and Melinda Gates Foundation, Merck and Company, Wyeth-Lederle Vaccines, SmithKline Beecham, and PATH/Children's Vaccine Program have contributed *project* support to the IVI. There is considerable support for the IVI from both public and private sector institutions across the globe. However, continued UNDP core support, both moral and financial, which confers credibility and impartiality is considered critical to the IVI. In order to be managed professionally, the IVI requires core support to match project support.

Sustainability of Products

The IVI is working tirelessly to ensure that the products of its research efforts are sustainable into the future. Through the DOMI project, the IVI is overseeing the introduction of two locally produced vaccines (typhoid (Ty21 a) and whole-cell cholera). In addition, IVI will coordinate the technology transfer of Hib conjugate vaccine from RIVM (The Netherlands) to Bio Farma (Indonesia).

Sustainability of Research Techniques

In addition to financial sustainability and the sustainability of research products, is the broader question of sustainability of research techniques in the field. The current epidemiological burden of disease studies employ high-cost diagnostic and research tools. The sustainability of such high-quality techniques in the field is at risk, unless concerted efforts are made to target strategic research to develop cheaper, more effective

diagnostic tools. The IVI should be expected to contribute to sustainability through targeted developmental research in its laboratories.

J. Follow-up

Notwithstanding the important role UNDP plays as Chair of the Institute

Support Council (ISC) (IVI's advocacy group of donors, supporters, and beneficiaries that is intended to assist the IVI in advocacy and resource mobilisation), UNDP, ROK, and the IVI need to work collectively towards enhancing the visibility and activities of the IVI, particularly related to developing a broader base of donor support for IVI activities.

VI. **FINDINGS**

In the course of this mid-term review of UNDP's role in the establishment and implementation of the IVI, the evaluation team reached the following conclusions.

General

- UNDP demonstrated exceptional vision and leadership in the establishment of the first ever international centre devoted to vaccine research and development.

- The Republic of Korea, as host country, has provided substantial and unstinting support to the IVI and has demonstrated its strong commitment to the IVI's long-term success.

- The Republic of Korea anticipates continued UNDP support, both financial and moral for the IVI, and rightly considers such support essential to IVI's international and impartial status.

- There is general and widespread support and enthusiasm for the role IVI plays and can play in the future from many quarters, including developing countries, private industry, public sector organizations and institutes in a number of countries, international organizations, and other key players in the vaccine arena.

Achievements

- The IVI has developed an impressive network of partnerships and collaborators in 13 countries, including Bangladesh, China, Denmark, Egypt, France, Indonesia, India, Korea, Myanmar, The Netherlands, Sweden, Thailand, United Kingdom, United States, and Vietnam. IVI is itself a member of WHO's Global Training Network.

- The IVI has performed remarkably well since its establishment. It has successfully initiated important activities related to measuring the burden of disease, establishment of multicountry field trial sites, training programs in Good Manufacturing Practices, intensive international collaboration and

partnerships, and information dissemination.

- IVI is emerging as a unique global centre of excellence dedicated to original and collaborative scientific and technical vaccine research against diseases that strike the most vulnerable segments of society.

- Although the IVI is based in Asia, the vaccine research and development projects underway are of global significance. Shigella, typhoid fever, cholera, and meningitis are important diseases in Africa, the Middle East, and Latin America.

- IVI has succeeded in initiating a population-based project activity in measuring disease burden in selected sites in Korea, China and Vietnam *(H. influenzae* type b meningitis). The study is underway in Korea and will commence in Vietnam and China in the near future. The ongoing project in Korea has the following features
  1. Sound study design and site selection, including pilot studies before project commenced 2. Quality assurance and control incorporated in both epidemiological and laboratory components
  3. Good communication and coordination among all investigators involved through regular meetings
  4. Setting up of a computerised standard database management tracking system that is accessible from the IVI.

- IVI is forming a core group of committed and highly skilled personnel in various key areas including clinical/field epidemiology, project management, human resource & financial management, information systems, vaccine production and vaccine policy, economics and financing. The Institute's first Director, appointed in July 1999 is a world-renowned scientist.

Partnerships

- The IVI has established an impressive network of collaborators across the globe with an emphasis in Asia.

- With the awarding of a $40 million grant from the Gates Foundation for the Diseases of the Most Impoverished (DOMI) project, the IVI has demonstrated its success in obtaining outside project support.

- IVI has developed, in close collaboration with WHO, an impressive in-house capacity for providing technical assistance and consultancy advice in relation to vaccine production and quality control with emphasis on GMP issues.

