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PUBLIC AND PRIVATE ROLES IN
IMMUNIZATION:
THE DONOR RESPONSE

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Public and Private Roles in Immunization:

The Donor Response

I. INTRODUCTION

A. Purpose

Donor agencies typically face hard decisions when it comes to the allocation of limited resources across their development assistance project portfolios. Classically, the trade-offs have been geographic -- this country or region versus that one; sectoral -- agriculture versus health versus industrial development versus any number of other options; longitudinal -- short-term demonstration projects versus long-term projects; and/or structural -- investment in physical plant versus investment in personnel and skills versus support for the commodity "inputs" of development. Recently, another set of choices has been added to the complexity of the resource allocation decision -- public donor support for public programs versus the use of public funds to encourage private sector roles thereby at a minimum freeing up public funds for activities least likely to attract private resources or, at most, leveraging public resources in the private sector.

Now that matrix of complexities also faces donor agencies on one of the most fundamental of public health issues -- the development, production, delivery and use of vaccines to immunize the children of the developing world. The need to make the most of limited public resources has driven the search for effective, cost-efficient public and private roles to

the heart of public health programs in the developing world.

This paper is intended to examine the nature of immunization program needs; to set out, within each, the problems and priorities as seen by the public and private sectors; to suggest possible public/donor agency responses to expanded private sector cooperation in the interests of broadening immunization availability; and, to evaluate briefly the benefits of and barriers to each possible response.

B. A Balance of Roles

Much of the private sector discussion in other areas of development has emphasized the efficacy of reduced public sector roles in development. It has advocated the overall efficiency and resource-maximization effect of using public resources to leverage expanded private involvement in development, thus reducing the ratio of resources needed from public coffers to accomplish development goals. The argument is usually that, with less of a reliance on public roles, both development resources and development quality would be increased.

That may or may not be the case with immunization programs.

Because overcoming communicable diseases is so basic to increased national welfare and productivity and yet is characterized by such externalities, governments and donor agencies have and will continue to have an entirely necessary role in the initiation, regulation, and (at least in part) delivery of immunization products and services. That role is made all

the more likely given the economics of the vaccine market -- the necessary purchasing power is not present in LDC's to ensure a large, ongoing market, thus few private producers are motivated to service the LDC market without a significant level of ensured public procurement. Indeed, even in the United States, fully 50% of the vaccine produced is purchased by government-financed agencies and programs.

Moreover, the need for public regulation of vaccine production and delivery is generally acknowledged by both government and private sector executives. Assurance of adequate safety testing in product research; adherence to Good Manufacturing Practices in plants; adequate product storage; provider and consumer education on vaccine delivery and use; and, producer protection from spurious tort actions in cases of vaccine-induced medical problems -- all are areas of appropriate existing and future government regulation (albeit increasingly carried out in consultation with the private sector).

Thus, when it comes to immunization programs, some problems may, in fact, require increased public roles -- either in terms of financial resources or in terms of more aggressive public policy -- rather than simply the shift of reliance toward the private sector. What can reasonably be sought, therefore, is a balance of public and private roles; a public stance which, perhaps with increased financing or public policy, utilizes, encourages and/or expands private roles and resources by creating the requisite incentives for long-term private sector commitment to immunization problems and programs.

C. Structure of the Paper

The major analytic divisions of this paper are those of the National Council for International Health developed for its March 18-20 conference on Private Roles in Immunization.

Within each section, the nature of program needs is set out and the major problems specified, both as seen by the public sector and as seen by the private commercial or non-profit sector.

Possible donor responses, linking public and private resources, are then examined. These are analyzed in terms of:

- whether the response would increase or decrease the public financial or policy role in the problem;
- where in the donor agency arsenal of project techniques the response would fall (technical assistance provision, commodity procurement, investment, policy dialogue, and/or demonstration projects);
- the identity of likely private sector partners;
- the nature of the requisite private role (pro bono donation of goods or services, contracting for services with public sponsors, and/or private or cooperative investment in new or expanded business);
- the likely level of host government involvement in the response;
- general barriers to the response, including the differing time frames with which public and private actors would see the opportunity, existing policy constraints, level of funding needed, etc.

II. VACCINE R&D AND MANUFACTURE

A. Nature of the Need

1. Status of Vaccine R&D

To date, vaccine research in the U.S. private sector targeted at developing new vaccine products or delivery systems has not been particularly significant. With the cost of vaccine research and development pegged at between \$50 and \$70 million per entity up to the point of marketing, the benefits of vaccine markets (see below) have seldom outweighed the costs of product development.

There have been and continue to be exceptions, of course. On its own initiative, Merck, Sharpe and Dome (MSD) has developed live attenuated vaccines against measles, mumps and rubella, and non-living vaccines against influenza, meningococcal meningitis, pneumococcal pneumonia and Hepatitis B. With vaccine R&D budgets at a fourth to a third of vaccine sales (the U.S. industry overall spends only about 2.4% of vaccine sales on R&D; overall, Merck itself spends about 10% of sales of all products on R&D) MSD is the U.S. leader in the vaccine research field within the private sector and has ongoing research or development programs targeted at an additional six disease problems.

Nevertheless, even here, the private sector relies most heavily on publicly-supported research for the basic science that makes its product development capability most effective and profitable. Indeed, Jordan and Galasco of NIAID have noted

that "most of the fundamental discoveries and technological developments that offer the prospects for new vaccines have been made ... in universities and other non-profit institutions largely with federal support." As regards LDC-endemic diseases, such support is increasingly augmented by private foundation funds (notably from the Rockefeller Foundation and the Edna McConnell Clark Foundation) and WHO/World Bank/UNDP support via the TDR program.

Given the capital and production costs of the vaccine business (vaccine production requires separate facilities and highly trained technicians), it is likely that public support for the basic research, technical training and clinical testing will continue to be requisite in the future, with industry emphasizing its ability, subject to the resolution of legal and market problems discussed below, to play the major role at the product development stage.

Within that R&D pattern, the driving force behind innovation in new vaccines is the application of recombinant techniques both to basic research and to product development. While this trend may not significantly reduce the costs of vaccine production, it may (1) expand the number of diseases susceptible to the basic research required for vaccine identification and development; (2) increase the number of firms involved in vaccine production by increasing the number of production opportunities; and, (3) increase the purity of vaccine products thereby reducing the likelihood of tort liability.

A closing note on world-wide R&D expenditures for vaccines is appropriate here. Accurate estimates are difficult to obtain; data for comparable years are also elusive. A recent study by Julia Walsh for the Rockefeller Foundation, based on correspondence, personal interviews and public documents, contains the following estimates for major research and development support for human vaccines:

	(\$ million)	
U.S. Government	\$70.09	(FY 1984)
WHO	11.37	(1982-83)
U.S. Pharma industry	49.6	(1982)
U.S. Biotech industry	10.0	(estimate)
Europe Pharma industry	50.0	(estimate)
U.S. Foundations	2.0	(1985 estimate)
Total	\$193.06	

Within the U.S. government expenditures, AID was the third largest vaccine R&D supporter in 1984 with a total expenditure of \$8.5 million, after the Department of Defense (\$45 million) and NIAID (\$9.1 million).

Of course, part of the WHO R&D expenditure is also based on U.S. government support, but the percentage cannot be derived from the WHO R&D budgets.

These figures represent total R&D for all human vaccines. As such, therefore, they do not help very much in comparing AID's tropical diseases role to overall vaccine R&D for tropical diseases vaccines alone. Disease-grouping specific finance data are not available from the private sector, nor for many DOD projects. It is striking, however, that AID's R&D support is nearly as large as that of WHO; four times that of U.S. foundations; and, nearly as large as that of the entire National Institute for Allergy and Infectious Diseases.

2. Status of the Vaccine Market

Despite the potential represented by new R&D techniques and the drive for public/private cooperation in vaccine R&D, four aspects of the vaccine market may make the transition from research to marketable product problematic. These characteristics, even now, severely constrain product availability and profitability.

In 1981, the total value of shipments of vaccine from U.S. producers was \$130.6 million, less than 1% of the value of total drug-plus-vaccine shipments from U.S. pharmaceutical producers. The vast majority of that vaccine was destined for U.S. markets; only 7% of U.S. biologicals were shipped to developing country markets in 1983.

The international market is simply not viewed as profitable by U.S. producers. In 1983, the EPI Revolving Fund purchased DPT and polio vaccine for about \$.02 per dose each and measles vaccine for \$.30 per dose. In the same year, Connaught, a Canadian firm with U.S. operations, raised the price of its DPT vaccine ten-fold, from \$.27 per dose (already 10 times the EPI procurement cost) to \$2.80 per dose. In 1984, Connaught got out of the market altogether because it could not get insurance against product liability. The basic reason for the 1983 price increase was market shrinkage, the costs of insurance, and, importantly, the differing economic structures of innovative (e.g., Connaught) versus non-innovative (e.g., most of the companies from which EPI procures) companies.

A second market factor facing both U.S. and European industry is the flight of producing firms from the market. In the U.S., over half of the vaccine types under production are supplied by a single producer. 29% of the licenses actually issued for production are not used by license holders. The profitability of the market -- given its size, its liability dangers and its international competitors -- is not sufficient to support greater competitiveness. In itself, this may or may not be a problem. Indeed, one can argue that this "flight" is merely a market shake-out, ridding a small market of relatively non-competitive companies. However, the effect of that "flight" on price, security of vaccine supply, and, perhaps most importantly, sites for innovative development of basic research discoveries may be extremely negative.

A third market characteristic -- price -- has already been mentioned. In the U.S., market size, product development costs (capital and ongoing), and liability insurance have pushed product prices up over the last two years. On the other hand, the international market has seen prices stabilize or decline due to price undercutting from cheap sources of supply, notably from East Bloc producers.

Finally, in terms of sales and profitability, the vaccine market is also problematic. Between 1968 and 1981, U.S. vaccine producers saw a 17% drop in real vaccine sales. Again, the

convergence of effective market size and product liability (damages claimed in whooping cough litigation against Lederle Labs in 1983 were 200 times the company's sales of the vaccine) acts so as to reduce private incentives for market involvement. This is as true in Europe as in the U.S.

Thus, the innovative side of the vaccine manufacturing industry upon which the market (and public health) depends for the development capability to turn basic research discoveries into new products to serve increasingly vulnerable diseases (including those endemic to LDCs) is hesitant to commit scarce investment resources to vaccine innovation and production when they could be used to address more profitable research.

This point must be emphasized. While, internationally, the supply of vaccines may not be as constrained as in the U.S., the converging market and litigation forces of today are forcing innovation, R&D-based companies from the market. As a consequence, the product development capability necessary for the realization of new vaccine opportunities is being sacrificed just at a time when scientific tools are bringing those opportunities within reach. Without the market commitment of innovation-based companies, those possibilities have little chance of becoming reality.

3. Special Aspects of LDC Markets

Because research, product development, and trade cross national boundaries, all of the above problems and considerations affect the developing world. In addition, however, LDC's face special disease problems and market characteristics which compound the complexity of immunization programs.

First, of course, is the disease problem. Research and product development targeted specifically at the major parasitic diseases of the developing world is poorly financed, in both the public and private sectors, relative to that focused on more world-wide diseases. As a problem, this situation may be overstated in that, especially in private sector research programs, basic research in one aspect of biochemistry, for example, may have implications for a number of diseases. Few laboratories are organized by disease; they are organized by process. Thus, it can legitimately be said that, as R&D commitment to disease control overall increases, the ultimate consequences for LDC-specific diseases are positive.

Nevertheless, tropical diseases R&D remains a "poor cousin" in terms of the market interests of private companies and, even with the efforts of the Rockefeller Foundation and WHO, in terms of the scientific interests of a wide range of university researchers.

Second, the LDC market for vaccines is not an effective one in terms of purchasing power. Despite the fact that less than 20% of children in the developing world have received

basic vaccinations, the purchasing power of developing countries, even with existing donor procurement programs, is not sufficient to attract major product development and manufacture commitment from the private sector. Increasing this purchasing power within developing countries themselves means increasing the hard currency (not local currency) component of the national health budget, a difficult undertaking at best. Increasing and/or altering the donor portion of vaccine procurement for LDCs would require either alterations in the internal allocation of donor agency resources in favor of immunization programs or the appropriation of new resources for donor immunization efforts.

Finally, LDCs face a "make or buy" decision, with political and industrial development pressure exerted in the direction of establishing more local autonomy in vaccine production. Such production may or may not be a reasonable choice in economic or quality terms; nevertheless the tendency is there. However, as of 1983, only 14 developing nations had significant vaccine production capability. Of these, only two produced measles vaccine; five produced polio vaccine (three of those producing only from imported bulk); 8 produced DPT; and, 10 produced BCG.

B. An Example of Corporate Decision-Making

At this point it might be useful to take an in-depth look at how a private corporation, within the problems and LDC-specific constraints in the vaccine field, assesses the

potential attractiveness of participation in a vaccine venture involving the developing world.

In 1983, David Martin of Genentech set out for the Institute of Medicine of the National Academy of Sciences the process by which Genentech assessed benefits of participation in the development and manufacture of a malaria vaccine. While Genentech is a relatively small, high-technology firm, and therefore not totally representative of the industry, the considerations governing its decision can be generalized to other companies.

In essence, Genentech, a publicly-held company responsible, therefore, to its shareholders, had to compare the malaria vaccine opportunity to its other corporate opportunities, even though it made that comparison in an explicit recognition of the humanitarian aspects of malaria vaccine development.

There were two contextual parameters of the decision. First, Genentech had limited financial discretionary resources for product development. The company already had major commitments to finance product development in a variety of areas, and thus needed to carefully target further opportunities. Second, the malaria vaccine market, even under the best of circumstances, was likely to remain diffuse and dependent on government sponsorship and advertising. (Recall that this is for a malaria vaccine; how much more so for vaccines for other diseases endemic to the developing world!) Furthermore, that market would largely be abroad, with attendant problems of foreign regulation, marketing and distribution.

In this context, there were six sets of considerations.

First, was the project scientifically attractive? Was the vaccine feasible on its merits, given the work to date? The answer to that question was clearly in the affirmative.

Second, therefore, was the market attractive? Clearly not, at least relative to other product opportunities destined for U.S. and European markets. However, could that market problem be overcome by siting the manufacture overseas? If the company pursued this strategy, it would be forced to deal with multiple governments and their unfamiliar regulatory agencies, as well as with costly clinical studies required by the U.S. If the company simply licensed the products manufacture abroad (or were forced by national law to do so), technology flow out of the company and out of the U.S. would result.

In spite of these difficulties, were there overriding reasons for developing the vaccine?

Third, therefore, were there humanitarian arguments that over-shadowed market concerns? Clearly, there was a humanitarian issue. The company concluded, however, that the necessity to displace other potential products (also having humanitarian value) from its development/manufacturing process might jeopardize the future of the company, including the malaria vaccine itself.

Fourth, then, would the malaria vaccine establish with WHO and foreign countries a positive reputation for the company which could be of importance for other Genentech products?

This seemed unlikely, and, in any event, would not be significant enough to override market concerns.

Fifth, would the experience of producing the vaccine push the company up a learning curve, in terms of technology or skill development, which would be unique to vaccine development? Again looking at the market, it was clear that if the company wished to learn the skills unique to vaccine development it should do so with a vaccine for which a market exists in the U.S.

Finally, company image was considered. However, there appeared to be more harm from a possible early product failure than there was gain from the development of such a vaccine.

Without a change in market potential and/or public-sector incentives in terms of strong support for product R&D, management saw no clear rationale for allocating scarce resources to the malaria vaccine opportunity.

C. Problems Needing to Be Addressed

Understandably, the public and private sectors view the R&D and manufacturing situation above with varying degrees of concern. Public sector priorities are often different from those of the private sector. Government/donor priorities are six-fold:

- assuring secure, long-term sources of vaccine supply;
in host government perspectives, preferably from local sources;
- minimizing prices paid for vaccines;
- increasing the number of manufacturers, thereby introducing competition into the market and lowering prices;

- expanding basic research in and product development for diseases of the developing world;
- expanding research in improved vaccine delivery technologies;
- developing a smoother, more assured transition between basic research in the university and non-profit sectors and the product development/marketing capabilities and commitments of the private commercial sector.

While the non-commercial private sector (i.e., universities and not-for-profit organizations) tend to share these public priorities, the private commercial sector has a six-fold but quite different set of priority problems when it views the vaccine research situation and the vaccine market:

- assuring an adequate rate of return from vaccine research and manufacturing investments;
- assuring an adequate price in the market;
- increasing market size and ensuring its long-term reliability;
- resolving liability problems*;
- resolving proprietary issues regarding corporate products;
- overall, making vaccine investments more competitive relative to the variety of R&D alternatives in the company.

*For example, in the Swine Flu program in the U.S. in a three-month period there were 3700 claims filed against companies alleging Guillain-Barre Syndrome reactions to vaccination with total damages claimed over \$3.3 billion.

D. Possible Donor Responses

In the areas of R&D and manufacturing, there are a variety of ways that donor agencies can work through and with the private sector in expanding vaccine research and product availability. As noted in the response matrix on the following page, however, most will require an increase rather than a decrease in the financial and policy commitments of the government and donor agencies involved.

Page 18 contains a comparison in broad terms of the possible donor agency responses to R&D/manufacturing problems and opportunities. The paragraphs below describe each response in a bit more detail.

1. Research and Development Responses

A. Research Funding

Problem: Inadequate levels of funding available for basic tropical diseases and immunization research.

Response: Donor agencies could dramatically increase the level of their support for basic research in tropical diseases and especially in vaccines for such diseases.

Such a response would involve an increased public role in research, both in terms of financial levels and in terms of the general project regulation which accompanies such public funding. Within many agencies, it might also involve fairly major programmatic reorientation, since most donor agencies now pursue health service delivery projects (with immunization components) rather than provide major support for basic scientific research.

Private partners in the research ventures would be in all three "private sector" categories: universities, non-profits, and

Donor Response: P&D and Manufacture

Area	Response	Direction of Public Role	Donor Method	Private Partners	Private Role	Host Govt Role	Barriers
R&D	- increase financial support for basic research	↑	operating grants	-universities -non-profits -indus. labs	contract	-	- availability of financing - alteration in program priorities
	- longer-term, more reliable research support	-	policy change	-	-	-	- scope of regulatory change
	- support for delivery technology research	↑	operating grants	-universities -non-profits -industrial labs	contract	-	- availability of financing - programmatic change
	- RFP system change	↑	policy change	-indus. labs	contract	-	- scope of regulatory change
	- apply Orphan Drug Act	-	policy change	-indus. labs	investment	-	- scope of regulatory change
Manufacture	- finance or be broker between univ & indus research	↑	operating grant	-universities -non-profits -indus labs	contract investment	-	- see DVDC discussion
	- change market struc. via PL480 analogy	↑	procurement	-MNC industry	contract investment	very active	- legislation required -appropriations required
	- LDC local manuf. or joint ventures	↑	feasibility/ investment	-local industry -MNC industry	investment	very active	- LDC capabilities - LDC policy - MNC skepticism - donor agency capabilities

industrial laboratories. The private role would be a contractual one with public funding agencies, although in the commercial sector some investment in facilities and personnel would be implied. To the extent that such investment was necessary, private companies would need to view the contracts as substantial in size and reliable in duration (see below).

There are several barriers to pursuing this donor response, not the least of which is the availability of funds. Within most agencies, funds would need to be re-programmed out of other areas of activity, or increased funds would need to be appropriated from legislative sources (e.g., for AID) or from sponsoring governments (e.g., for the World Bank).

In addition, increased research, assuming it is targeted at ultimately developing vaccine products, would run into industry concerns over proprietary rights to discoveries and subsequent support for clinical trials of any potential product. These concerns would need to be addressed if research advances were to give rise to marketable products.