•IVI provides a unique venue for public and private sectors to join together to assess burden of disease, conduct clinical trials, and participate in scientific and technical research and collaboration. IVI's Hib disease burden studies currently underway are unprecedented not only as the first ever multi-country population-based studies in Korea and Vietnam, but also as the first time collaboration among three private pharmaceutical firms in a disease burden study. The latter illustrates the importance with which private industry views the role of the IVI in conducting epidemiological research..

- Although IVI is a member of the Global Alliance for Vaccines and Immunization (GAVI) Research and development Task Force, there is potential for enhanced cooperation and communication between IVI and GAVI.

- Initial resistance among certain segments of private industry to possible abuses of intellectual property rights and perceived competition in the domain of vaccine production has diminished. *In the opinion of the Evaluation Team, there is no justification whatsoever for concern that the IVI is less than totally committed to maintaining intellectual property rights. In addition, it is clear and evident that the IVI will never be involved in the manufacture and sale of vaccines at any time, now or in the future.*

- WHO's initial concern (1993-4) with specific regard to IVI's mandate and demarcation of activities has been replaced by widespread support and approval of the role IVI is playing in global vaccine activities and strategies.

Administration and Financing

- There remains some confusion regarding expected levels of financial commitment from the UNDP and ROK. Part of the confusion surrounds the definition of "operating expenses." In the future, the IVI should develop a multi-year budget including the total costs of the institute and its projects. In this context, the ROK/IVI may wish to consider a fixed donation to the IVI rather than a predetermined percentage formula. It is estimated that the IVI will, when fully operational, have a total budget of approximately $20 million, at least 40% of which will need to be in the form of unrestricted core funds to cover overhead and indirect costs (i.e. costs not immediately attributable to a given project.) This would imply that the ROK contribution be approximately $5-6 million annually in perpetuity.

- UNDP, as the co-founder and initial project sponsor of the IVI, is satisfied with the way the project is currently managed.

- The policies and procedures established at the IVI, including human resources, financial, administration, budgeting, and reporting, have been professional although on-going review is essential to ensure relevance as the IVI evolves.

Future Directions for the IVI

- IVI's research programme will focus on its key mission to facilitate introduction of inexpensive vaccines in developing countries and thereby contribute substantively to poverty alleviation, good governance, capacity building, and institution building.

- The IVI's planned GMP pilot plant facility will not only produce high-quality GMP pilot lots of bacterial and viral vaccines, but also provide a unique hands-on training facility in Asia for developing country nationals in GMP/QA/QC production practices.

VII. RECOMMENDATIONS

Based on a mid-term evaluation of on-going IVI activities, the Evaluation Team has the following recommendations for both UNDP and the IVI.

A. UNDP Involvement

1. UNDP should continue its support of the establishment phase of the IVI for an additional 3 years at a minimum of current funding levels. Continued UNDP commitment, both moral and financial, is critical to the sustainability, credibility, and stature of the IVI as an impartial scientific organization dedicated to the research and development of vaccines of importance to developing countries. Should UNDP decrease its level of support for the IVI, the future of this evolving institute and its activities will be in jeopardy. Whether UNDP support is drawn from the Regional or Global programmes is a matter for internal UNDP discussion and resolution. Although based in Asia, and although its current research projects are Asia-based (but with global implications), the IVI will increasingly and necessarily evolve into an international institute.

2. The UNDP-chaired IVI Institute Support Council (ISC) lends itself to advocacy with a commensurate emphasis on enhanced communication and resource mobilization. The UNDP should consider continuing its leadership of the ISC. The evaluation team recommends that the ISC build on its reputation to work with the IVI to develop a formal policy for international fundraising. Such a fundraising initiative, "Friends of the IVI" could draw

upon international expertise in global fundraising and contribute substantially to the development of an endowment for the IVI.

3. In light of the goodwill and trust between the UNDP and the Republic of Korea, and the role the Republic of Korea intends to play within the emerging donor community, the importance of a continued partnership and communication between UNDP and the ROK with regard to the IVI cannot be over-emphasised.

4. Cooperation and communication between IVI and the Global Alliance for Vaccines and Immunization (GAVI) should be continued and expanded in well-defined areas. GAVI appears excellently positioned to receive ear-marked donations from bilateral donors for the IVI. In this context, and as also recommended in *UNDP's External Evaluation of the Global Programmes, Health and Development (February 2000),* UNDP should reconsider its decision not to be a participating board member of GAVI. In the current unprecedented global effort to enhance immunization worldwide, UNDP can and should play a pivotal role in country coordination. In addition, UNDP is uniquely positioned to assist countries in developing appropriate polices and institutions; disseminate knowledge and experience among member countries; mobilize public and private sector resources; and, promote technical cooperation and transfer.

5. With regard to the relationship between IVI and UNDP, consideration should be given by both organizations to a different kind of future relationship-not one of donor-recipient

only, but one based additionally on a strong partnership to achieve IVI's objectives. Such a partnership, building on UNDP's presence in 136 countries, policy expertise, extensive network and outreach capabilities, is, in fact, consistent with UNDP's new direction and may facilitate continued financial support.

B. Future Directions For IVI

1. The IVI should strive to develop itself into a fully international institution. The current network of collaborators should be enlarged wherever possible to include centres in Africa, Latin America, and former Soviet republics. IVI should consider formalizing the cooperation arrangements that have been made with partners in various countries in order to secure the continued loyalty of partners in the IVI network. Participation in the network should be formally agreed to describing and delineating the area(s) of collaboration. It should

clearly articulate and define what it really means to be "international" and incorporate this view into its strategy and work plan.

2. The future research efforts of the IVI should be closely linked to its ongoing activities in epidemiological field studies of disease burden and vaccine effectiveness. It should utilize its comparative advantage and unique position in having access to patient materials in disease-endemic areas (e.g. strains/ isolates, sera, CSF, tissues, good clinical and epidemiological information) and in having extensive networks of collaborators in place. In this regard, IVI should focus its efforts on strategic and applied research rather than dealing with basic research in vaccine-related areas. Examples of potentially valuable research areas would include study of human immune responses to candidate vaccines, improvement of laboratory diagnostic tests, molecular epidemiology of selected pathogens (and building a repository of isolates and strains), and improvement of vaccine delivery and formulation. Another potentially important 'niche' for IVI is to focus on the implementation and application issues related to novel vaccine technologies, e.g. DNA vaccines and oral vaccines. The linkage of IVI's research efforts to the established networks will also facilitate training and research capacity building efforts in the collaborating countries.

3. IVI needs to communicate more effectively its existence, mandate and mission to developing countries. This could be done in cooperation with key stakeholders, especially UNICEF, UNDP, WHO, and the World Bank, all of which have extensive regional and national networks in place.

4. IVI needs to continue to communicate its mission to private industry, given previous misunderstandings related to IVI's involvement in full-scale vaccine production. This is a critical step in the process to obtain industry's future cooperation and support. A similar recommendation can be made regarding the IVI's relationship with the United States State Department. *This should be given a high priority to encourage the U.S. government to ascend to the IVI establishment agreement.* United States support for the IVI will be instrumental in securing support from other nations, notably Japan. It is the express view of the evaluation team that the IVI has taken all possible steps to put in place a solid IPR policy fully aligned with policies and practices in OECD countries.

5. IVI's GMP pilot plant facility will fulfil a critical niche worldwide not only for improving access to pilot lot production but also for training local vaccine producers and national regulatory authorities in GMP standards. The IVI must first develop and better define plans for the financing and administration of

this important facility, including the identification of "launching customers" at the earliest. The IVI should not exclude the option of subsidizing, either in whole or in part, the pilot production of low-market value prototype vaccines, and this should be explored with multilaterals, UNDP, and GAVI.

6. IVI should maintain and improve its capacity in policy research related to the economics and financing of vaccines. This is a key area which requires minimal capital expenditure and addresses a key need in developing countries. If such a capacity cannot be maintained in-house, this type of study could be out-sourced and results made available through IVI.

7. In recognition of its status as an independent international institute, IVI should continue to ensure good external review of its future activities (e.g. research programme, vaccine production, conduct of clinical trials) to ensure objectivity and transparency.

8. Given the partners' confusion surrounding the definition of "operational" and " fixed" costs, and the responsibilities of the partners toward contributions to the IVI budget, it is recommended that a given annual contribution be made, since a fixed percentage for a developing institution provides for too many uncertainties.

9. The IVI, as an organization seeking to work with industry, should not hesitate to protect its developed know-how and file international patents whenever possible, not for commercial purposes, but to force a dialogue with organisations and companies eager to apply technologies developed at IVI.

VIII. LESSONS LEARNED

There are some key lessons learned in this evaluation that are relevant to planners of future institution building and capacity building projects at UNDP. Among the lessons learned which can contribute to the success of an institution such as the IVI are:

- Committed individuals working in identified niche areas, and focussing on early results, can be crucial to raising awareness of and visibility of a new institute.

- To safeguard goodwill and prevent future misunderstanding, explicit agreements should be reached at the outset of a project on financial support and other expectations from all parties concerned. These agreements should be formally agreed upon, reviewed and updated at regular intervals.

•Public-private initiatives related to products with commercial potential (and associated concerns with intellectual property rights), will invite concerns from both sectors. However complex and time-consuming, these concerns must be confronted and resolved on an ongoing basis, so as to ensure that each group contributes its best and maximum to the given initiative.