B. Research Funding Mechanisms

Problem: Public sector research support is often short-term and episodic.

Response: Donor agencies could attempt to provide, if not increased levels of research support, at least a more reliable, longer-term form of support.

By assuring researchers of multi-year support at firm funding levels not subject to periodic review and change, both commercial and non-commercial research institutions might feel

more confident about the investments needed for and the opportunity costs involved in commitments to tropical diseases research.

Again, this would involve contract relations with all aspects of the private research community, but would not necessarily involve greater public roles.

For many agencies, the biggest barrier to this response is a regulatory one. Government regulations for research contracting and oversight, as well as the method of determining year-to-year research contract budgets, would need to be altered. Change in the structures and processes of public agencies is always slow and difficult; thus, the incentives for agencies to initiate such change would need to be quite significant.

C. Technological Research

Problem: Little public or private research is focused on improved technology for equipment and supplies needed for immunization programs.

Response: Donor agencies could expand their support for research into vaccine delivery technologies, seeking ways, for example, to reduce the need for cold chains at the delivery end of the immunization process, or to reduce the need for multiple vaccinations. An objective would be to develop products attractive for commercial production.

Since relatively little of this type of research is now supported, this response would increase public roles in the research process and, for many agencies, would involve both a programmatic shift in research budgets and a need for subsequent support of demonstration projects to test the utility of new technologies in the field.

Again, all private constituencies are potential partners, although the commercial sector probably only at the point of product development. At early stages, contract relationships would be the method of cooperation, but subsequent product-development stages would involve investment commitments from the commercial sector.

Barriers to such research involvement from the donor agency point of view are both the need for increased or re-allocated funding and the need to introduce new program priorities into the donor agency health sector portfolio.

From the private sector's point of view, many of the new or improved products needed for immunization programs in developing countries are not of interest to commercial companies. Likely profit margins do not justify R&D costs. Thus, significant effort would need to be placed in convincing commercial companies of the depth and reliability of markets for the new technology if subsequent product development investments are to be expected.

One approach to matching publicly-funded technology research with corporate product development might be to replicate the BIRD Foundation of Israel which has successfully developed products through public "venture capital" funding, turning those products over to the commercial sector for production and marketing. Discussion of the U.S. Drug and Vaccine Development Corporation (below) will elaborate on this point.

D. Efficiency of Research Cooperation

Problem: In the United States, it has been the experience of public agencies that industry hesitates to cooperate with government research programs in some measure because of the perception of the amount of "red tape" involved in obtaining research funding. In some cases, commercial manufacturers have expressed interest in projects, only to decline to submit proposals for support when they receive the public Request for Proposal (RFP) detailing the large amount of information required if their proposal is to be considered.

Response: To the extent that this research proposal/approval process can be made more efficient, greater collaboration with the commercial private sector may be possible.

The problem with this response, of course, is that regulatory change would be required. Moreover, that change would involve aspects of government contracting that apply not only to donor agencies, but often also throughout the government. Donor agencies have no special leverage within governments to accomplish system-wide reforms in such areas as contracting procedures or procurement, and so might hesitate to spearhead such efforts.

E. Orphan Drug Act

In the United States, a law known as the "Orphan Drug Act" came into being in January of 1983 to provide incentives for the development of drugs which address "a disease or condition that is rare in the U.S.". Research financing, exclusive marketing, and tax credits are some of the incentives provided to industry by the bill. Initially, \$500,000 was made available for the program; 13 projects were funded in fiscal 1983.

Problem: However, according to the regulations published subsequent to the law, the Act will not cover diseases which, though rare in the U.S. itself, are not rare world-wide. That decision effectively eliminates product research and development for such diseases as malaria and schistosomiasis.

Response: One U.S. donor response might be to attempt to change Act regulations to allow the inclusion of diseases endemic in the developing world but rare in the U.S.

The primary private partners in subsequent research are likely to be in the commercial sector, with a need for significant investment on their part for research and product development.

Although the incentives provided by the Act might induce industrial laboratories to be interested in tropical diseases investments, the markets are probably not sufficiently reliable and large (of their own accord) to convince industry to join with donor agencies in an aggressive attempt to change current regulations. On their own, donor agencies will face a number of barriers to achieving changes in the regulations, since the decision to rule tropical diseases out of consideration was made after considerable policy reflection within the FDA and HHS.

2. Manufacturing

A. Transition from University Research to Industry Product

Problem: Ensuring that vaccine research supported by public funds reaches the market requires a smoother transition between universities and corporations. It also requires that both the public interests of government sponsors and researchers and the market and income interests of corporations be addressed with equal care.

Response: Donor agencies could serve as, or finance another institution to be, a broker between university basic research and industrial development capability.

Such a broker institution could hold discovery patents in the public interest, license manufacturers for product development and marketing, provide extra funds for the additional testing of the discovery on which industrial interest might be contingent, and, ultimately and perhaps most importantly, redistribute royalties and reserve part of those royalties to establish a constant fund to be allocated solely for further research on tropical diseases.

Such an initiative would require a major commitment from donors, in terms of financing and in terms of program commitment to tropical diseases drug and vaccine research. It would significantly increase the public role in such research and in product development, although it would also expand private commercial and non-commercial roles in tropical diseases drug and vaccine R&D and manufacture

Experience has shown that there are a number of significant barriers to the successful implementation of such a broker role.

In 1980, with support from the Rockefeller Foundation, the Drug and Vaccine Corporation was incorporated as a non-profit organization for just such a purpose. A copy of the DVDC prospectus is attached.

The DVDC is currently operational, and has begun taking in some university research products in anticipation of industrial

development licensing. The problems involved in the startup of the DVDC have been complex, and are worth an analytic paper in and of themselves. In short, they fall into three categories:

- the timing and level of capitalization needed for the DVDC to achieve its goals. Without adequate staff, and especially without adequate capital to fund necessary pre-licensing trials, attracting corporate interest in laboratory discoveries is difficult.
- the need for universities to place patent rights to discoveries in the DVDC. Universities have been hesitant to to agree to give up potential sources of revenue in this way, hoping that they themselves can market discoveries directly to industry and thus retain all royalties income. It has proved difficult to argue that a) that income is not cost free and b) the DVDC concept also addresses the need to trap part of that income solely for further research grants. Unless research fundors and researchers -- public or foundation -- exert leverage, based on their research support, to encourage management to adopt a longer-term view of the royalties-development-income-research process, there is little that can be done to force university agreements such as those used by the DVDC.
- hesitancy within the industry that, if companies agree to participate in the DVDC and alternative sources of

capitalization are not found, companies would be relied upon as capitalization sources. This is compounded by corporate doubt as to the validity of claims of near-term "discoveries" within university laboratories, as well as continued concern over the size and depth of the ultimate market for any product (see discussion of the PL-430 analogy option below).

As regards the vaccine discussion in this paper, the broker-institution response also faces a further barrier. The DVDC was thought to be ultimately self-financing because it encompassed both drug and vaccine products. Thus, there was increased likelihood that a "cash-cow" discovery would be made (probably in the drug field, rather than in vaccines) that would produce significant royalties and serve as the financial base of the operation. If the concept were to be limited to vaccines, it is doubtful whether ultimate self-financing would ensue.

On the other hand, the DVDC organization is currently performing the bridge function outlined above -- albeit on a limited scale -- and, with adequate resources, could be efficiently expanded to address more large-scale university-to-industry transition needs.

B. Vaccine Market Structure

Problem: Market structure -- size and reliability -- as regards vaccines, and particularly vaccines for the developing world, remains the chief disincentive to expanded commercial roles in vaccine R&D and manufacture.

This market problem is all the more serious since it is denominated in foreign exchange not in local currency. Therefore, local solutions to the problem are long-term and complex, necessarily involving, as they do, not a reallocation of existing health budget line-items, but, rather, an expansion of national exports and then an allocation of the increased foreign exchange available to vaccine purchases.

On the donor side, the problem is compounded in development programs by a donor agency hesitancy to increase commodity support for vaccines (and drugs) because such strategies are simply support for recurrent costs, and do not involve development of host government health systems to a point of self-sufficiency.

Response: Again in 1980 and with Rockefeller Foundation support, a strategy was investigated and pursued which would respond both to the market-depth problem in the eyes of the private sector (i.e., increased procurement levels) and the recurrent cost support problem in the eyes of the donor agencies. A copy of the resultant PL-180 analogy paper is attached. In brief, the strategy described attempts to overcome the recurrent costs problem by linking significantly expanded hard currency pharmaceuticals (including vaccines) procurement by donor agencies to increases in local currency host government investments in the health sector.

In short, dollar denominated loans for pharmaceuticals procurement are foregiven (i.e., converted to grants) as additional local currency is made available for investments in the primary health care system or (preferably) in the pharmaceuticals management and logistics systems of recipient countries. Additionally, the strategy contains an option for pharmaceuticals procurement and distribution via private voluntary organizations.

Recognizing that it is ministries of finance not of health that control increases in resource allocation to health budgets, the strategy not only expands hard-currency procurement, but also gives ministries of health leverage (hard-currency loan reduction) over ministries of finance (increasingly concerned about such things) to argue the merits of health sector budget increases.

The strategy is analogous to, but expands upon, the agricultural loan program of the United States, administered under the PL-480 Food-for-Peace Program.

Implementing such a strategy would certainly increase the role of the public donor agencies, although it would also have the potential for significantly expanding private commercial and non-profit roles in the provision of vaccines to the developing world. By altering the structure of the market, it also provides an incentive for increased private commercial investment in vaccine R&D for developing world diseases.

The barrier to such a donor response is the degree to which it would entail new legislation and increased appropriations. The strategy reached fairly high levels of approval in the Carter Administration prior to the election of 1980. Thus, considerable support for the concept at high U.S. political levels has been demonstrated in the past and might prove possible now, given current concerns over developing world conditions and foreign policy.

It should be noted that there are a variety of other options for responding to the market-size problem as faced by manufacturers. Among these are:

- granting of exclusive licenses to individual manufacturers for the supply of specific vaccines for all donor programs;
- granting long-term contracts for vaccine supply to manufacturers;
- increasing the price paid to manufacturers for vaccines, in the hopes that the increased resources will find their way to R&D expansion and/or will entice more manufacturers into the market.

While each of these options clearly has its merits and problems, from the donors' perspective none deals with the key problem of transforming vaccine procurement into something other than a pure financing of recurrent health program costs. While the PL-480 analogy is a more complex option, and probably requires a greater level of bureaucratic gymnastics for its implementation, it does have potential as a resource-leverage tool and thus addresses, to some extent, the recurrent cost barrier to expanded donor vaccine financing.

C. Local Manufacture

Problem: As noted earlier, relatively little vaccine production occurs within the developing world, yet ensuring local sources of supply is often a host government priority.

Response: An additional donor response to manufacturing problems would be to support feasibility studies for the development and/or the expansion of local vaccine manufacturing capabilities. For some agencies, actual participation in joint venture investments might also be possible.

Again, such endeavors would imply an increased public role, at least at initial phases of investment consideration and structuring, but they would also have the potential for leveraging significant and long-term levels of private sector commitment to vaccine manufacture.

Whether or not such efforts would be either economically or financially rational in terms of the use of public agency finances and scarce local investment capital, however, can only be judged on a case-by-case basis. It can be expected that, where financially and economically feasible, expanded local production would not encounter market-size disincentives, since small local producers are more likely to be attracted to smaller LDC markets than are the major MNC producers. Indeed, it may prove financially useful to consider "local manufacture" as a two-step industrial problem, with major production facilities at the regional level (perhaps in joint venture with multinational producers), reserving local investment for final stages of filling and packaging.

The fact remains, however, that economies of scale operate

in vaccine manufacture, with large-scale, centralized manufacturing facilities being more cost effective overall than smaller operations. For example, industry executives estimate that an effective population of 40 million is required for a multinational corporation to calculate a positive cost/benefit in investing in vaccine manufacturing. Less than that size reduces the attractiveness of the investment. Thus, the question of economies of scale limits local production opportunities, irrespective of the other barriers donors might face in becoming involved in such projects.

And those other barriers are not insignificant. At a minimum, they are six-fold.

First, donors and investors might face local policy opposition from host governments which might oppose private investment in such a key public health area as vaccines.

Second, even given market size, donors would face limited investment sites, since many developing countries would lack adequate levels of trained personnel or industrial infrastructure to support such local industries.

Third, quality assurance considerations are complex in vaccine manufacture, even under the best of circumstances. Skilled personnel and adequate technology are scarce in the developing world. Thus, quality assurance may be problematic. Furthermore, unless the product of local manufacture was purchased by donor agencies, WHO standards could not be assured. Enforcement would

be left virtually entirely to host governments, with possible problems in assuring that safe and effective products are reaching the local population.

Fourth, development agencies normally have extremely long lead times between the identification of possible projects and the decision to support those projects. Eighteen-month or two-year decision processes mean that, if private investors are to join with public fundors, public donors need to be sensitive to what will almost surely be private sector frustration with the pace of the "cooperative" venture. With a few exceptions, donor agencies face considerable difficulty in reducing these project decision timeframes since these are usually tied both to bureaucratic procedures, legislative requirements, and budget cycles.

Fifth, such efforts to support local, private manufacture of vaccines might incur opposition from donor-country multinational manufacturers already serving developing country markets and/or skepticism from any multinational manufacturers which donor agencies might approach for participation in such investments.

On the other hand, the international pharmaceutical industry has demonstrated an ongoing willingness to aid in the development of the pharmaceutical production capabilities of the developing world. For example, the International Federation

of Pharmaceutical Manufacturers Associations (IFPM.) initiated a training program in 1980 for LDC manufacturing personnel to receive on-the-job training in multinational pharmaceutical companies in manufacturing and quality control skills. Between 1980 and 1984, twenty-nine LDC personnel completed such training programs; 8 are in the process of training; and 10 are awaiting company offers of posts.

While this effort is pro bono in nature and not an investment commitment of the pharmaceutical industry, it certainly reflects an active concern with the quality of local manufacture among those companies.

Finally, of course, for some agencies the pursuit of such efforts is itself problematic, since many public donor agencies are not structured, either in terms of policy or in terms of personnel skills, to assess investments in health product industries. Overcoming that barrier would require both policy change and personnel skill development, both likely to be long-term alterations within most agencies.

III. MANAGEMENT AND DISTRIBUTION OF VACCINES

A. Nature of the Need

1. Status of Management Needs

Even if the research, manufacturing and market problems outlined above could be resolved, the ability of developing country public health systems to absorb and manage greater quantities of vaccines are limited.

Funding aside, determining what to buy, how much, from whom, when, in what rotation, and for how long requires management system "software" of adequate health and product information as well as the "hardware" of trained management personnel. Typically, developing countries have neither prerequisite in sufficient availability to support existing immunization programs, let alone expanded, nation-wide efforts.

Moreover, assuring that product quality is maintained after supplies are procured and received -- irrespective of whether systems are in place for distribution of those supplies -- also requires trained personnel and adequate facilities (public or private) which are in short supply in developing countries.

Finally, managing the money made available for immunization programs is an essential skill if limited resources are to be expended with as much impact as possible, and if public authorities charged with overall decisions on the allocation of

scarce LDC investment capital and operating resources are to allocate even greater amounts to immunization programs. This local financial skill question is not insignificant; fully 80% of the costs of an immunization program are local in nature and are normally covered from an LDC's own resources. Better management of, or the initiation of private alternatives to, the 56% of vaccine budgets normally consumed by salary and operating costs, for example, would free up resources for expanded training and for capital investments, as well as possibly convincing financial authorities that careful financial management of such programs deserves resource rewards in the form of increased budget support.

2. Status of Distribution Needs

There are four major aspects to the distribution personnel and systems required for immunization programs:

- (1) the establishment of an adequate and widespread cold chain system for storage of vaccines;
- (2) the maintenance and repair of the equipment and facilities in that chain;
- (3) the availability of transport for both personnel and materials between shipping, storage, and delivery points;
- (4) the maintenance and repair of that transport.

In the public sector of LDC's, all four aspects are usually problematic. Moreover, even where adequate public systems have been established, capital and recurrent costs of their use and maintenance are significant. In one AID-supported

immunization program in Kenya, transport costs consumed fully a third of the program operating budget. In general, amortized capital costs for cold chain and transport total nearly 20% of all operating costs for public vaccination programs.

Fortunately, the distribution problems faced by public immunization programs could be eased by greater cooperation with the local, indigenous private sector, probably at less cost than the establishment and maintenance of purely public systems.

Widespread warehousing and distribution systems for consumer goods; widespread cooperative systems in rural areas; commercial vehicle repair shops -- all are possible for-profit contractors available to public and donor agencies to lower costs and expand the distribution of vaccines for immunization programs.

B. Problems Needing to Be Addressed

Again, the nature of and priority among the problems facing vaccine management and distribution systems differs as between public and private organizations. Government and donor agency officers have five priority concerns:

- development and implementation of systems for the selection of appropriate vaccines and for their procurement;
- development of managerial capabilities in the public sector;

- obtaining investment capital for the development of cold chain facilities and equipment;
- financing of recurrent costs for immunization programs;
- development of maintenance capabilities for both equipment and transport used in public programs.

Private sector representatives have differing priorities, depending on whether they are viewing the problems from local industries, international companies, or non-profit agencies. In general, it can be said that both local industries and non-profit agencies are primarily interested in those problems whose resolution involves public or donor contracting to maximize the use of existing local (for-profit or non-profit) resources and systems.

International companies, from their own perspective and given their own expertise, have three sets of priorities:

- minimizing demand-side regulation in the pursuit of those solutions (e.g., minimizing the use of formularies for procurement);
- assuring public sector regulatory consistency in the development of licensing and import laws*;
- assuring that public or private distribution systems protect product quality and prevent product pilfering and subsequent counterfeiting.

*A recent set of interviews with 100 top U.S. MNC executives indicates that the decision to become involved in LDC economies turns not on the severity of their regulations but on the consistency of their enforcement.

C. Possible Donor Responses

The summary matrix of possible donor responses to increased private participation in problems of vaccine program management and product distribution is contained on Page 39. Overall, what is striking about these possible responses, compared to those for R&D/Manufacturing issues, is:

- (1) their greater degree of non-profit presence in the private partner category;
- (2) the greater degree of local industry involvement possible in resolving distribution problems;
- (3) greater reliance necessary on pro bono relationships with the commercial sector, rather than on contract or investment relationships. In turn, this implies that public/donor agencies will need to develop more aggressive incentives for private involvement than would be the case if opportunities were more market-based ;
- (4) the greater degree of host government involvement required in any donor agency response.

1. Management

A. Management Skills and Systems

Problem: The lack of adequate public sector management skills for vaccine distribution systems is one of the most important constraints to the success of immunization programs.

Response: Donor agencies could expand their training programs available for public managers of vaccine procurement and distribution. This would simply be an expansion of or a variation on the theme of existing training programs offered by most donor agencies, and could be carried out through classic technical assistance channels available to agencies.

Donor Response: Management and Distribution

Area	Response	Direction of Public Role	Donor Method	Private Partners	Private Role	Host Govt Role	Barriers
Management	- training of vaccine mgrs	—	-demo projs -tech asst	-universities -non-profits -MNC industry	contract pro bono	active	- industry incentives
	- improved info. systems	—	- demo projs -tech asst	-MNC industry	pro bono contract	active	- industry incentives
	- development of private QC capability	↓	- policy dialogue - feasibility/investment	-local indus -MNC indus	investment	very active	- current local policy - donor agency skills and policy
	- financial mgmt training	—	-tech asst	-universities -non-profits -MNC industry	contract pro bono	very active	- public sector priorities
	- equipment maint and repair	↓	-demo projs -tech asst -feasibility/investment	local indus.	contract investment	very active	- ROR for industry - current local policy
Distribution	- private warehousing	↓	-demo projs -feasibility/investment	-local indus -non-profits	investment contract	very active	- ROR for industry - current local policy
	- logistics training	—	-tech asst	-non-profits -local indus	contract	active	- industry incentives
	- PL 480 analogy to leverage investment in p.h. system	↑	-procurement	-MNC industry -local indus	contract investment	very active	- legislation required - appropriations required
	- distribution coordin. with existing private networks	↓	-demo projs -policy dialogue -tech asst	-non-profits -local indus	contract investment	very active	- current local policy

An active host government role would be needed in planning and carrying out the training, since it would be public personnel being trained.

On the other hand, despite the simplicity of their implementation, such training programs are not likely to leverage much in the way of private resources. Contracts with non-profits or consulting groups to carry out the training would increase private roles, but industrial involvement would be on a pro bono basis.

This latter donation of effort might not be insignificant. In the United States, many multinational corporations have policies and procedures in place which require senior executives to second part of their time to community organizations for service work. At this point, much of that donation of expertise, materials and training resources remains allocated to domestic programs within U.S. cities. However, there is a clear opportunity for immunization program authorities to access this reservoir of management/distribution expertise, especially from companies operating within countries of international immunization concern.

B. Information Systems

Problem: Both disease and health status data tracking and the management of vaccine procurement and inventories require extensive and often sophisticated information systems. Such systems are generally lacking in developing country immunization programs.

Response: Using private sector technology and expertise, donor agencies could initiate information system improvements in public health agencies in the developing world.

Again, the method by which donor agencies would initiate the projects would be consistent with existing programs -- either via technical assistance, demonstration project, or procurement channels.

To the extent that such projects purchased technology and expertise from the international communication and computer industries, there would be clear industry incentives for participation. To the extent that such projects are conceived as outlets for donations of industry equipment or expertise, industry might only be interested in participation in those countries with potentially large markets for purchase of information system products. In those cases, pro bono participation might have market spillover effects. However, that would limit donor projects to the more affluent countries of the developing world.

Finally, if the response involves simply procurement of equipment and expertise, the response is not particularly "private" in nature.

C. Quality Assurance

Problem: Quality assurance is an issue of importance both to public/donor agencies and to private vaccine producers. Adverse reactions due to spoiled products and/or the adverse public outcry which would accompany such reactions is in the interests of neither public nor private participants.

On the other hand, quality assurance is generally viewed as a public agency responsibility in the developing world, with the private role being one of technical assistance donations for training and systems establishment.

Response: One alternative to this problem would be for donor agencies to engage in policy dialogues with host governments to explore the possibility of opening quality assurance to private investment.

For example, a donor agency could suggest to a host government that some combination of private and public finance could be offered to the local private sector to establish quality control laboratories with standards set by the public ministry. Alternatively, the host government could build, with donor concessional funding, quality control facilities and lease these to the private sector, so that operation and costs were absorbed by the private sector (lessees and private companies using the facilities), but with close public ministry supervision of quality.

Donor money would be used as a catalyst for the private investment process, either to finance the feasibility work or as a partner in the loan. In the former case, the assistance could be structured as a loan, repayable with interest if the investment is actually made. The donor could also serve as a technical assistance bridge by providing experts from its home drug regulatory authority to aid in system design.

The two largest barriers to such an approach to quality control problems are (1) the precedents and expertise in donor agencies which have long dealt with quality problems from a purely public viewpoint; and (2) existing host government policy.

D. Financial Management

Problem: The limited local resources available for immunization programs require careful management if they are to be stretched to meet ever expanding needs, and if their effectiveness is to attract greater levels of private and public sector support.

Response: Within structures similar to those described in Response A above, donor agencies could place more emphasis on the development of financial management skills in public ministries charged with immunization program management.

Again, this would involve contract relationships with the non-commercial private sector (probably universities), but most likely only pro bono relationships with the commercial sector.

The major barrier to such projects would be a requisite change in public policy attitudes which have not historically viewed financial management skills as a priority in public health ministries or programs.

E. Maintenance and Repair

Problem: Keeping the transport and equipment used in immunization programs functioning, and repairing it when it breaks down, is crucial to adequate, consistent vaccine distribution.

Response: Rather than replicating in the public sector maintenance and repair capabilities already present in the private commercial sector, public immunization authorities could make greater use of contracting mechanisms to utilize private M&R resources.

For donor agencies, this might also involve provision of feasibility financing for new local or joint venture businesses to serve these needs.

Given the reliance to date on public systems and the development of public sector capabilities, host governments would need to be very active in the development of such projects. Existing

government policy would thus be a barrier -- possibly a major one -- to such a donor response.

2. Distribution

A. Commercial Logistics Networks

Problem: The availability and condition of facilities and transport in the public sector to move vaccines to outlying areas is a serious problem in most developing countries. As a result, much vaccine does not reach actual delivery systems in a timely or safe fashion, thereby compromising the effectiveness of local immunization efforts.

Response: Within immunization projects, donor agencies could begin to make greater use of existing private commercial warehousing and transport capabilities.

This would involve a decrease in public roles and an increase in commercial contracting. Realistically, however, there are likely to be few commercially attractive opportunities as programs move from the provincial level to outlying areas. Thus, reliance on commercial systems is probably feasible for distribution systems between points of import and province capitals, but not beyond.

Again, host government involvement would have to be significant since such strategies cut across the traditional methods of public program warehousing and transport.

A second barrier to this strategy is information. Few countries have conducted comprehensive inventories of the private commercial resources actually available into which public immunization programs might link. Without some sense of what is available and how it might relate to local problems, expanded cooperation is difficult.

B. Public Sector Skills

Problem: Poorly skilled public sector distribution managers are often greater barriers to effective vaccine distribution than is the lack of distribution facilities.

Response: To the extent that expanded use of private logistics networks is not possible due to government policies, donor agencies could place greater emphasis on training public sector personnel in logistics skills.

Private sector partners could then be non-profit or consulting organizations which would provide the training on a contract basis and/or commercial companies which would donate materials or expertise for such training programs.

Such training would be consistent with the way in which donor agencies and governments have approached public program bottlenecks in the past, but would not be particularly "private" in nature.

C. Investment in Distribution

Problem: Public distribution infrastructure is inadequate and often decades old.

Response: See PL-480 Analogy discussion on Page 27+ as well as strategy paper attached.

D. Use of Non-Profit Systems

Problem: In many countries, public health infrastructure is totally lacking in remote outlying areas, thus limiting the coverage of immunization programs.

Response: Rather than (or in addition to) using purely public or commercial distribution networks for vaccines donor agency programs could expand their use of existing private non-profit networks.

Religious organizations, private voluntary organizations, cooperatives, all have significant distribution networks -- often the only health networks in remote areas -- which could be more effectively plugged into immunization programs.

Doing so involves neither major changes in the way donor agencies design programs nor major changes in government policy. Thus, the major barrier to such strategies seems to be simple system inertia, a barrier that can easily be broken by innovative, creative donor agency professionals working together with host government program officers.

IV. DELIVERY AND USE OF VACCINES

A. Nature of the Need

1. State of Vaccine Access

According to UNICEF, at present 5 million children per year die from measles, diphtheria, pertussis, tetanus, tuberculosis or polio -- diseases which are preventable via immunization. Another 5 million per year are disabled by these diseases, which are also a major cause of childhood malnutrition. Yet, in 1984, less than 20% of LDC children were protected against all or most of these infections by immunization. Indeed, for some diseases and in some regions, the percentage of protected children is far less than the average. In the Eastern Mediterranean region, for example, only 9% of the children have received BCG against tuberculosis and only 15% have been vaccinated against measles. In Southeast Asia,

only 1% of the children have received measles vaccine.

For the most part, public immunization programs in the past have focused on the delivery of immunization services via public health outlets and programs: public health huts, clinics, and hospitals; vertical government disease control programs; specialized programs for maternal and child health in government clinics. Long neglected have been private outlets, from private hospitals and clinics to corporate or union health services to individual private practitioners to pharmacies to the myriad of non-profit or religious organizations (local or international) operating health and social services in the developing world.

The availability of commercial outlets for vaccination delivery is not limited to countries at the higher ends of the development scale. For example, a mini-survey in Khartoum found 114 commercial health care service operations (private hospitals, clinics, laboratories, pharmacies, dentists) in 7 blocks of commercial outlets and 236 such operations in 18 blocks of retail services.

The child-care and education system, public and private, provides another possibility for vaccination service delivery. Indeed, in this case the opportunity exists for making vaccination mandatory for educational enrollment.

The access problem is not only one of physical outlet availability; it is also one of regulatory scope, personnel

training, and the link between the two.

In most LDC's, public health regulations seriously limit the types of non-physician health workers permitted to give vaccinations. Pharmacists, nurses, paramedical personnel, traditional practitioners -- all of whom are the primary sources of initial contact between health systems and the public -- are severely limited in their immunization roles. In part, this situation is a result of physician-dominated policy mechanisms in the health sector; in part, it is a product of a very real concern over the lack of adequate training of alternative vaccination providers, both technical training and training in community education regarding side-effects and reactions.

Nevertheless, in an environment of less than 20% vaccination coverage, the problem of expanding outlets becomes so serious as to render these concerns negotiable at the point of immunization policy and program design.

2. Vaccination Program Use

Establishing adequately widespread outlet sites for immunization is insufficient if the target population does not take advantage of the available programs. Available data suggest that use is indeed a key problem in immunization programs. In 81 immunization campaigns surveyed by WHO between 1979 and 1983, the average dropout rate between the first and third shots of DPT was 40%. The rate was as high as 78% in the

Yemen Arab Republic, 68% in Mozambique, 60% in Sierra Leone, and even 60% in Ecuador.

The problem of public perception of the need for consistent use is particularly problematic for vaccines -- such as DPT -- where multiple injections are necessary. But, demand is also a problem for even single-shot vaccinations. Lack of information or understanding among mothers regarding the need for immunization; lack of community information on the sites and times for vaccination availability; or even the pure energy required to obtain these vaccinations for older children (too heavy for mothers to carry to vaccination sites, too small to walk the distance themselves), all act to reduce program use.

B. Problems Needing to Be Addressed

From the public sector perspective, there are four priority areas in the drive to diversify vaccination delivery points and to increase use:

- heightened public and policy-maker awareness of the value of vaccination programs;
- increased national political commitment to such programs;
- expansion in the outlet network;
- increased public demand for vaccination.

In viewing partnership opportunities with public sector programs, the concerns and priorities of the private sector are somewhat different and encompass five areas:

- regulatory change to permit expansion of outlet networks;
- availability of financing for contracts to permit private delivery of vaccinations and/or policy change to allow fee-for-service payments for such vaccinations;
- availability of provider training;
- protection from liability for side-effects;
- private participation at the initial stages of planning for private involvement in the expansion of immunization networks

C. Possible Donor Responses

Page 51 contains the donor response matrix describing possible project areas for private sector involvement in immunization delivery and use. In general, these responses (1) involve greater roles for non-profit organizations than for the commercial sector; (2) require very active host government participation; and, (3) are highly consistent with donor programs and modus operandi, and thus face few barriers to implementation, except for questions of donor funding levels.

Donor Response: Delivery and Use

Area	Response	Direction of Public Role	Donor Method	Private Partners	Private Pole	Host Govt Role	Barriers
Delivery	- use of alternate private outlets	↓	policy dialogue demo projs	*	contract investment	active	- local government policy re fees
	- require immuniz. reimbursement in ins/HMO schemes supported	↓	demo projs	local commercial	contract	active	- few
	- union clauses specifying free immunization	↓	policy dialogue tech asst	local industry MNC industry unions	contract pro bono	active	- industry cooperation/incentives - donor agency contacts
Use	- fund, with prof assns, "state of nation" conferences in host countries	↑	operating grants	*	contract pro bono	very active	- funding availability
	- fund host country equiv of "White House Conf" on immuniz to develop broad constituency	↑	operating grants	*	pro bono	very active	- funding availability
	- media/public relations campaigns	-	demo projs tech asst	local firms MNC firms	contract pro bono	active	- few

* including, traditional practitioners, private medical and paramedical personnel and facilities, women's organizations, religious organizations, PVO's, cooperatives, credit unions, social security organizations, labor, MNC's, professional organizations, local industry

1. Immunization Delivery

A. Private Outlets

Problem: Public infrastructure for the delivery of immunization services is limited both in terms of its geographic presence and in terms of populations reached.

Response: Donor agency project teams could place more emphasis on the use of private outlets as alternatives to or complements for public sites.

Such private partners include traditional practitioners, private paramedical personnel, women's organizations, private physicians/hospitals/clinics, religious organizations, PVOs, cooperatives, credit unions, social security organizations, labor unions, professional medical organizations, and private manufacturing facilities whether local or multinational.

Private sector relationships would be either contract (in which case the government or agency would pay the vaccination provider); investment (in which case the private provider would be allowed to charge for the service); or pro bono (in which case the provider -- e.g., multinational companies with operating facilities -- would provide vaccinations to workers' children free-of-charge). The opportunities and combinations of roles are myriad. The major barrier to investigating such program changes is existing government policy which places emphasis on public delivery and indeed, in some cases, actively discourages cost recovery through such arrangements as fee-for-service mechanisms.

B. Links to Insurance Schemes

Problem: Few immunization programs take advantage of existing health service reimbursement mechanisms for expanding vaccination delivery sites.

Response: Another possibility for expanding vaccination outlets could be to require immunization reimbursement in any insurance or HMO schemes supported in whole or in part by donor agency or government funds.

Again, active host government involvement in this response would be necessary, but there would be few policy or financial barriers to its implementation.

C. Organized Labor

Problem: As developing countries expand their industrial bases, the employed population forms something of an as yet untapped "captive audience" for many health programs.

Response: Another possibility is for donor agencies to work with unions in countries with strong organized labor systems (e.g., Tunisia) to develop contract clauses specifying employer provision of immunizations.

Hopefully, employers would be involved in the development of such clauses at an early stage, to prevent later opposition. In addition, governments might develop incentives for employers to accept such clauses (e.g., tax breaks or investment credits).

Donor agencies in the health sector have not traditionally worked with or through labor organizations. Thus, a lack of contacts, or a hesitancy to set programmatic precedents might be a barrier to aggressive donor agency pursuit of these possibilities. Yet, in many parts of the developing world, industrialization and urbanization are proceeding at a rapid rate, and the service outlets represented by private companies and unions can no longer be overlooked.

2. Immunization Program Use

A. Developing Professional Constituencies

Problem: A variety of private and public leaders, professional as well as political, need to be galvanized around immunization needs within developing countries.

Response: In order to increase the professional and policy making constituency for immunization programs, donor agencies together, perhaps, with the national private medical association could sponsor annual "state of the nation" conferences in key developing countries.

Such a conference would examine, on a national basis, many of the issues and problems outlined in this paper. It would also serve as a platform for key professional leaders to urge program commitment and cooperation from their public private colleagues.

The largest barrier to such an effort would be the availability of donor funds. It might also be possible to obtain multi-national corporate donations for such an effort, particularly from producer companies and/or companies with operations in the countries at issue.

B. Increasing Public Demand

Problem: The importance of national immunization programs needs to be placed in the forefront of public attention in such a way as to convey not only the importance of the disease control opportunity, but also the support of national leadership at its highest levels.

Response: In the United States, an effective way to mobilize both public and professional awareness around major issues is the "White House Conference". These are well-planned, extensive, multi-day meetings which bring together, with great fanfare, public interest groups, private and public executives to place national spotlights on key public problems. Similar conferences could be sponsored in key developing countries.

These meetings would be focused on developing a broad public constituency for immunization, and on giving immunization a sense of national urgency. Involvement would be targeted at the nation's highest leaders. The experience of Colombia is illustrative of how a nation's chief executive can be publicly involved in immunization program development and delivery, thus conveying to all groups the immediate importance of vaccinations.

Again, a key barrier to the development of such a meeting strategy is the availability of funds both for the extensive time and effort needed to develop the sponsoring commission and meeting plan, as well as for the meeting itself.

A second major barrier to the effectiveness of such an approach to increasing public demand for vaccinations is the difficulty in sustaining the momentum created by such highly public conferences. If a wide variety of institutionalized public advocacy groups is not present within the national social and political structure to keep the immunization issue before the public eye, single conferences are unlikely to create long-term, sustained demand for vaccinations.

C. Media Campaigns

Problem: Reaching all components of the national population with information on immunization programs, and motivating that population to seek vaccinations requires media-based information and "pr" strategies.

Response: Donor agencies could place more emphasis on extensive media and public relations campaigns, contracting with major international public relations firms to develop multi-media approaches to the problem and/or seeking pro bono expertise from such organizations as the U.S. Advertising Council.

Support for such campaigns has many precedents in both donor and host government immunization programs. The largest barrier to expanded use of this technique is ensuring that the private as well as public outlets for immunizations are capable of responding to that demand, and that the logistics and distribution systems are able to get the vaccine to its points of delivery.

As an adjunct to the use of alternative delivery sites and to the constituency-building strategies described above, however, extensive public relations campaigns, using private sector expertise and taking advantage of private sector outlets, are essential to increasing public demand for services.

V. IMMUNIZATION PROGRAMS OF AID

A. Current Efforts

From Fiscal 1984 through Fiscal 1986, AID will have allocated an estimated \$61 million of development assistance funds, and another \$3.5 million in ESF funds, to immunization efforts. An additional \$25 million was made available by Congress in FY 1985 for the Child Survival Fund. At least part of that money is likely to be available for immunization efforts.

How has AID spent these monies in the past, and what implications might that have for its future roles in immunization and its cooperation with the private sector?

Detailed figures -- and even these are only estimates -- are available only for the DA funds.

Overall, immunization as a percentage of development assistance health expenditures is expected to decline from 18% in FY 1984 to 12% in FY 1986. As Table I below indicates, however, there is no significant change in the internal allocation of resources with that decline.

Table I

Immunization:
Program Area as % Total Imm Expenditure

Bureau/ Office	FY 1984	FY 1985	FY 1986
Africa	22%	25%	20%
Asia	16%	21%	18%
LAC	6%	6%	8%
Near East	2%	1%	1%
S&T	54%	47%	53%

S&T's vaccine development program -- focused largely on malaria but recently also on measles and rotovirus -- is the major recipient of immunization funds. 80% of S&T's immunization funds are spent on research.

Within the regions, Africa and Asia are the major foci of immunization concerns, although Africa's funds are accounted for not by national project components but by the regional CCCD effort.

From the limited information available, it appears that, within national development projects which have immunization

components, project emphasis is on the training of field workers to deliver vaccination services and the development of public demand via the use of media.

Within regional projects focused on immunization, the CCCD program in Africa is the largest effort, but 50% of its funds from FY 1984 through FY 1986 are allocated to technical assistance.

B. Future Possibilities

Given the private sector opportunities described throughout this paper and recognizing AID's priorities to date, to which opportunities could AID respond that strike a balance among the various considerations which must be factored into its immunization protfolio?

What could AID do that

- is not inconsistent with its current programs, yet is usefully innovative in its private sector connections;
- takes advantage of private sector opportunities or resources, yet meets both public interest and market priorities;
- is financially feasible, given AID's current and expected level of resources, yet makes long-term economic sense;
- balances resources allocated to its central S&T activities with those allocated to the regions;
- both promotes current immunization program needs and looks toward the research and technology future in this highly complex and rapidly changing field of scientific endeavor;

-- develops a variety of immunization activities within AID's programs, yet assures adequate resources to any one such activity over a sufficient period of time to ensure success.

Any amount of debate on these trade-offs is possible and no doubt will ensue. In the interests of beginning that discussion, let me forward what appear to me to be four priority areas of opportunity for AID, each of which is objectively necessary for successful immunization programs now and in the future and which, taken together, satisfy the balancing criteria set out above.

1. Central Efforts

A. Transition from Basic Research to Marketable Products

AID has between 40% and 50% of its immunization program resources allocated to vaccine research, much of this for malaria but recently for other diseases as well. Since launching the malaria vaccine program in 1966, AID has spent roughly \$35 million. Before the vaccine is ready for use, an additional \$15-25 million will be spent. Moreover, in 1985 AID, with NIH and the FDA, will embark on a special human vaccine research project, costing AID between \$5 and \$6 million over 5 years. Additional U.S. vaccine research funding is contributed to the WHO TDR program and to fertility regulating vaccine research.

Most, in some cases all, of this research taken place in university or non-profit settings. Yet, as discussed in detail earlier, the product development expertise rightly remains in

2. Regional Efforts

A. Training

AID has long focused on -- and has become very good at -- human resources development in the health sectors of the developing world. It would thus be a relatively straightforward process for AID to develop, perhaps at the regional level, expanded training opportunities for immunization program and financial management. Such an effort will attract more in the way of non-profit than commercial resources, although pro bono technical assistance from the latter sector may be possible (see below).

Without such expanded management skills, the resources currently poured into research and development, procurement, and public demand generation will face a serious bottleneck in achieving immunization goals.

B. Technical Assistance

As noted earlier, 50% of CCCD's immunization budget between 1984 and 1986 was allocated for contracted technical assistance. However, as described throughout this report, significant resources and expertise exist within the private sector which would be of importance in a number of immunization program areas, e.g., distribution, management, media development, quality assurance. Regular access to this expertise could not only assist AID's project work, it would also provide AID officers with the beginnings of a professional network among their private commercial sector counterparts. Moreover, by exposing corporate executives to the

problems of developing world immunization and health programs, it might begin to create something of a corporate constituency for development issues and resources.

Domestic precedent exists for corporate executive secondment to community organizations. International precedent exists in the area of environmental protection. Based on previous discussions with industry executives regarding a health sector "Technical Assistance Clearinghouse"; there appears to be broad willingness within industry to participate in such an effort provided that

- (a) companies have a clear idea of the maximum time to be requested in any year;
- (b) the individual missions are no more than 3 weeks in duration;
- (c) the individual best able to meet the technical skills required is determined by the company from its world-wide operations, not by outside organizations;
- (d) a third party handles all administrative needs, briefings, etc., so as to avoid any conflict-of-interest charges regarding direct corporate involvement in AID Projects.

Possible third-parties for the siting of such a clearinghouse might be PRITECH or the Bellagio Vaccine Task Force. The first year of operation could be on a trial basis, with subsequent locus and operations designed on the basis of an evaluation of its utility both to AID and to participating companies.

3. Country-Level Efforts

Expanded immunization program efforts, with private sector linkages, at the country level are, of course, region and often country specific. The viability of any endeavors are also dependent on the nature of AID's health project portfolio in any particular country, since immunization efforts have usually been components of health projects rather than free-standing projects themselves.

One initiative which AID might undertake, irrespective of region or project portfolio, is a concerted effort to develop private (commercial and non-profit) resource inventories for key immunization program countries. This information would then be available to program personnel and to policy makers in assessing the private-sector linkages possible for immunization programs within the countries. As noted previously, private sector cooperation within the country level is difficult until one knows the level and nature of private resources available which might be brought to bear on immunization problems.

There would be a number of options for the development of such inventories, from manual systems to machine-based systems. To the extent that such information is important to and could be shared with other donor agencies beyond AID (e.g. the EPI), an intensive undertaking to develop the inventories might be arguable. To ensure that sufficient resources were

available to see the job through, AID might want to concentrate on only one or two regions -- Africa and Asia for example -- rather than on developing individual inventories for all countries.

Some of the inventory work could be carried out within AID missions, provided that the data protocols were made available to health officers. Some could be done with independent researchers, local personnel to the extent possible.

In any event, the effort would not be extremely costly, but is pre-requisite to any hope for longer-term leveraging of private resources in national immunization programs.



NOT FOR QUOTATION

Drug and Vaccine Development Corporation
Prospectus

Revised May 1981

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Drug and Vaccine Development Corporation

Draft Prospectus

I. Summary

Over two billion people in less developed countries (LDCs) suffer from a wide range of infections which lower life expectancies, reduce productivity, and react synergistically with already low incomes. For many of these diseases, there currently exists no safe, cost-effective therapeutic or preventive technology. Even where a drug or vaccine exists, however, its delivery to those in need is often hindered by logistics, managerial, or technical barriers.

This prospectus describes an institution designed to address some of the constraints to drug and vaccine research and development for diseases of developing countries. It should be recognized from the outset that resolution of many of the health problems of LDCs requires a wide range of health system improvements, of which drug and vaccine availability is only a part. Nevertheless, it is a crucial component if many of the more widespread debilitating diseases are to be cost-effectively controlled.

The Drug and Vaccine Development Corporation (DVDC) described here was conceived to utilize scientific discovery more effectively in the development of drugs and vaccines for LDCs via a public-private partnership between university scientific capability and corporate drug development

expertise. As such, the DVDC would respond to a number of current structural problems in the field of research and development in tropical diseases.

One significant problem is that academic investigation has not been aggressively transformed by academe for application in the market place. As a consequence, a great deal of important work remains underutilized. Another problem is inadequate (and possibly declining) funding for tropical diseases research. To achieve a critical mass of effort, new sources of research support must be identified.

The DVDC is a nonprofit corporation organized to monitor tropical diseases research for its patent, licensing, and product potential with the objective of licensing industry to apply and make available such discoveries. In exchange for research grants, leading investigators transfer proprietary rights in their investigations to the DVDC. The DVDC aggressively patents promising discoveries and licenses them for production and marketing. Royalties are returned to individual investigators and/or their sponsoring institutions, and to the DVDC for further research on the diseases of the tropics. This patenting process is carried out with the greatest speed and efficacy in order to ensure minimal delay in the publication of academic research results.

In addition to its monitoring and licensing functions, the DVDC has a broader agenda of interests which respond to the range of bottlenecks to drug and vaccine availability in developing countries. For example, the DVDC will take an active role in the additional development and/or toxicity studies which may be required to attract pharmaceutical interest in product marketing and distribution.

Since some discoveries, particularly in the area of tropical diseases, may not be marketed profitably by pharmaceutical corporations, the DVDC will also be active in developing private-public partnerships, or surrogate markets, e.g., purchases supported by multinational funders or other public agencies.

Structurally, DVDC staff regularly would call on international expert panels to identify and/or make final assessments of the patentability of research discoveries offered to the Corporation. These expert panels are also closely involved with the design of additional chemical compound studies and the identification of promising areas of research for grant awards.

Financially, the DVDC initial operation budget is \$244,000 per year. It is anticipated that the full corporate operational plus grants program budget will be \$1.5 million by 1985. Financial support for the DVDC in the near-term must come from foundations, corporate philanthropic, government and international funding organizations. Since the ultimate receipt of royalties will create an income stream for the DVDC, longer-term financing may be possible using any of a number of debt mechanisms.

II. Tropical Diseases in Developing Countries

A. Disease and Its Impact

While the exact pattern of tropical disease epidemiology varies from country to country, many characteristics are shared. Most residents in developing countries harbor at least two parasitic infections. In many poorer areas, over half of the children die by age five. For those who do survive, life expectancy is as much as 10-15 years less than in

industrial countries. Some studies estimate that one-tenth of an average person's life in an LDC is disrupted by disease.^{1/}

Even in urban areas, where health services are generally more readily available, infant mortality rates and communicable disease prevalence are rising, especially in squatter settlements. In Manila, for example, the incidence of tuberculosis and gastroenteritis in squatter areas is two to eight times that of non-squatter urban areas.^{2/}

In the face of such health problems, most developing countries themselves spend less than \$3 per capita annually on public health services. The majority of these local resources are allocated to maintaining large and expensive urban hospital facilities.^{3/}

In addition to local resources, bilateral, multilateral, and private voluntary agencies contribute much-needed outside capital and recurrent cost financing to the health sector. The focus of most external agency programs is currently on rural and urban primary care targeted at poverty groups. Even with this outside assistance, however, scarce resources for health programs place increasing emphasis on the design of cost-effective disease control strategies. This is so particularly since (a) past investment programs for disease control (e.g., in water management) are proving increasingly expensive, (b) recurrent costs of general health programs are escalating with general inflation rates, and (c) local and international resources for health financing are being constrained by domestic and international economic pressures.

B. The Role of Drug and Vaccine Research and Development

While the scope of health problems in developing countries calls for a broad-based approach to health systems development, one of the crucial factors involved is the availability of drugs and vaccines for disease prevention and therapy. This availability is affected by barriers ranging from gaps in basic biomedical knowledge to lack of drug delivery systems in LDCs themselves.

For a wide range of the most prevalent tropical diseases, however, the major problem is a lack of safe, effective drugs and vaccines. Since World War II industrial and academic biomedical research, in the United States alone, has grown into a vast effort, supported by over \$4 billion in government and private funds. Little of this funding, however, has been directed to the development of drugs for treatment or prevention of tropical diseases. Since tropical diseases are not prevalent in the U. S. and other industrialized countries, research programs in these countries have lacked economic and political incentives to generate research financing in any way comparable to that targeted on their own domestic disease problems.

Thus, while many avenues of drug research are now open, relatively little tropical disease research is underway, either in the academic sector or in the pharmaceutical industry. Constraints operate on both the not-for-profit and the for-profit sectors conducting such research.

Nonprofit medical research centers are engaged in basic medical and clinical research, as well as in the development and testing of new drugs for the pharmaceutical industry. In academic settings, scientific

research is typically stimulated by financial incentives in the form of grants from government, private foundations, and industry. In the U. S., the Federal government has by far the largest funding capacity. But the statutory limitations of the Department of Health and Human Services (formerly HEW), which emphasizes the study of disease problems important in the U.S., poses a major obstacle to any expansion of programs for research on tropical diseases.

Tropical disease research also has a low priority with, and receives little support from, other Federal funding agencies. The result is a situation in which little tropical research can be planned, at precisely the period when recent advances in cell and molecular biology, comparative biochemistry and immunology, along with sophisticated laboratory technology and the technical capacity to conduct large-scale chemical investigations, have opened a new era for drug development.

Where such advances have taken place, university and public laboratory research programs are not suited for transforming discovery into technology. Research findings are published, but few find their way to actual drug/vaccine development. Such public programs have neither the production facilities nor the expertise to carry through on the patent/licensing process necessary to attract industry to drug development and production.

For its part, the pharmaceutical industry over the past 10 years has been reducing its investment in tropical diseases drug research and development. This trend has been particularly noticeable in U. S. -based parent companies, but, to a lesser extent, many European companies have

also been reducing such investments. Industry cites several barriers to greater involvement in developing tropical disease drugs and vaccines, including (a) lack of market incentives sufficient to justify major corporate investments in either the relevant basic biochemical research or the further development of existing discoveries potentially relevant to tropical diseases, (b) specific regulatory barriers rendering testing and clinical trials difficult, and (c) lack of patent protection in developing countries.

In spite of the barriers to tropical diseases research, however, major new initiatives in basic research are being mounted, including major schistosomiasis research funded by the Edna McConnell Clark Foundation, the Tropical Diseases Research and Training Programme co-sponsored by WHO, UNDP, and the World Bank, and the Great Neglected Diseases Network sponsored by The Rockefeller Foundation. Outstanding scientists are being attracted by these programs, in part for humanitarian reasons and in part because of the potential for practical research outcomes.

Nevertheless, the capabilities and potentials of current basic research programs remain underutilized in the face of (a) an inadequate supply of research financing, (b) the lack of an attractive linkage between university tropical diseases basic research and the development/production capabilities of industry, and (c) limited market-based motivation for expanded industrial initiatives in tropical disease drug development. Thus, in the context of a recent resurgence of interest in tropical diseases research, a major initiative is now needed to remove the barriers both to increased research and to the availability of technology based on that research.

III. Drug and Vaccine Development Corporation

A. Objectives

The Drug and Vaccine Development Corporation (DVDC) was conceived to address the above problems by providing a mechanism for more effective use of scientific discovery in the development of drugs and vaccines for developing countries. The DVDC, a nonprofit corporation, has three priority goals:

1. to aggressively monitor basic research so as to identify and obtain patent protection for academic discoveries in tropical diseases;
2. to pursue the further development of new or existing compounds, submitted to the DVDC either by universities or by industry, the design and, where necessary, the financing of further laboratory, clinical or field trials in order to bring discoveries to a point of development which generates industrial interest in licensed production;
3. to provide increased financing for tropical diseases research via the development of a research grants program financed from patent royalties reinvestment and independent funding.

Achievement of these objectives will require the DVDC to assume a number of functions both toward the public sector and toward private corporations. These functions are described in detail below.

In addition to its immediate goals, the DVDC must address many of the previously described problems via longer-term objectives. While these may be subsidiary in the initial years of DVDC operation, they do indicate the potential impact of the DVDC on the broader system of bottlenecks impeding drug and vaccine development for tropical diseases. These secondary objectives are as follows:

1. to expand industry's investment incentive by reducing risk capital requirements and expanding potential markets, the latter in part via the development of surrogate markets;
2. where cost-effective, to stimulate the development of drug production capabilities in the developing world by licensing appropriate technological work to local industry;
3. to investigate and give opinions on the safety, efficiency, and risk/benefit aspects of unused or newly developed drugs;
4. to develop uniform testing procedures and criteria enabling drug evaluation in the socio-economic and health context of less developed countries.

B. Organizational Precedents

While several institutions exist linking basic scientific research to industrial product development, none has the mandate, process, or structure to meet the range of objectives described above. For example, the Research Corporation only rarely aggressively pursues research discoveries. It chooses to respond to requests for patent activity rather than to seek out such opportunities. Such a passive approach would not help to build the critical mass of effort and attention that is required by tropical diseases.

For the most part, existing programs rely on internal staff assessments to judge the patentability and licensing potential of any discovery offered to the organization at issue. The highly complex issues related to tropical diseases, however, and the relatively circumscribed availability of research expertise both call for discovery evaluation by outstanding panels of international experts. None of the existing programs provides for such reliance on broad-based technical expertise.

Finally, the need for expanded resources for basic tropical disease research requires that royalties be targeted specifically for grants in such research areas. In other programs currently in operation, royalties for specific patents are placed in a central grants fund which finances a variety of research proposals. Royalties are generally not earmarked for specific areas of activity. The extensive need for financial support for specific tropical diseases research efforts, however, argues for specific earmarking of tropical disease drug/vaccine patent royalties for tropical diseases research proposals. While such consolidation is necessary in order to overcome previously inadequate research resources and to build a critical mass of research effort, its creation is not within the purview of existing institutions.

The organizational precedent most analogous to the DVDC is the International Contraceptive Committee which was created to encourage both public and industrial research and development in contraceptive technologies. In exchange for giving the Committee access to information and experimental compounds and ensuring public supplies at a reasonable price, industry receives regular research results, licensing rights and broader market opportunities. However, the Committee limits its activity to the area of contraceptive technology and does not have the capability of expanding into the broader areas of grants programs, procurement, field testing, etc., envisaged by the DVDC.

Thus, although when possible building on the patent/licensing experience of such organizations as the Research Corporation and the Wisconsin Alumni Research Foundation, achievement of the above objec-

tives requires the DVDC to fill a broader role including active pursuit of research, specific channeling of royalties to tropical diseases research, private sector market expansion, and provision of improved drug and vaccine information to developing countries. All of these functions are, of course, subject to antitrust review.

Creation of the DVDC has taken place in the context of full cooperation with WHO, other U. N. agencies, and The Rockefeller Foundation to ensure coordination of efforts.

C. DVDC Functions

To achieve the objectives described, the DVDC will carry out a number of tasks from the outset. The sections which follow describe these initial DVDC functions. The anticipated operating procedures and the organizational structures to be established for pursuit of the functions are described subsequently.

Monitoring of Research

The DVDC will actively track laboratory research world-wide in an effort to identify ongoing research of potential value to tropical diseases. Such monitoring will involve the research work of both industry and university laboratories. Although the DVDC and its periodic publications consequently will also act as a communications channel between industry, academic and developing country research leaders regarding research trends, full confidentiality of crucial research findings will be maintained to ensure patent and publishing rights.

It is anticipated that the monitoring effort will concentrate initially on research being carried out by the individual research insti-

tutions affiliated with the Great Neglected Diseases Network, organized by The Rockefeller Foundation.* Individual agreements between each institution and the DVDC will be sought to ensure compatibility with institutional and national policy. Initially, members of the Executive Committee of the Network will be asked to monitor the research of their laboratories, identifying the potentially patentable discoveries. If, during this initial period, the DVDC is approached by non-Network university programs, assessment of research/discovery potential will lie with the Network Executive Committee. DVDC staff will stay in close and regular contact with these Network scientific leaders to ensure that the identification/assessment/patent process proceeds as quickly as possible, and thus does not delay academic publication of research results. As monitoring experience builds, the range of monitored universities and laboratories will be increased and the monitoring burden will shift increasingly to DVDC staff.

Patenting/Licensing

As described earlier, a major barrier to the expansion of tropical diseases drug and vaccine research and development has been the failure to aggressively patent and license academic investigation for use in the

*Institutions involved in the Network include: Tufts University; University of Virginia; Case Western Reserve University; University of Washington; Oxford University; Biomedical Research Centre for Infectious Diseases (Cairo); Harvard University; Universities of Stockholm and Uppsala; Weizmann Institute of Science (Israel); Walter and Eliza Hall Institute of Medical Research (Australia); The Rockefeller University; the Centro de Investigacion y de Estudios Avanzados (Mexico); and Mahidol University (Bangkok). Annex II of this prospectus contains a description of the operations of the Network, and a list of the major research leaders involved in Network governance.

market place. As a consequence, much important work has not been utilized. One of the primary functions of the DVDC will be to identify and attract patentable research discoveries, pursue patents for such discoveries, license industry to develop and market technologies from the discoveries, and channel patent royalties back to the research institutions both through administrative agreements regarding the DVDC and research institution royalty percentages, and through research grants for specific projects or programs.

This function should prove attractive to researchers and their sponsoring institutions for several reasons. First, it provides a practical mechanism for transforming discoveries into marketable technologies capable of addressing the health problems toward which the initial research was targeted. Second, it provides a royalties share to the institution/researchers without the latter individually incurring the time and expense required to pursue patent and licensing rights. Third, it provides potential increased resources for research in any one institution by establishing a grants fund from a percentage of royalties of all patented sales. Again, such funds are made available without the need for individual institutions to incur program costs. Moreover, grants resources will also be generated by independent funding mechanisms.

Similarly, the patent/licensing function would assist industry by providing access to the research products of an international group of top academic tropical disease researchers. Such licenses would allow development and marketing of drugs and vaccines without research and/or in international patenting by industrial laboratories themselves. Furthermore, the DVDC-based international network of research scientists

and institutions offers to industry the potential for collaboration on the field clinical testing of its own research discoveries in tropical diseases.

Developing countries would benefit from the patenting/licensing activities in several ways. First, it would provide greater assurance that tropical disease research discoveries, in industry or academe, would be transformed in to useful products. Second, the return of royalties to the DVDC would expand the resources available for tropical diseases research. Third, for those drugs patented via the DVDC, developing countries would receive adequate cost and quality protection in exchange for patent protection. Finally, where cost effective, the licensing of local drug production facilities to carry out further product testing and development would both increase LDC industrial capability and help to reduce product prices.

The process of discovery receipt, patent/licensing pursuit, and royalties division is described in detail below.

Financial Support for Drug and Vaccine Development

Where research products have been submitted to the DVDC for patenting, further product development (e.g., field testing) may be necessary prior to gaining active corporate licensing interest. Similarly, existing corporate discoveries with potential tropical disease significance may require further testing before their safety and efficacy are clear. Yet, private sector capital budgets for such development often are limited, extending funding only to the top ten percent of corporate laboratory discoveries. Thus, the financing required for such development stages may not always be fully available from private sources.

In such cases, the DVDC, using interested panels of scientists, will seek to design the development stage tests, with attention to meeting needs in the downstream licensing process. When necessary, public sector funding and in-kind corporate contributions will be sought to finance the testing and developments required.

Expand Research

The DVDC will pursue two approaches to expanding the funding available for tropical disease drug and vaccine research. Independent fund-raising for such research will take place immediately to create a grants program. In addition and as royalties profits are received, a portion of royalties received by the DVDC on marketed drugs and vaccines will be channeled into that program. Research funds will be granted to applicant university or public sector laboratories which have administrative agreements with the DVDC patent program. The major criterion for such agreements is a demonstrated capability in tropical diseases research.

An outside international panel of experts will evaluate the research applications and recommend final grant awards. Care will be taken to ensure that conflicts of interest between panel experts and applicant institutions are minimized.

Subsidiary Functions

Market Expansion: Presently, a small number of pharmaceutical companies are supplying the tropical diseases drug needs of the developing world. The developing world lacks, for the most part, the capability to develop and distribute tropical disease drugs on its own. While bilateral and multilateral funders have made some contributions in this area, notably through the WHO

Special Programme for Research and Training in Tropical Diseases, the gap between what exists and what is needed remains substantial. For the near-term, drugs for tropical diseases must be supplied by the pharmaceutical industry.

However, even if opportunities are created for expanded research in tropical diseases, there would remain an absence of incentives for actual drug development. Until LDCs can afford adequate supplies of tropical disease drugs, the incentive for industry to provide these drugs lies in the creation of surrogate markets, with national or international aid programs at least partially absorbing the initial costs of supplying essential drugs. This concept has been accepted in other areas of international assistance (e.g., food supplies and educational infrastructure), and seems to be the only medium-term solution for assuring the effective supply of adequate drugs and vaccines to developing countries.

Through its attempts to provide opportunities for expanded drug and vaccine development, the DVDC will work closely with bilateral and multilateral funders to develop models for financing of drug and vaccine procurement for LDCs.

Expanded Drug Information for LDCs: If new technologies are to be appropriately and effectively used, it is essential that developing country health leadership be fully aware of the progress on tropical diseases research and the methods for and implications of new drug or vaccine use. The DVDC will pursue a broad information dissemination program focused on LDC leadership. Moreover, it will sponsor cost/risk studies of the drugs and vaccines at issue and assist LDC leaders in making safety and efficacy

judgments on drug use. An additional longer-term function is the development of testing procedures for drugs and vaccines to assure drug evaluation that is both relevant to the social, economic and health context of less developed countries and in conformance with international standards.

Testing Procedure Improvements: The presence of inappropriate drug and vaccine regulations also has inhibited the development of drugs and vaccines for tropical diseases.

For the pharmaceutical industry, an overdeveloped regulatory system means increased cost and risk in new drug research and development, adding up to a risk/benefit ratio that is unfavorable and discourages long-term projects in favor of shorter-term, less bold ventures. For academic research, the delay and waste involved in satisfying U. S. requirements for NDA and IND approval (for new and innovative drugs) means that many important discoveries do not reach the stage of clinical trial and remain forever on the shelf.

United States laws affect all pharmaceutical research, not only programs intended to benefit developing countries. Certain restraints, however, make research aimed at tropical diseases even more difficult. These regulations make it difficult to send experimental drugs out of the country for trial (although the logical environment for drug testing is the one where it will be used), and at the same time make it difficult to manufacture in this country a drug whose sole market is elsewhere.

Aspects of government policy in LDCs and in Europe also constrain innovation in tropical disease pharmaceuticals. The patent process has become expensive, time-consuming, and unreliable. Inadequate patent and

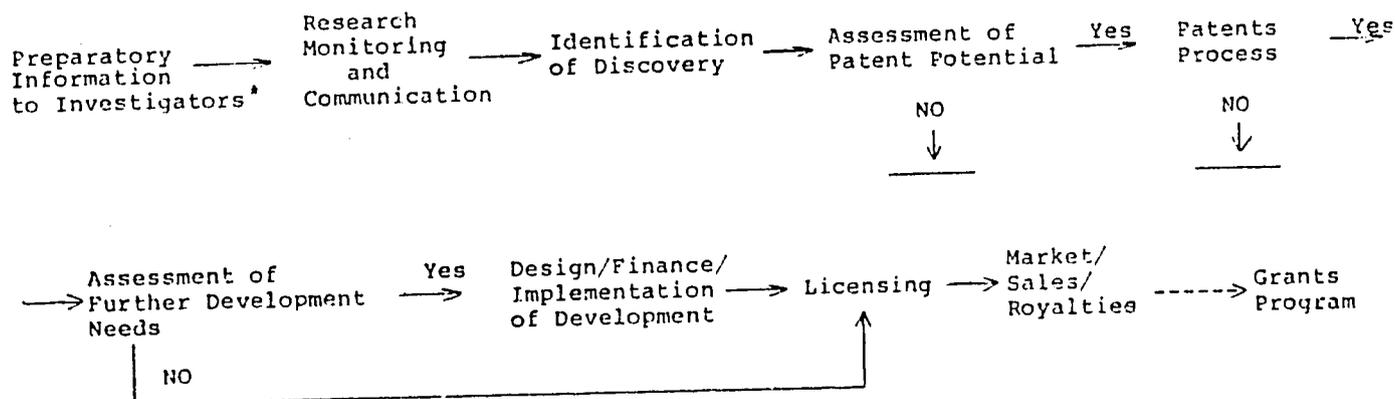
trademark protection of compounds and the legal framework which discourage the drug industry from investing in tropical diseases research.

Moreover, while individual drug companies are often deterred from innovative research ventures by the risk and expense described, cooperative ventures within industry which could make such efforts feasible are often prevented by the uncertainty of antitrust laws. The international reach of U. S. antitrust laws also inhibits the pharmaceutical industry from participating in cooperative efforts to supply tropical disease drugs to the developing world.

DVDC staff and committee experts will work with national and international agencies to attempt to reduce these regulatory constraints to tropical disease drug and vaccine research and development.

D. Operating Procedures

While details of the procedures by which the DVDC carries out its primary goals vary according to the needs of individual discoveries, the following represents a brief description of the major stages and activities within that process:



* i.e., Development of Patent Manual

Preparatory Information

In many cases, individual scientists are not aware of the prerequisites for successful pursuit of patents. Most universities provide little or no information to the scientist regarding data necessary for patent approval, the process, timing and conditions of patent application, or the rights and responsibilities involved in patent issues. Without such information, the scientist often either is discouraged by the apparent maze of effort required or, having attempted to solve the maze once, is unwilling to undertake the process a second time. The problem is even more complex when the research at issue has been financed by a number of sponsors or cuts across research programs in one or more research institutions.

Recognizing these barriers to the effective participation of investigators in the DVDC research monitoring and patenting process, the DVDC will develop a manual for research scientists describing the details and prerequisites of patent efforts in general and the DVDC process in particular. This manual will identify the key issues to be taken into consideration early in the research process (e.g., issues of data records or inter-institution agreements) and will suggest means for their management. The full DVDC process will also be described in detail. The manual will be made available to all researchers in institutions having administrative agreements with the DVDC as well as to research directors responsible for monitoring discoveries.

Monitoring/Communication

Given the extend of research activities as well as the need to isolate those discoveries having practical merit, the monitoring process represents a key point in the patenting process. As described earlier, this process will be managed initially via the Executive Committee of the Great Neglected Diseases Network. DVDC staff will maintain very close communications with these research directors, however, since an external pragmatic view may be necessary to identify the practical options from a set of biochemical research discoveries.

The monitoring itself will be an ongoing effort by each research director, with the annual Network meeting representing an opportunity for comparison of possible directions for pursuit of patents. This meeting will also serve to identify inter-institutional research areas which might lead to practical, patentable results.

As the monitoring grows beyond the Network, DVDC staff will assume greater substantive monitoring responsibilities. However, since research laboratory work is highly technical and since discoveries of a practical but not necessarily scientifically "interesting" nature might otherwise remain uncovered, DVDC staff will continue to rely on research directors for detailed and regular reports of research findings.

To ensure that the monitoring process also becomes a technical and patent communications channel, the DVDC will initiate a series of periodical publications for distribution to researchers, industry, developing country health leadership, bilateral and multilateral organizations, public medical institutions, and private international organizations.

These publications, beginning with a bimonthly research bulletin and possibly developing into a more technical periodical, will serve to communicate the progress of the DVDC program, to keep investigators informed regarding the directions of an international research network, and to maintain momentum for the inflow of practical discoveries to the DVDC.

Discovery Identification/Patent Assessment

Once the monitoring process in any institution has identified a potentially important discovery, that discovery, under the terms of the sponsoring institution's administrative agreement with the DVDC, will be submitted to the DVDC for patent investigation. The DVDC Patent Advisory Committee, whose structure and membership is described in subsequent sections of this prospectus, will assess the submitted discoveries for their patent potential. Those which are accepted will enter the DVDC patent process; those which are not accepted will be returned to the sponsoring investigator/institution.

Patent Process

Every effort will be made to speedily obtain patents in order to minimize the delay of publication of research results by the investigator and sponsoring institution. Patent submission will be monitored by DVDC staff and will be managed by outside legal counsel. Submission will be made in the United States and in those other countries which DVDC management feels are relevant. Costs of patent submission will be borne by the DVDC.

Further Development

In some cases the patented discovery may not be sufficiently developed to attract industry interest in the initial stages of its further testing. In these circumstances, industry opinion will be sought and an ad hoc, highly credentialed group of DVDC-affiliated scientists will meet to examine the technical needs for further testing and development of the discovery. Testing protocol will be developed and financing sought for these further steps. It is anticipated that much financing will be sought from a consortium of sources including bilateral and multilateral donors, foundations, and industry. The actual implementation of the testing/development design will be carried out by DVDC institutions and investigators, coordinated by DVDC staff. The development advisory group will supervise the technical aspects of the tests and will evaluate the resultant data.

Licensing

At the appropriate stage, DVDC staff will conclude licensing agreements with interested corporations for the final development, production and marketing of the pharmaceutical. Such licenses will specify the royalties return from sales, a portion of which royalties would revert to the DVDC research grants program.

E. Organization and Management

In order to effectively carry out the above functions, the DVDC must respond structurally to several prerequisites. It must (a) have the quality control capability necessary for judging both patent offers and research grant applications; (b) build a sound network of research leadership in academe; (c) relate effectively to industry leadership; (d) involve LDC

health and research leadership to ensure program appropriateness, especially regarding surrogate markets; (e) be able to work with patent and regulatory bodies within the United States and abroad; and (f) have the ongoing staff and financial means to support activities prior to royalties receipt.

The diagram which follows on page 24 briefly illustrates the structure of the DVDC for the first five years of operation. Subsequently, new positions will be required for portfolio management. Each operating section is described in turn below for purposes of clarification. Further detail will be contained in the DVDC Bylaws.

Board of Directors

The Board of Directors of the DVDC would be made up of not less than 10 and not more than 20 persons. The chair would be elected from the Board and serve a two-year term. Members of the Board would include the interim Advisory Committee and any further member(s) elected by the Board. The Board would be responsible for overall management of the DVDC and will meet annually.

Executive Committee

The Executive Committee of the DVDC would be responsible for regular oversight of DVDC activities. It would be comprised of seven members elected for two-year terms from within the Board of Directors, as well as the Chief Executive Officer of the DVDC, the Vice President, Finance, and the Vice President, Operations. The Committee would be chaired by a president elected from within the Committee, who would serve for a two-year term.

Chief Executive Officer

The Chief Executive Officer (CEO) would be a salaried officer responsible for daily management of the DVDC and for all major liaison between DVDC staff and operations, the Board, and the Executive Committee. The CEO would also be the main external representative for the DVDC (unless otherwise designated), and would be responsible for coordinating all program development.

Counsel

In its initial years, DVDC legal matters, including patenting and licensing formalities, would be handled by outside counsel. Subsequently, in-house counsel would probably be required.

Vice President, Finance/Administration

The Vice President, Finance/Administration would be a salaried staff member responsible for financial management of the DVDC as well as for the establishment and administration of its standard operations, procedures, and personnel policies. Financial management duties would include tracking of revenues and expenditures, management of earning asset portfolios, and, together with the Board, Executive Committee, and the CEO, development of non-royalty based funding. In consultation with other officers, the VP, Finance/Administration would also be responsible for establishing fiscal year operation program budgets.

Vice President, Operations

The Vice President, Operations would be a salaried staff member responsible for management, implementation and coordination of all patent, development, licensing, research grant, and external communications func-

tions of the DVDC, as well as for development and administration of agreements with participating universities and laboratories. Advisory evaluations committees would also be convened, chaired, and managed by this officer. Actions on all patent, license, and grant recommendations would be the responsibility of this officer, answering to the CEO and to the Executive Committee/Board.

The Vice President, Operations will also be responsible for concluding and administrating agreement on discovery-receipt and royalty-distribution with individual researchers and/or laboratories involved in the patent/licensing program. These agreements will be negotiated on a case-by-case basis, but, in general, will specify the coverage of research applicable, the duration of the agreement, and the specific royalty split anticipated. The standard royalty split will be 25%-75% in favor of the DVDC on product sales in developing countries* and 75%-25% in favor of the laboratory/individual on product sales in developed countries. Further laboratory (or university) splits with individual scientists will be determined by the laboratory (or university) in question. Criteria for deviation from this standard formula are to be determined.

* Defined by the World Bank income categorizations and excluding capital surplus petroleum exporting countries.

Patents Advisory Committee

Members of this outside committee (not less than 10 nor more than 20) would be senior international experts in tropical diseases research and would serve for four-year terms. The initial committee would be appointed by the Board of Directors for staggered terms. Subsequent members would be elected by the Committee and approved by the Board. On the basis of staff research, the Committee would be responsible for evaluating the patentability and licensability of research discoveries offered to the DVDC and for advising the Vice President, Operations on patent/licensing pursuit. The latter, however, would retain responsibility for final decisions and their implementation. The Committee would also be asked to identify potentially important research programs in universities not part of the DVDC program, and to assist DVDC officers in soliciting the inclusion of that research in the DVDC patent portfolio.

Grants Advisory Committee

Members of this outside committee (not less than 10 nor more than 20) would also be senior international experts in tropical diseases research and would serve as volunteers for four-year staggered terms, with subsequent members elected by the Committee and approved by the Board. The Committee would be responsible for evaluating requests for grant allocations made to the DVDC via the Director of Grants Programs. Evaluation would be according to explicit criteria, to be set out by the Committee and not to include consideration of institutional DVDC affiliation. The Committee would then advise the Vice President, Operations on useful grant awards. Again, the latter would retain responsibility for final decisions and their implementation.

It is likely that the grants program will not be operational for the first year of DVDC existence. This Committee, therefore, would be constituted when needed.

Director, Patents/Licensing

The Director of the Patents/Licensing operations would be a salaried DVDC staff member responsible for seeking out patentable research and unused industrial research findings and presenting basic information on such research to the Advisory Committee, and seeking corporate interest in receiving licenses for the development of patented research. The Director will be sufficiently familiar with the scientific issues in question to be capable of following up potential opportunities and to be competent in licensing discoveries.

Director, Grants Program

The Director of the DVDC Grants Program will probably not need to be recruited for the first two years of DVDC operation. When recruited, the Director will be a salaried DVDC staff member who will be responsible for soliciting, reviewing, and gathering information on grant applications from research laboratories. Initial screening will be carried out on the basis of criteria established by the Grants Advisory Committee, and that Committee shall make all awards recommendations. The Director will also develop non-royalties sources of grants program support, in association with the DVDC Vice Presidents and Chief Executive Officer.

Director of Publications

The Director of Publications will be a salaried staff member responsible for all external written communications of the DVDC. This will

include initiating a series of international newsletters, reports, or other materials to provide information flow among tropical diseases research programs in general and regarding DVDC programs specifically; ensuring that the DVDC receives all relevant publications from external programs; developing DVDC promotional material; managing the publication of the annual report; coordinating all DVDC publishing efforts; and handling all press notices and liaison.

Finances

Until at least 1986-87, DVDC financing will need to be non-royalty based. Even after that time, it is likely that outside budget support will be required.

The following assumptions apply to the first five-year budget estimates.

1. In 1981, the Chief Executive Officer and Vice President positions are staffed by core CPR program personnel, entailing only partial salary need.
2. From 1982 onward, the DVDC operating budget (if not full staffing) is separate from that of the CPR core budget, even if it continues to be physically lodged within the CPR program.
3. Staffing is gradual, keyed to portfolio expansion, itself determined by the DVDC Board.
4. Unit costs are in 1981 U. S. dollars; inflation is calculated at 10% per year over the previous year.
5. Overhead is calculated on base cost; inflation is calculated on base-plus-overhead.

The five-year DVDC budget represents a phasing of research grant activities and a gradual assumption by the DVDC of broader areas of responsibility. By 1984-85, it is anticipated that the DVDC will house a developed patent/licensing/grant function and will be well positioned to serve as a center of activity for broader drug and vaccine interests, such as quality studies, cost-risk analysis, etc. The five-year budget, therefore, represents three phases of DVDC operation:

1. 1981: Start-up investments and gradual growth to ensure the initiation of patent activities and to lay the groundwork for subsequent growth into research grants activity.
2. 1982: Initiation of grant activity and consolidation of patent/licensing operations.
3. 1983-85: Expansion to full operation of patent/licensing activities including growth in institutional networks and industrial agreements; marked increase in grant activity; initiation of some quality and cost-risk studies.

Budget growth from \$224,000 to \$1.4 million thus also reflects a gradual assumption of the broader DVDC goals and objectives described at the beginning of the prospectus. It should be pointed out that this growth pattern represents only budget approximations as the size of the patent portfolio and grants program have yet to be determined by the Board.

Annex I contains three-year budget projections.

Annex I

DVDC Three-Year Budget

Annex I

Three-Year Start-Up Financing
Drug and Vaccine Development Corporation
(\$ '000)

	<u>1981</u> ^{1/}	<u>1982</u> ^{1/}	<u>1983</u> ^{1/}
<u>Salaries</u> ^{2/}			
Chief Executive Officer ^{3/}	27	27	27
Vice President, Operations ^{4/}	18	50	50
Director, Patents/Licensing			35
Director, Publications			35
Assistants	1.8	20	20
Secretarial ^{5/}	5.0	30	30
Researchers		<u>14</u>	<u>14</u>
Subtotal	<u>51.8</u>	<u>141</u>	<u>211</u>
<u>Meetings</u>			
Ad Hoc Development Panels		8	8
Patent Advisory		16	16
Grant Advisory			8
Advisory Board	<u>30</u>	<u>30</u>	<u>30</u>
Subtotal	<u>30</u>	<u>54</u>	<u>62</u>
<u>Other Travel</u>			
Domestic	10	10	10
International	<u>10</u>	<u>10</u>	<u>20</u>
Subtotal	<u>20</u>	<u>20</u>	<u>30</u>
<u>Other Operating</u>			
Technical Consultants	25	10	15
Materials ^{6/}	10.8	10	15
Communications	6.3	8	10
Printing/Publishing ^{6/}	<u>15</u>	<u>15</u>	<u>20</u>
Subtotal	<u>57.1</u>	<u>43</u>	<u>60</u>
BASE TOTAL	158.9	258	363
Overhead - 10%	<u>15.8</u>	<u>25.8</u>	<u>36.6</u>
Subtotal	174.7	283.8	399.6
Inflation - 10%	<u>--</u>	<u>17.5</u>	<u>30.1</u>
BASE PLUS	174.7	301.3	429.7
Accounting/Legal (includes patents)	20	20	30
Grants			<u>250</u>
TOTAL OPERATING ^{7/}	<u>194.7</u>	<u>321.3</u>	<u>709.7</u>

Annex I

NOTES

1/ As is specified in the text of the prospectus, 1981-83 represent DVDC start-up years. Costs, therefore, are somewhat lower than for subsequent years of full operation and grant-making activity.

2/ fully loaded

3/ One-third time from CPR staff for purposes of management, marketing, constituency development, pursuit of funding, and liaison with the Board of Directors and Executive Committee.

4/ Half-time from CPR staff until 1982; functions will include those of Vice President, Finance until 1984.

5/ full time equivalents

6/ including publication of external reports, newsletters, etc.

7/ exclusive of ad hoc funds for financing postpatent stages of development

Annex II

Great Neglected Diseases

Network Summary

Great Neglected Diseases

International Network of Biomedical Research Groups to Study the Great Neglected Diseases of the Developing World

Description. In December 1977 the Trustees approved funding for the creation of an international network of biomedical research groups to study the great neglected diseases of the developing world. By 1979, the network consisted of the following research units:

Clinical units

Tufts University, Division of Geographic Medicine
University of Virginia, Division of Geographic Medicine
Case Western Reserve University, Division of Geographic Medicine
University of Washington, Division of Geographic Medicine
Oxford University, Tropical Medicine Research Unit
Biomedical Research Center for Infectious Diseases, Cairo, Egypt

Immunology units

Harvard University, Immunoparasitology Division
Universities of Stockholm and Uppsala, Joint Immunoparasitology Unit
Weizmann Institute of Science (Israel), Unit for Molecular Biology of
Parasitic Diseases
Walter and Eliza Hall Institute of Medical Research (Australia),
Immunoparasitology Research Unit

Biochemistry/pharmacology units

Case Western Reserve University, Pharmacoparasitology Research Unit
Rockefeller University, Pharmacoparasitology Research Unit

In 1980 two more biochemistry/pharmacology units have been brought into the network. Both are from the developing world and both are doing excellent work in the crucial new area of membrane chemistry. These are Dr. Martinez-Palomo's Parasite Biology Unit at the Centro de Investigacion y de Estudios Avanzados in Mexico City and Dr. Yongyuth Yuthavong's Parasite Biochemistry Unit at Mahidol University in Bangkok. The network units organized in centers of excellence in developing countries in South America, Africa, and Asia will function as research and training centers for their country, their region, and for investigators from the developed world.

The units sited in the developed world devote approximately one-third of their time and funds to collaborative work with developing world institutions, at present in Brazil, Mexico, Guatemala, Jamaica, Saudi Arabia, Kenya, Liberia, Gambia, Thailand, Indonesia, The Philippines, New Guinea, and Fiji. Each of the 14 units is led by an outstanding scientist who has

attracted cadres of excellent students and young investigators, thus creating a critical mass of young investigators with a high output in terms of both quality and quantity. Annually, all of the units gather together to present their data and their plans and budgets for the following year. The work of each of the units in the network is detailed in the attachments.

Importance. The sophisticated biomedical research establishment of the industrialized nations has thus far largely ignored many of the diseases that afflict hundreds of millions of people in the developing world.

Recently, however, international agencies have become concerned about these neglected problems, which are perceived to be a significant hindrance to both economic development and acceptance of population control. The World Health Organization has embarked upon a Special Programme for Research and Training in Tropical Diseases for which they have now received commitments of \$20 million, largely from European countries. But the WHO must work under several constraints, political, geographic, and economic. In the second annual report of its tropical diseases programme, the WHO recognized the particular importance of programs like the GND network in fulfilling needs not met by its own Special Programme.

The overall result of mobilizing the best of the scientific establishment should be the development of new and better tools for diagnosis, treatment, and prevention, leading to more rapid and complete control of these widespread infections.

Previous Interest. In 1974 a grant of \$525,000 was made to Case Western Reserve University School of Medicine to develop a unit in its Department of Medicine devoted to research on the great neglected diseases of the developing world. Since 1977, three appropriations have provided \$3,450,000 toward the initiation, continuation, and further development of the network.

Supplementing this program are the Foundation's Career Development Fellowships in Geographic Medicine. These fellowships provide a career incentive for outstanding young researchers in the great neglected diseases. Two five-year fellowships are awarded annually in a widely-advertised international competition. To date, the five fellowships awarded have gone to a Brazilian, a Sri Lankan, a German, a Canadian and an American.

In addition, the Foundation has provided over \$6 million since 1965 for support for schistosomiasis research projects on St. Lucia.

Staff Involvement/Officer Responsibility. The Director for Health Sciences is responsible for the project. He is assisted by a Visiting Research Fellow and the Program Associate for Health Sciences who spend 25 percent of their time on the project. The director of each of the

network's units serves on the Executive Committee which reports to and advises the Director for Health Sciences. In addition, there is an Advisory Committee to the GND program consisting of one representative each from the medical schools, research institutes, government, philanthropy, industry, and the World Health Organization.

Cooperation with other organizations in funding or implementation.

Cooperation with other agencies has been an integral part of the program since its inception. The latest annual meeting of the network units was attended by representatives from the World Health Organization, the Macy Foundation, the Edna McConnell Clark Foundation, the National Institutes of Health, the Consejo Nacional de Ciencia y Tecnologia (CONACYT) of Mexico and the Wellcome Trust. The Director of Health Sciences is a member of the WHO's Joint Coordinating Board for the Tropical Diseases Research Programme and the Director of the WHO Programme serves on the Foundation's Advisory Committee to the GND program. The Foundation has worked in close collaboration with the Edna McConnell Clark Foundation on several projects. They jointly support a course in the Biology of Parasitism at the Marine Biological Laboratory in Woods Hole, Massachusetts. With the Josiah Macy, Jr. Foundation a meeting on the Present Status and Future of Parasitology is scheduled for October 1980. The National Institutes of Health has recently initiated Program Project Grants in Parasitology (\$500,000 a year) and the two institutions chosen to date (Case Western Reserve University's Division of Geographic Medicine and Harvard University's Immunoparasitology Division) are both members of the GND network. CONACYT in Mexico is providing joint support for the new Mexican unit which has been added to the network. The Wellcome Trust has been reviewing its program in tropical medicine, and in their latest annual report is the following statement: "These new developments, which it is hoped will be consolidated in the next two years into a Division of Medicine in the Tropics at the Trust, has similarities to the Rockefeller Foundation network. It is anticipated that the linkage with the Rockefeller Foundation programme will be of benefit to the two foundations as well as to the development of the subject."

Current obligations. The current grant of \$1,600,000 is available for allocation during the period ending December 31, 1980.

Implications for future support. The officers plan to recommend support for each of the units at an annual level of up to \$150,000 for a maximum of eight years and a total of \$14,400,000 in appropriation funds.

Great Neglected Diseases Network

Research Directors

- Dr. Gerald T. Keusch
Tufts-New England Medical Center
- Dr. Richard Guerrant
University of Virginia
- Drs. Adel Mahmoud and Leslie T. Webster, Jr.
Case Western Reserve University
- Dr. Seymour J. Klebanoff
University of Washington
- Professor D. J. Weatherall
Nuffield Department of Clinical Medicine
Oxford, England
- Dr. John R. David
Harvard Medical School
- Dr. Aziz El Kholy
Biomedical Research Center for Infectious Diseases
Cairo, Egypt
- Dr. Peter Perlmann
University of Stockholm
- Dr. Hans Wigzell
Uppsala University Medical School
Uppsala, Sweden
- Dr. Ruth Arnon
The Weizmann Institute
Rehovot, Israel
- Dr. Graham F. Mitchell
Walter and Eliza Hall Institute of Medical Research
Australia
- Dr. Anthony Cerami
The Rockefeller University
- Dr. Adolfo Martinez-Palomo
Centro de Investigacion y do Estudios Avanzados
Mexico
- Dr. Yongyuth Yuthavong
Mahidol University
Bangkok, Thailand
- 78

Annex III

1/
Health Policy Paper, The World Bank, March 1980

2/
World Development Report, 1979, The World Bank, 1980

3/
Health Policy Paper, op. cit.



DISCUSSION DRAFT

IMPROVING THE AVAILABILITY OF PHARMACEUTICALS
IN DEVELOPING COUNTRIES

A Proposal for Action from
The Center for Public Resources

November 1980

40

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IMPROVING THE AVAILABILITY OF PHARMACEUTICALS IN DEVELOPING COUNTRIES

A Proposal for Action from
The Center for Public Resources

Executive Summary

During the last 40 years, some of the most important advances in medical care and health status of people living in the United States and other industrialized countries have come through the development of new drugs and vaccines. Major fatal or crippling diseases, such as polio, measles, diphtheria, and tuberculosis, have been sharply reduced. Moreover, the populations of these countries have benefited from these advances not only in terms of physical well-being, but also in terms of increased life spans, higher productivity, and enhanced capacity to learn and to progress economically.

In many instances, pharmaceutical interventions have proven to be the most cost-effective way of treating and preventing disease. This is particularly evident in the case of vaccines, which can prevent disease episodes whose treatment costs are a vast multiple of the cost of immunization.

These major advances have yet to take place in many developing countries. In part, the health status of people living in less developed countries continues to be low because they suffer from certain diseases for which effective methods of prevention and treatment have not yet been developed. But more importantly,

they are missing major improvements in health status that lie within the scope of existing technology because of inadequate utilization of already proven methods of treatment and prevention. This is especially true with respect to the major causes of mortality and morbidity among children.

Moreover, the inability of developing countries to make full use of certain already available drugs and vaccines has a strong negative influence on research and development efforts with respect to many tropical diseases. Private companies (who have developed nearly all successful drugs and vaccines) are discouraged from committing private funds to research on diseases of the tropics both because of the lack of effective purchasing power on the part of the people in need, and because of the inadequacy of public health care delivery and pharmaceuticals distribution systems.

However, the solution to the problem of inadequate utilization of existing drugs and vaccines does not lie in simply transferring funds to developing countries. In many instances, existing pharmaceuticals cannot be utilized effectively without significant improvements in health care delivery and in pharmaceutical supply systems. The capacity to import, store, prescribe, dispense drugs and vaccines, and to instill patient compliance must be developed hand-in-hand with an expansion of the financial resources which poor countries can devote to pharmaceuticals and their health delivery systems. Thus, the question is not so much whether to seek additional funding for pharmaceutical purchases by developing countries, but how best to administer a program aimed at

increasing developing country purchasing power.

This report describes a financing strategy intended to strengthen significantly the assistance provided by the United States for the purchase of pharmaceuticals by developing countries. A key emphasis of the approach is to ensure that this expanded assistance is provided as part of a broad effort to improve health care delivery, rather than as an isolated program to finance the supply of additional commodity imports. Details of the reasoning behind the proposal and its specific design are set out in separate sections below. Very briefly:

Section 1 describes the need for more and better drugs and the linkages between better utilization of pharmaceuticals and improvements in health care in developing countries. It analyzes the major components of health problems (e.g., ignorance of how to maintain health, dietary inadequacies) and describes the relationship between inadequate availability/utilization of pharmaceuticals and the other components of the health problem. Section 1 goes on to discuss the major underlying reasons for the pharmaceutical supply problem, namely:

- lack of an adequate health care delivery system to reach underserved groups;

- . inadequate distribution systems for pharmaceuticals themselves;
- . weakened incentives for new R & D;
- . inadequate mobilization of domestic resources for the health sector.

Section 2 briefly reviews the present U. S. foreign assistance program in health, summarizing the program's efforts in terms of the major dimensions of the ill health problem set out in Section 1. Expanded financing of pharmaceuticals is concluded to represent a major opportunity for expansion of U. S. foreign assistance efforts in the health sector. Such expansion is a natural complement to the present training and primary health care focus of U. S. programs, and would build on the commodities experience in the population area.

Section 3 describes the actual approach to expanded funding of pharmaceuticals imports by developing countries and addresses the major hindrances to effective utilization of drugs and vaccines in developing countries.

The financing mechanism is somewhat analogous to the present-day PL480 Food-for-Peace Program. In a similar manner, the U. S. foreign assistance program would extend concessional and non-concessional loans to developing countries

for the purchase of needed drugs and vaccines from U. S. companies or their overseas subsidiaries in developing countries. Of course, such a procurement program in the U. S. context would have to give due consideration to the avoidance of any antitrust implications.

These pharmaceuticals would be distributed to the people of the recipient countries primarily through public channels but also through private voluntary organizations and multilateral agencies. Wherever appropriate, the loans would include cost-recovery provisions (and incentives for cost-recovery) aimed at increasing the mobilization of local resources for health sector financing. Provisions would be made in the loan agreement for some or all of the loan repayment obligation to be cancelled if a mutually agreeable increase in health care expenditures is made by the recipient country.*

We believe this approach (which is described fully in Section 3) will make a major contribution to removing the obstacles to better utilization of pharmaceuticals in developing countries. Specifically, it should:

- . increase the volume of resources available to purchase needed drugs and vaccines;
- . link together financing for pharmaceutical imports and improvements in health care delivery and in pharmaceuticals distribution;

*

While this report focuses on a change in the foreign assistance program of the United States, the proposal could equally well be an appropriate component of other bilateral and multilateral assistance efforts.

- . promote an increase in domestic resources allocated to health care;
- . strengthen the incentives for development of new drugs and vaccines;
- . ensure appropriate standards and quality.

The amount of financing of this type that could be absorbed by developing countries runs into the hundreds of millions of dollars. However, we believe a successful pilot program could be launched on a much more modest level to assess its viability. Once the concept has been proven and experience has been gained in a few small lending operations, the program could be expanded to a more reasonable scale.

IMPROVING THE AVAILABILITY OF PHARMACEUTICALS IN DEVELOPING COUNTRIES

SECTION 1:

THE NEED FOR MORE AND BETTER DRUGS

Inadequate availability and utilization of pharmaceuticals is a major problem in developing countries. Seventy percent of the population of these countries have little or no access to modern drugs and vaccines. The result is that many diseases that have been controlled in developed countries remain major causes of suffering and death in less developed nations. The World Health Organization estimates, for example, that about five million children in developing countries die each year from measles, pertussis, tetanus, poliomyelitis, diphtheria, and tuberculosis. All of these diseases have been substantially conquered in developed countries through immunization programs and other public health efforts. Probably 20% of the deaths among children under five years of age in developing countries could be prevented by currently available vaccines, saving perhaps 2 1/2 million lives each year. Malaria is another example of a disease that can be prevented or treated with modern drugs but which continues to kill one million people per year, mainly children. Several hundred million people lack the benefits of either vector control programs against malaria or access to treatment, although they live in areas where this disease is endemic.

Beyond these preventable or treatable diseases, however, there remain major challenges for the development of new drugs

and vaccines. As in the case of the principal infectious diseases in the industrial world, pharmaceutical interventions appear to promise the most cost-effective means of intervening to prevent or cure these (mainly parasitic) diseases. At present the only way of dealing with several of these diseases is through vector control programs requiring education, behavioral changes on the part of the affected population and often major capital investments in waste disposal, water supplies, housing, and the like. Safe and effective vaccines for some of these diseases may be possible in the not-too-distant future. For others, hope lies in finding better methods of treatment. In all cases, substantial research remains to be done. Improvements are also needed in existing vaccines and drugs to make them easier to store and administer (e.g., more thermo-stabile) and less toxic. The recent eradication of smallpox on a worldwide basis was made possible by the successful development of a freeze-dried vaccine. Although it is perhaps an exceptional case, smallpox eradication illustrates both the capacity for use of medical technology to solve major health problems and the highly cost-effective nature of such solutions.

Inadequate availability and utilization of pharmaceuticals is, however, only one aspect of the health problem of developing countries. More effective use of existing agents and potential new drugs and vaccines must be seen as part of a much broader effort to improve the health status of people living in developing countries. Moreover, efforts to improve the supply of

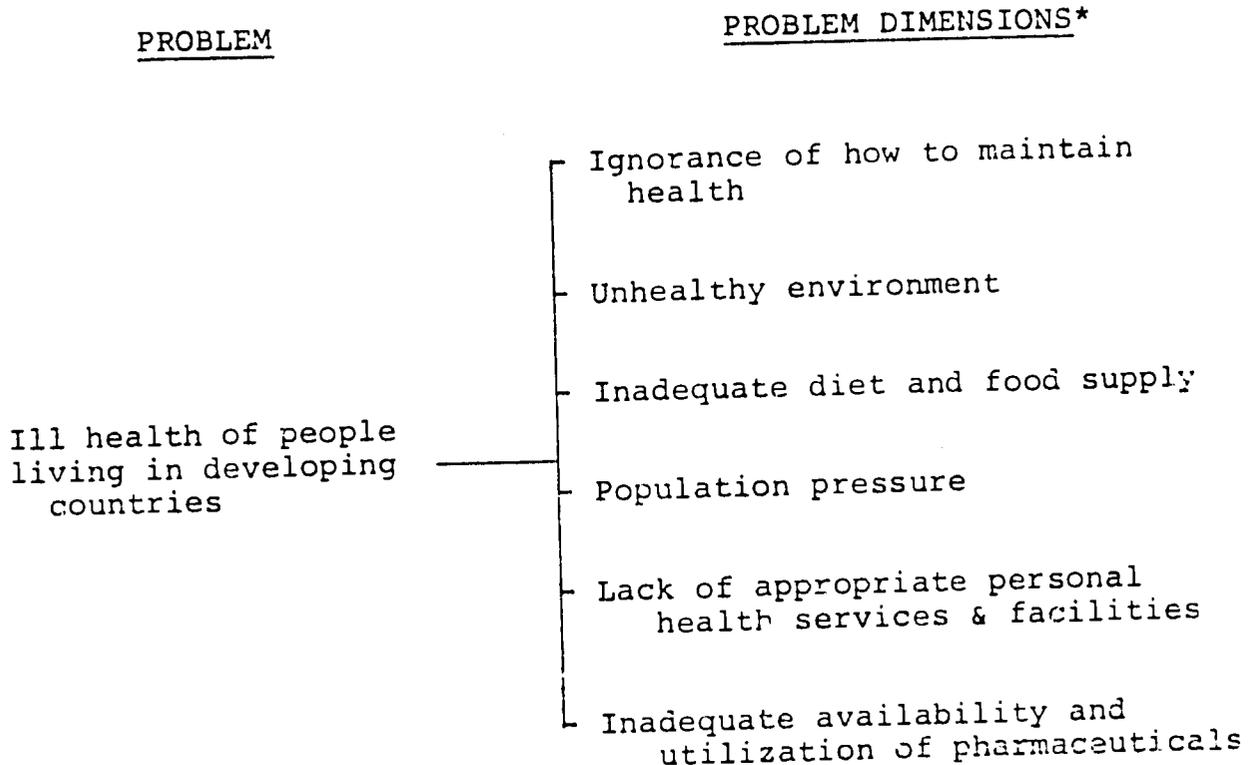
pharmaceuticals must take into account the specific obstacles that presently stand in the way of the flow of drugs and vaccines to people who need them the most.

Major Dimensions of the Ill Health Problem

Exhibit 1 on page 4 illustrates diagrammatically the major dimensions of the problem of ill health among people in less developed countries. Ignorance of how to maintain health lies at the heart of many aspects of ill health. It compounds the effects of the other dimensions of the health problem. Many people in developing countries live in disease-ridden, parasite infested environments; their lack of knowledge about both the origin of disease and the importance of simple personal hygiene exposes them to more or less continuous infection from the environment in which they live. A prime example of how ignorance contributes to disease problems is the infant diarrhea complex. Too frequently mothers react precisely the wrong way to this endemic problem among their children: they cease feeding. A large portion of the deaths among young children due to the complications of diarrhea can now be prevented through (a) education of mothers in how to handle diarrhea, and (b) widespread distribution of packets of oral rehydration salts (together with instructions in their use).

The unhealthy environment, already mentioned, plays a dominant role in the high proportion of the disease problems of developing countries. Because of a lack of even simple waste disposal, water supplies are frequently contaminated, leading to the rapid

PROBLEM OF ILL HEALTH IN DEVELOPING COUNTRIES
HAS SEVERAL MAJOR DIMENSIONS...



*

The description of the health problems of less developed countries contained in this exhibit is admittedly somewhat arbitrary and general. It is intended only as a framework to set the problem of inadequate pharmaceuticals in perspective. A similar framework can be found in the World Bank's Health Sector Policy Paper, Second Edition.

transmission of all types of communicable diseases. Some diseases are hazards of the tropical environments in which people live (e.g., malaria) and can only be eliminated through extensive vector control programs. It is estimated, for example, that perhaps 800 million people are exposed to the risk of schistosomiasis. Exposure to various types of worms is so extensive that multiple infections are the rule rather than the exception.

An inadequate diet also is a major contributory factor in disease problems, especially for maternal and child health. Ignorance of basic dietary requirements is part of the problem; shortages of basic food requirements are, of course, part and parcel of the poverty syndrome. Weaknesses due to malnutrition lower resistance to disease, and certain diseases in turn compound the problems of malnutrition. Moreover, diseases directly traceable to malnutrition are a major health problem in themselves.

Population pressure both contributes to, and is fostered by, the health problems of developing countries. It contributes through inadequate birth spacing (which increases risks to the mother's health, lowers the birth weight and physical development of newborns, and forces premature weaning), through nutritional deficiency arising from pressures of scarce food supplies and through overcrowding. Pressure to maintain high fertility, however, is closely linked to high infant and child mortality rates, with the consequent threat to the future security of parents. Population control measures may not be fully effective

until progress is made on increasing the life expectancy of people living in rural and semi-urban areas.

The lack of appropriate personal health services, especially in rural and poorer urban areas, is a somewhat different dimension of the problem of ill health. Ignorance, an unhealthy environment, and inadequate nutrition are major causative factors of ill health; the absence of needed health care personnel, their sometimes inappropriate training, and their frequent geographic maldistribution allow the problems of ill health to continue. Building up primary health care services is now generally accepted as the first priority of developing country health programs and the foreign assistance efforts of the major donor countries. It is important that these services be appropriate, i.e., that they are integrated and comprehensive, and that they emphasize prevention and primary care for the broad spectrum of the population rather than intensive high cost care for the few.

Inadequate availability and utilization of pharmaceuticals as noted above, also a major dimension of the problem of ill health in developing countries. Just as a lack of personal health services contributes to the perpetuation of the poverty-disease syndrome, so also the shortage of appropriate drugs and vaccines prolongs preventable and curable suffering and death. It is clear that a lack of needed pharmaceuticals is not the only reason for poor health status in developing countries, but it is an essential component. Providing a cost-effective means of preventing and treating diseases is indispensable to the improve-

ment of health status; this is a role that has been played by pharmaceuticals in the past and is one that will continue in the future. Indeed, because of the large capital expenditures required to develop extensive health care facilities and manpower for secondary and tertiary care, pharmaceuticals may be the only possible method of intervention for some time to come (albeit a less than complete solution to many health problems).

To a large degree, the roles of personal health services and pharmaceuticals have been de-emphasized in the health policy arena in recent years. This has perhaps been overdone. While other measures in addition to the development and distribution of drugs and vaccines are required to conquer fully these diseases, the failure to provide effective pharmaceutical means of intervening in the disease problems of developing countries will consign the people of these countries to a generations' long process of economic and social development -- involving vast expenditures of sanitation, irrigation, water supplies, housing, and education -- before many disease problems can be overcome. The issue should not be seen, however, as an "either/or" situation but as "both/and". Drugs and vaccines by themselves are not, and will not be, a total solution; they are one part, albeit an essential part, of a broad strategy needed by developing countries in tackling the problem of pervasive ill health of their peoples.

Developing countries are estimated to spend 30-50% of their total health care budgets on pharmaceuticals (compared to 10-15% in developed countries). On the surface, this might indicate

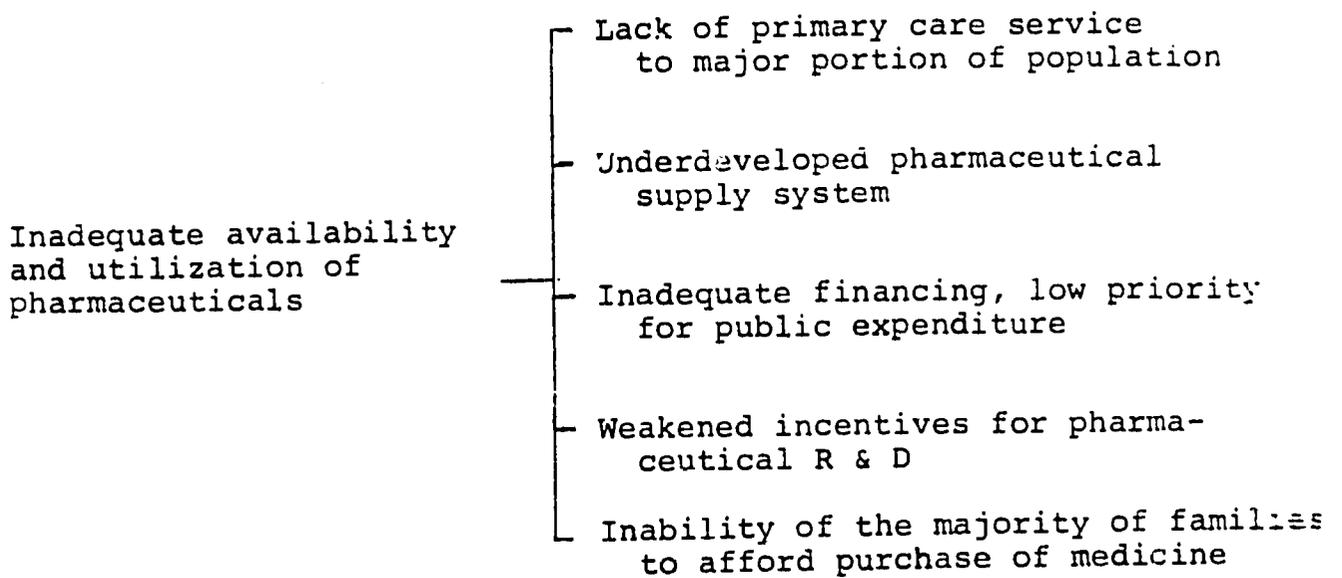
that too great a proportion of scarce health resources is being devoted to pharmaceuticals. These figures are misleading, however, for several reasons. Per capita health budgets in developing countries are themselves often quite small; a high proportion of total expenditures may translate into absolute purchases of pharmaceuticals on the order of \$1-2 per person per year, compared to expenditures in the industrial countries of \$35-50. Moreover, developing countries are constrained in their ability to control costs by lack of efficiency in purchasing and distributing pharmaceuticals. In addition, pharmaceuticals are often expensive relative to other health care inputs regardless of whether such pharmaceuticals are imported or produced domestically.

Total consumption of pharmaceuticals by developing countries was estimated to be about \$7 billion in 1977. According to one estimate of need made by a UN agency (UNIDO), the absolute minimum consumption should be more than 2 1/2 times that figure.

The Pharmaceutical Supply Problem

Viewed in isolation, the problem of inadequate types and amounts of pharmaceuticals in developing countries could appear to be solvable by a combination of (a) some form of subsidy for the purchase of needed drugs and vaccines, and (b) increased support for research and development on diseases of the tropics. However, there are several aspects of the problem that go beyond the lack of financial resources in developing countries (Exhibit I, page 9).

INADEQUATE UTILIZATION OF PHARMACEUTICALS
STEMS FROM FIVE MAIN FACTORS...



1. Lack of an adequate delivery system to reach underserved groups. More drugs and vaccines, whether imported or produced domestically, will not help reduce morbidity and mortality unless they reach those in need. The shortage of primary health care in developing countries not only deprives their populations of the attention of physicians, nurses, and health assistants, it also effectively blocks them from receiving the preventive and therapeutic agents needed to maintain or regain health. Without substantial further development of primary care delivery, additional pharmaceuticals cannot be utilized with complete effectiveness.

2. Inadequate distribution system for pharmaceuticals. While a sound health care delivery system is essential to the effective utilization of more drugs and vaccines, present shortcomings in the pharmaceuticals supply system within developing countries often restrict availability of needed products. In recent years, much has been written about the supply of pharmaceuticals in the developing world. Several UN agencies have recommended widespread development of domestic industry as a means of reducing the cost of pharmaceuticals and saving foreign exchange. While it is by no means clear that developing countries should embark on extensive local manufacture of pharmaceuticals, there are nonetheless real problems with current logistics, managerial and quality control aspects of the public pharmaceutical sectors of most developing countries.

In brief, many countries (especially the poorest ones) are not able to store and distribute drugs and vaccines adequately. They lack such fundamentals as a complete cold chain for vaccines needing special handling, inventory control systems, and transportation. Out-of-stock and out-of-date problems are common, especially in outlying areas. Spurious drugs, duplication of products, poor price comparisons, and inappropriate packaging are also frequently cited problems. Effective quality control mechanisms to ensure the safety and efficacy of both imports and domestically produced drugs is missing; this shortcoming is becoming more critical as developing countries seek to expand purchases of non-branded (generic) drugs from non-traditional suppliers and to engage in more domestic manufacture.

Through their bulk purchasing and procurement programs, WHO and PAHO are attempting to mitigate the financial constraints to pharmaceutical and vaccine procurement by small nations. However, an additional major roadblock to better utilization of pharmaceuticals is the state of development of the domestic pharmaceutical sector within countries themselves. Steps are needed to strengthen this sector, initially not so much in manufacturing as in packaging, quality control, and distribution.

3. Weakened incentives to new drug research and development.

For several years now, concern has been mounting about the adequacy of research and development on diseases of the tropics, that is, on diseases that predominantly affect people in develop-

ing countries. As discussed above, there are major health problems for which no, or inadequate, preventive therapeutic agents exist. The vast majority of new drugs and vaccines have been developed in the Western industrialized countries, almost exclusively by the profit-oriented multinational companies. In part, certain disease problems have not yet been adequately addressed due to severe market limitations, themselves a result of the poverty of the people who suffer from the diseases. Limited markets make it highly difficult for private firms to recover R & D costs from a new product. Nor has there been any significant government support for research in this area.

Steps have been taken in recent years to improve this situation, although public funds for such research in the U. S. and elsewhere remain miniscule compared to the financing available for non-tropical disease research. Official funding has been found for such efforts as WHO's collaborative tropical disease research program. Also, the expanded awareness of the need to control certain diseases whose spread has been increased by economic development (e.g., schistosomiasis) has helped build up market incentives for private firms. However, these incentives have been weakened by other factors such as a lack of patent protection, price controls, and the prospect of severe restrictions on the range of products that can be marketed in particular countries. In short, market uncertainty has increased and with it the risks associated with decisions to make major R & D commitments to drugs and vaccines whose potential is restricted to developing countries.

4. Inadequate mobilization of domestic resources. The relative poverty of developing countries restricts their ability to finance health care for their people. Hence, major contributions to the health sector have come from private and public external resources, and will need to continue to do so for many years into the future. However, the priority accorded to health has in some instances been low. Health care expenditures in many developing countries amount to only about 2-3% of GDP compared to 5-10% in developed countries. As national and international inflation continues, energy import costs rise, and external payments positions are put under severe pressure, the economic problems facing developing countries are likely to discourage increased domestic investment and recurrent budget allocations to the health sector. Domestic health allocations, measured in real terms are, at best, likely to remain constant.

Within this total, the pattern of expenditure is commonly biased towards secondary and tertiary care for the urban elite. The underdevelopment of the public delivery system affects, to the largest extent, the rural and urban poor who are dependent on that system for provision of health care. In almost half of the developing countries, government expenditures on health are no more than \$2 per person per year (compared to more than \$200 for some industrialized countries).*

Part of the reason for the low priority accorded to health sector financing in developing countries has been an excessive

* World Bank Health Sector Policy Paper, pp. 27-28, Annex 7.

emphasis on investment in physical capital as the primary means of development. However, treatment of social services (such as health) merely as a form of consumption is waning; instead, health care expenditure is seen increasingly as an investment in human capital that can increase productivity and total output within the economy. Improving the utilization of pharmaceuticals depends on building on this trend and increasing the perceived value of drugs and vaccines in the development process (along with personal health services) so as to raise the priority and funding for the health sector itself.

These four main dimensions of the pharmaceuticals supply problem -- lack of personal health services for large segments of the population, weak pharmaceutical distribution systems, inadequate incentives for the development of new drugs and vaccines, and insufficient mobilization of domestic financial resources -- must all be addressed in any program to increase utilization and availability of drugs and vaccines in developing countries. More importantly, the overall problem of pharmaceuticals must be seen within the perspective of the broader causes of ill health and their solutions, namely education and training in the health area, improvements in environmental sanitation, population control, better nutrition, and expansion of appropriate personal health services. The next section reviews present U. S. development assistance policy and considers how expanded support for pharmaceuticals imports would fit into those efforts.

SECTION 2:

U. S. FOREIGN ASSISTANCE FOR HEALTH

In recent years, U. S. development assistance has become more focused on basic human needs (e.g., health). The purpose for this focus is twofold: First, to ensure that the benefits of development reach those most in need; second, to foster economic development by contributing to the development of human resources. Accordingly, there has been a shift in the U. S. assistance away from physical infrastructure projects (e.g., roads) and toward investments in education, training, nutrition, and health care. This twofold purpose springs from a recognition that access to health care is (or ought to be) a basic human right and that the broader goals of development are to secure such rights for all the people of the world.

Improving the health status of people in developing countries, especially the underserved poor in rural and urban areas, is recognized in U. S. foreign assistance planning to be a multifaceted problem. Reduction in the incidence of death and disease involves a wide range of social and economic advances, including the provision of clean water for drinking, bathing and washing; more adequate nutrition; sanitary disposal of human wastes; better housing; education with respect to personal hygiene and nutrition; and, access to personal health services. Indeed, policy makers tend to see the health sector in quite broad terms, encompassing a range of activities traditionally not directly linked to health.

This breadth of focus is reflected in the character of the specific projects financed by the U. S. aid program. While some projects are fairly narrow, most have multiple components; that is, they incorporate to various degrees activities such as primary care, sanitation, training, and water supply improvements. U. S. financing also covers a range of inputs to these projects, with the determination of items financed and financing terms (e.g., grants, long-term loans) flexibly determined according to both project characteristics and the status of the recipient country. This flexibility is important in developing cooperation with other donors.

Exhibit 3 on page 17 gives a broad assessment of the present U. S. assistance program in terms of its coverage of the major dimensions of developing countries health problems discussed earlier. As Exhibit 3 indicates, existing U. S. assistance efforts represent a balanced response to the problem of ill health of people living in developing countries. One of the main opportunities for expansion of health care assistance lies in the area of pharmaceuticals.

With respect to the dimension of ignorance about the causes and treatment of illness, present U. S. programs lay strong emphasis on training and education efforts. Much of this training is directed toward the promotion of primary health workers who can provide basic services to the rural and peri-urban poor. The focus of such training, however, is on general problems of health, especially in rural areas, so that the health care worker

PRESENT U. S. HEALTH ASSISTANCE LEAVES
SCOPE FOR EXPANDED SUPPLY OF PHARMACEUTICALS...

EMPHASIS IN PRESENT
U. S. FOREIGN ASSISTANCE PROGRAM

PROBLEM

PROBLEM DIMENSIONS

<p>Ill health of people living in developing countries</p>	<p>Ignorance of how to maintain health</p>	<p><u>Strong:</u> Training programs emphasize development of appropriate skills and knowledge for rural health workers including health education.</p>
	<p>Unhealthy environment.</p>	<p><u>Strong:</u> Sanitation and water supply major priority. Also, vector control programs for specific diseases.</p>
	<p>Inadequate diet and food supply</p>	<p><u>Strong:</u> U. S. accounts for majority of world-wide food assistance. Increasing development emphasis on nutrition and domestic agricultural projects</p>
	<p>Population pressure.</p>	<p><u>Strong:</u> U. S. leadership widely acknowledged. U. S. supplies bulk of family planning materials (including pharmaceuticals).</p>
	<p>Lack of appropriate personal health services and facilities.</p>	<p><u>Growing:</u> Now number one priority. Emphasizes poorest/underserved groups. Integrated services approach.</p>
	<p>Inadequate availability and utilization of pharmaceuticals.</p>	<p><u>Growing:</u> Part of primary care emphasis. 20-40% of some projects devoted to pharmaceuticals and other commodities.</p>

can begin to prevent disease and foster self-treatment through education of the population themselves.

Similarly, U. S. assistance has traditionally made a major contribution to environmental aspects of the health problem through water supply and sanitation projects. Moreover, the U. S. participates in or contributes to vector control programs relating to specific disease categories (e.g., the Onchocerciasis Control Programme, and the WHO/UNDP/World Bank-sponsored Special Programme for Research and Training in Tropical Diseases). U. S. support for nutrition (through its food assistance program) and population planning dominates such problem-specific financing.

The expansion of primary health care has become the highest priority for U. S. health assistance policy. Allocations for primary care projects have increased in recent years. In some respects, these projects are intended to respond to the whole range of problem dimensions shown in Exhibit 3. Indeed, U. S. policy emphasizes the integrated nature of health problems and hence the corresponding need for the expansion of primary care to take place in developing countries in a balanced and comprehensive manner.

Provision of finance for pharmaceuticals has not been a major focus of U. S. policy until recently with the exception of the population program, which has the widespread distribution of family planning materials as its major goal. In keeping with the build-up of emphasis on primary care, more financing of drugs, vaccines and other medical supplies is being done. In some health

projects, commodities account for 20-50% of total project cost.

Expanded financing for pharmaceuticals represents a major opportunity for the U. S. foreign assistance program for three main reasons. First, because pharmaceuticals represent such a major component of total health care expenditures, especially of foreign exchange costs, the need for such financing is great and will become greater if access to primary health care is to be extended in developing countries. Second, unless the supply of drugs and vaccines can be assured, the benefits of primary health care projects will diminish over time and/or will fail to be realized from the outset. Experience has shown that unless a community can be assured that acute health crises are being met, a basis of trust -- the key to acceptance of preventive measures -- is extremely difficult to attain.

Lastly, since the supply of pharmaceuticals is the key commodity problem in expanding primary care, it lends itself to a type of financing that can be used as a tool to reinforce improvements in the health sector generally in developing countries. This last point is discussed in detail in the following section.

SECTION 3:

THE PROPOSED FINANCING STRATEGY

The suggested financing mechanism for expanded funding of pharmaceutical imports by developing countries is part of a much broader effort by the Center for Public Resources (CPR) to establish new forms of public/private partnership aimed at realizing the potential for better use of pharmaceuticals in developing countries. CPR's program includes efforts in strengthening the incentives for research on diseases of the tropics, in developing an industry-sponsored fellowships program in logistics training, and in creating a technical assistance clearinghouse, as well as in stimulating better financing for purchases of pharmaceuticals by developing countries. This proposal for expanded funding is designed to meet to a substantial degree all of the major hindrances to improved utilization of drugs and vaccines described in preceding sections of this memorandum. Section 3 first describes the mechanics of the proposal and then briefly reviews how its objectives match up with the major dimensions of the problem.

How the Strategy Would Work

The basic concept underlying the proposed mechanism is the financing of needed imports. For some time into the future, most developing countries will continue to rely on foreign sources for drugs and vaccines. This is especially true of those pharmaceuticals whose technical characteristics demand large-scale manufacture, and of many pharmaceuticals that can be imported in bulk for local formulation and/or packaging. Unfortunately,

the deterioration in developing countries' economic prospects in the last year has substantially reduced their capacity to pay for pharmaceuticals (or other imports) out of export earnings. As a result, developing countries' needs for external financing of pharmaceuticals imports has increased.

The discussion in preceding sections suggests, however, that several key conditions need to be laid down for this financing. First, its provision should be tied to improvements in health care delivery and internal distribution of pharmaceuticals. The emphasis should be on generating investments in the health sector. Second, the drugs and vaccines thus financed should reach the appropriate target groups (i.e., mainly the underserved rural and urban poor). Third, to the extent possible, the financing should be provided in ways that help mobilize the recipient countries' domestic resources for purchase of pharmaceuticals and other health care inputs. Recurrent costs, in the final analysis, must be met through the use of domestic capabilities.

We propose that this financing be provided under a program analogous to the Food-for-Peace Program. Under this similar approach, the U. S. would provide loans, with significant grant potential, to selected developing countries to cover the cost of importing pharmaceuticals that are needed and requested by the recipient country. Such pharmaceuticals would be imported directly from the U. S. or, with appropriate waivers, purchased from overseas subsidiaries of U. S. companies located in develop-

ing countries. Procurement would be by competitive bidding.

The repayment terms for loans would be appropriate to the particular country, following the policy guidelines already established in the foreign assistance program. Loans would vary in their degree of concessionality (i.e., the degree to which the interest rate and repayment terms are below prevailing private market terms) but all repayment obligations would be in dollars. Conditions would be laid down in the loan agreement which, while tailored to the specific circumstances of the recipient countries, would usually include provisions as to the type of pharmaceuticals to be financed, the method of procurement, and their use and distribution within the country.* To give a further incentive to the recipient country to build up the health sector, we propose that a loan forgiveness feature be included in the financing program. That is, a portion of the dollar repayment obligation would be cancelled (i.e., the loan would be converted to a grant) in line with pre-agreed and mutually acceptable increases in local currency health care funding.

While this approach could be applied successfully within specific health care projects, its main benefit would be in strengthening the financing of the health sector generally. Moreover, because such a large proportion of health care in many developing countries is delivered through private

* AID has a well-developed set of procedures to be followed in procuring pharmaceuticals, including a list of eligible items, price guidelines, and review of the need for, and appropriateness of, the pharmaceuticals requested by the country.

voluntary organizations (PVOs), a PVO-oriented grants program could appropriately be included in expanded financing for pharmaceutical imports.

Health Sector Lending

Nonproject lending for health sectors has not played a large role in U. S. assistance programs, yet it offers substantial potential for expansion of assistance. Such loans are usually popular with recipient governments because of their general character. Moreover, they have the potential to significantly enhance the policy influence of the donor governments. Finally, disbursement of funds from such lending generally takes place much faster under nonproject lending since the type of imports financed are commodities whose use does not depend on, for example, lengthy construction efforts, and thus can be readily absorbed by the recipient country.

Among the most common criticisms of nonproject assistance are the difficulty of ensuring that the appropriate target groups actually benefit from the assistance and the potential for long-term dependency on foreign financing.

It is expected that the major part of the proposed financing program would take place as this type of general support for the health sector. Most loans would be made for the purchase of pharmaceuticals not tied to specific projects, and the imported drugs and vaccines would be distributed through whatever channels are typically used in the recipient country. At the outset, it is

expected that most of the lending would be in the form of government-to-government loans for the purpose of improving the supply of pharmaceuticals in the public sector. But while the government of the recipient country would be the purchaser of the pharmaceuticals, actual procurement might take place through U. S. government agencies or multilateral organizations, as well as directly from the pharmaceutical companies.* Distribution of the pharmaceuticals could take place through official government channels (e.g., rural health centers), through the programs of private voluntary agencies or through multilateral organizations.

The specific operation of the loan forgiveness feature in these loans would be tailored to country circumstances. Two main options might be offered. The first would apply to countries in which cost-recovery policies are ruled out by severe economic constraints. In these countries, a portion of the dollar repayment obligation would be cancelled in line with an increase in local currency made available for health sector investment in primary care or drug/vaccine logistics systems. Attaching this sort of condition to the loan forgiveness feature would give ministries of health additional leverage in requesting increased sector funding from ministries of finance and planning. That is, an infusion of local currency into the health sector would cancel

* All purchases would be subject to established AID review procedures. It is recognized that specific procurements by multilateral organizations for a U. S. program would require prior general policy clearance by their administrators.

a dollar repayment obligation, thereby both encouraging investment in the health sector and reducing the general debt burden of the economy. Such an approach would require careful monitoring by U. S. authorities similar to that required for the collection and expenditure of counterpart funds generated by local sales of the pharmaceuticals. In particular, some assurance would be needed that expanded health care funding that is treated as counterpart expenditures for purposes of loan forgiveness was not previously programmed into the national investment budget.

In a second group of countries, local currency revenues may be generated through sales or program pharmaceuticals either to the public via a cost-recovery program or to public or publically utilized private distribution companies. These revenues, also called counterpart funds, would be earmarked for use in the health sector. In such cases, a portion of the dollar repayment obligation of the pharmaceuticals loan would be cancelled (i.e., the loan would be converted to a grant) in line with expenditures of the local currency counterpart funds for expansion of the primary care system or of the pharmaceuticals logistics and distribution system. Such a forgiveness procedure would encourage cost-recovery programs and help develop health sector self-reliance.

As with other types of sector lending, commodity loans could also be used to support major reforms or institutional changes in the health sector generally. For example, a country may wish to undertake a major reorganization of its health sector, cutting back on certain types of services and expanding primary care in

underserved areas. New services and charges may be introduced. Sector loans could facilitate such change by providing general support to the health sector during the period of transition and cover the initial cost of expanding certain services. Or, a country may wish to bring about substantial reform of the pharmaceutical distribution system; a sector loan would give the right sort of general support for such changes. The end result of such programs would be a larger or more efficient health sector, with an enhanced domestic priority for health.

In principle, the most straightforward way of providing support for the health sector generally would be through a general program loan rather than through commodity assistance. While this is true, there is one overwhelming practical reason for preferring the commodity approach: it is politically more acceptable in donor countries. This preference reflects both the desire to promote donor country (e.g, U. S.) exports as part of the foreign assistance effort, and a perception that it is easier to ensure that a tangible commodity produces the intended benefits than is the case with untied financial assistance. In part, this is because supplying a commodity puts a strong obligation on the recipient country (and the donor agency) to ensure that a distribution system is developed to handle the commodity efficiently.

Project Emphasis

As noted above, U. S. foreign assistance programs have already been expanded modestly in the area of support for health care com-

modities, including pharmaceuticals within specific health projects. While coverage of some local costs has provided a limited amount of free foreign exchange, the fact that relatively little commodity assistance is provided means that the recipient country must cover a major project cost component (i.e., pharmaceuticals) with other resources. This component also often represents the major portion of foreign exchange costs associated with health care projects; this is invariably true of the recurrent costs involved.

To some extent, developing countries have sought financing for the pharmaceutical component of these projects from other donors. However, as a matter of policy for most donors, foreign assistance is intended to be temporary or self-liquidating with respect to a particular project. This raises complex issues in the case of health projects where the benefits often take a long time to appear (in some cases the better part of a generation) and where it is difficult to "capture" these benefits financially in any clearly defined way.

These considerations suggest that, first of all, support for import of pharmaceuticals may need to be of a longer term nature than other project components. That is, the number of years in which assistance is provided may need to extend beyond other aspects of the project (e.g., training of health workers) and the terms on which the assistance is provided may be more lengthy and or concessional. Second, where economically appropriate, the pharmaceuticals should be provided in a way that generates local resources

to cover at least part of the costs of the health care system.

In many instances, the scope for prescription fees or sale of the pharmaceuticals is very limited, particularly in projects that are designed to meet the needs of the poorest population groups. In some projects, however, it may be possible to generate local currency funds from sale of the pharmaceuticals, particularly if some type of a fee-for-service approach is an accepted part of national health policies. For example, cooperative village pharmacies might be promoted under this program to stimulate "self-help" financing of health care. The counterpart funds thus generated might make a significant contribution to the financing of local health services. The loan forgiveness feature of this proposal would give the recipient government an incentive to seek to develop acceptable means of recovering costs since the cancellation of the repayment obligation depends on both the generation of local currencies and their use on health sector improvements.

Nevertheless, there will be situations where local cost-recovery is not possible but where prospects will be good for "leveraging" the resources provided through CPR's proposed program so as to promote increased funding in the health sector. In such cases, the loan forgiveness feature could be utilized in the same way as was outlined above for nonproject loans, i.e. part of all of the loan repayment obligation could be cancelled on condition that a measurable increase in health sector funding takes place. In this way, the benefits of increased donor influence

on health sector priorities and on the perceived importance of the health sector as a whole could be gained without requiring the introduction of cost-recovery mechanisms in situations where their implementation would be likely to generate severe problems.

PVO Grants Program

A significant portion of the PL480 food assistance is channeled through private voluntary organizations (PVOs). This is particularly the case with the targeted nutrition programs for the poorest population segments. In these programs, grants of food (plus handling costs) are made by the U. S. government to specific private agencies who take responsibility for distributing the food in the country.

CPR proposes that a similar PVO component be included in expanded funding for the importation of needed drugs and vaccines. In many instances, the same agencies that are engaged in nutrition programs also provide health care services.

Financing under this component would be on a grant basis. The PVO representatives in the country would work with the resident AID mission to develop specific proposals for funding. Once reviewed and approved, the U. S. headquarters of the PVO (or its agent) would arrange the purchase and shipment of the pharmaceuticals.

Potential Benefits

The financing proposal is designed to respond to the major problem dimensions described above. With respect to the shortage of financial resources, the gain to developing countries is obvious.

increases in loans and grants for the purchase of pharmaceuticals will directly assist funding for health care in recipient countries and thereby enable imports of needed pharmaceuticals to be expanded.

The proposal, however, would provide this additional finance in such a way that primary health care delivery would be built up in parallel with the increased supply of pharmaceuticals. This would be accomplished by tying the pharmaceuticals to specific projects, by attaching policy conditions to broad, sectoral loans and by forgiving a portion of the loan on condition that additional local resources are used in approved projects or other purposes aimed at strengthening the health care system.

Similarly, loan conditions could be shaped in appropriate cases so as to require strengthening of the pharmaceutical sector to ensure that needed drugs and vaccines can be imported, finished, stored, and distributed in such a way as to protect the safety and efficacy of pharmaceuticals reaching the final consumer. Indeed, the legislation setting up the program would probably contain provisions requiring that drugs and vaccines financed by the program are not subject to loss, spoilage or "profiteering". In some instances, improvements in the delivery mechanism may need to precede actual shipments.

Improving pharmaceutical supply systems in recipient countries could be an area where the resources of the pharmaceutical industry might be brought to bear through new forms of public/private partnerships. The industry is the dominant reservoir of expertise in

logistics management of pharmaceuticals. Moreover, because of its international character, this expertise extends to the problems of developing countries. The question is how to enlist the resources of the industry in an effective way that is also acceptable to a variety of developing countries.

One approach currently being explored by CPR is to create an industry-wide Technical Assistance Clearinghouse, in which experts from different companies would be temporarily seconded to assist developing countries draw up programs to improve pharmaceutical delivery within the public sector.* The program would be managed by an organization outside the industry, probably by CPR. These studies, which would be financed by multilateral or bilateral organizations or by developing country governments, would help give assurance that the pharmaceuticals supplied under the proposed financing program could be used effectively.

Beyond these initial studies, further industry involvement might be of two types: First, teams of industry specialists might be involved in implementing needed improvements (e.g., inventory controls) or in training local staff. Second, in appropriate instances, private companies might also be encouraged to make investments in local manufacturing and distribution of pharmaceuticals, perhaps as part of the programs of the Overseas Private Investment Corporation (OPIC). While OPIC has pursued some investment insurance activity in this area, additional incen-

* Annex A describes the proposed Technical Assistance Clearinghouse in more detail.

tives are needed to transform this effort into an aggressive pursuit of such opportunities.

Influence on the allocation of domestic resources to and within the health sector through the broader support for pharmaceuticals is expected to bring about a more balanced program of public expenditure. The goal would be to alter the pattern of investment within the recipient country towards a higher level of expenditure per capita on health and one that is more evenly distributed across the total population.

Finally, we believe that this approach can contribute significantly to strengthening incentives for development of needed new drugs and vaccines. It will do so in part because it will generate additional demand for pharmaceuticals by developing countries. This effect could become very important if the program is implemented on a substantial scale (as, for example, has been the case in the population control area). However, even without large expenditures, a financing program for pharmaceutical imports will help to improve markets for existing drugs and vaccines and thereby create a more robust, less risky environment for the development of new or improved means of disease interventions. Moreover, efforts to strengthen primary care and pharmaceutical distribution systems will make the utilization of drugs and vaccines more widespread and more effective. Both of these benefits to the people of developing countries will tend to create, or reinforce, pressures to make more and better pharmaceuticals available.

Developing countries clearly need more and better pharmaceuticals. In addition, without substantially improved utilization of existing drugs and vaccines, they cannot expect to advance towards the improved health status that their peoples have a right to. Every year millions of lives are lost to diseases that can be prevented or cured with existing technology.

Improvement in drug and vaccine availability is, however, more than a matter of manufacturing and shipping the pharmaceuticals. It is also more than a matter of additional research on diseases of the tropics. What is required is a broad-front effort to build up delivery systems for primary health care, strengthen distribution systems, tilt the allocation of resources towards primary care and underserved groups, and to ensure the availability to urban and rural poor of new drugs and vaccines.

Present U. S. assistance efforts cover all of the major dimensions of the problem of ill health in developing countries. But emphasis has been given to the supply of commodities only in the population program. Only modest amounts have been made available to cover the cost of other pharmaceuticals. The expansion of financing to cover needed imports of drugs and vaccines thus represents a major opportunity for greater effectiveness of foreign assistance in the health sector.

The financing strategy described above and developed by the Center for Public Resources outlines a network for packaging this assistance in the form of project and sectoral loans and grants,

tied to specific improvements in primary care delivery systems, pharmaceutical distribution, and overall financing for the health sector. We believe that such an approach has great promise of success in ensuring that badly needed pharmaceuticals reach those who will benefit most and in so doing make the greatest possible contribution to the alleviation of the appalling human misery that pervades the developing world today.

Annex A

Technical Assistance Clearinghouse

Technical Assistance Clearinghouse

Background

One of the most frequently recurring problems facing the implementation and expansion of primary health care programs in developing countries is the great need for basic drugs and vaccines in the public health systems of poor rural areas. Pharmaceuticals, whether imported or produced domestically, cannot contribute to a reduction in morbidity and mortality unless they reach those in need. Regular and recurring supply shortages or the supply of ineffective products undermines not only the technical effectiveness of health care workers but also the confidence of those workers and the communities which they serve. That latter confidence is the basic foundation fundamental to primary care services.

While the importance of pharmaceuticals quality and distribution is increasingly recognized as important to the design of primary care programs, neither development assistance agencies nor most developing countries themselves house the expertise needed to analyze and remove bottlenecks which plague primary care pharmaceuticals systems. That expertise is importantly concentrated in the private sector, within the pharmaceuticals corporations whose organizational success depends on the maintenance of product quality and its efficient delivery and distribution worldwide.

Proposed Technical Assistance Clearinghouse

Within the context of the Pharmaceuticals Program of the Center for Public Resources (CPR), it is proposed to establish a technical assistance clearinghouse to serve as a bridge between the needs of the public sector and the expertise of the private sector in assistance to the primary health care needs of the developing world.

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This clearinghouse would provide access to appropriate industrial expertise through the neutral, non-profit format of CPR itself so as to minimize the conflict-of-interest barriers which currently inhibit public-private sector cooperation on pharmaceuticals issues in developing countries. Based on agency discussions it is anticipated that the expertise sought by agencies and developing countries would initially involve two functions:

1. assistance both to agencies and to ministries of health to evaluate existing pharmaceuticals logistics systems and to assess the alterations necessary for increasing the availability and quality of pharmaceuticals to low-income rural populations;
2. assistance to multilateral and bilateral agencies in determining in recipient countries the quality and distribution patterns of pharmaceuticals financed by development assistance programs. This assistance might be in the form of service contracts developed in conjunction with specific agency procurement packages but, due to policy constraints and recipient country sensitivities, might be better managed via the neutral CPR forum.

Proposed Organization and Operation

Given its unique role as a joint public/private effort, the Pharmaceuticals Program of the Center for Public Resources would act as the intermediary among governments, agencies, and corporations in providing the above expertise. CPR would confirm the

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willingness of U. S. multinational pharmaceutical corporation to provide a fixed number of person-weeks (e.g., eight) per year in a given area or areas of expertise. The corporation would be reimbursed by CPR for the expert's time during any assignment.

Agreements would also be reached between CPR and development assistance agencies as to the scope of expertise likely to be requested and the methods of reimbursement.

Operationally, a typical project would function as follows:

- (a) an agency or LDC ministry would request expertise for a fixed amount of time and for a fixed scope of work, and would agree with CPR as to the skills needed, the prerequisites specific to the setting (e.g., language skills or country experience), and the rate of payment;
- (b) CPR requests from one of the cooperating companies secondment of an appropriate person to fill those parameters;
- (c) the above mentioned expert is seconded to CPR for the agreed period of time (e.g., four weeks);
- (d) CPR develops briefing material for the expert regarding the country, its health problems, the portfolio of activity of the sponsoring agency, etc.;
- (e) the sponsoring agency arranges one or two days of briefings regarding the assignment prior to departure of the expert;
- (f) the expert departs for the assignment; it is anticipated that this will often be in the context of a larger group of primary care analysts assigned to a broader health analysis for the agency;

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- (g) upon return, the expert's report is written at CPR and issued to the agency by CPR itself;
- (h) the expert returns to his/her parent company and regular duties, and CPR reimburses the company for his/her salary for the duration of the assignment.

It should be noted that all expenses incurred are reimbursed to CPR through the requesting agency, with the company contribution constituting a donation of the expert's time spent away from corporate responsibilities. Agency expenses include only the direct expenditures for the mission itself and the expert's reimbursement since the clearinghouse is administered through existing staff of the CPR Pharmaceuticals Program.

Recognizing that this clearinghouse effort would be a unique initiative, it is proposed that the first year of activity be maintained as a pilot effort. In 1981, only four to six requests for assistance would be accepted, and every effort would be made to ensure that each participating company receives only one CPR request for expertise during that period. At the end of 1981 the clearinghouse would be evaluated in terms of its utility to the agencies and developing countries requesting assistance, the benefits experienced by company personnel themselves in terms of increased understanding of the field conditions in developing countries, and the degree of demand such a system places on the corporations participating. At its 1982 meeting, the Task Force of the CPR Pharmaceuticals Program will review that evaluation, and will determine (a) the appropriateness of its continuation and (b) any need for expansion of the corporate network to include non-U. S. companies.



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