Chapter 7

Responding to needs: institutions, incentives and finance for future health R&D

This Report has highlighted a set of major challenges to global health at the end of the 20th century: an unfinished agenda of overcoming avoidable maternal and childhood conditions; a continually changing threat from microbes; rapidly emerging epidemics of noncommunicable diseases and injuries; and an acute shortage of data and knowledge to inform health policy and to combat inefficiencies and inequities in health systems. These challenges will place governments and health service providers under considerable strain, particularly in low-income and middle-income countries. And they will test, perhaps more than ever before, the capacity of the international health R&D community to respond with timely and appropriate solutions.

Yet that R&D community—a loose "system" made up of investors, research networks and research institutions in every specialty—is currently falling short of its potential to rise to these challenges. As the previous chapters have shown, the distribution of resources and effort across the spectrum of health problems appears to reflect uneven advocacy and special pleading rather than rational and coordinated responses to need. Some work is duplicated; significant gaps remain; and dispersion of resources constrains capacity to focus resources on the completion of high-priority R&D efforts.

At the crudest level, it is clear that the health needs of poor populations are receiving inadequate attention. The allocation of R&D resources in both public and private sectors reflects the preoccupations of the established market economies, with as little as 5% of total R&D resources being devoted to the health needs of developing countries where 90% of the world's disease burden is carried (Annex 5). The unevenness of this distribution appears to have persisted for some time, as the Commission on Health Research for Development observed a similar pattern when it began work almost a decade ago (Commission on Health Research for Development 1990). It is, of course, important to question the implicit assumption that these health problems are qualitatively different from those of the industrialized world, particularly as the distinction is being gradually blurred by demographic and epidemiological changes. However, in practice there are important distinctions. In particular, the responses that are appropriate to the emerging epidemic of noncommunicable diseases in developing countries must necessarily be different. If resource-poor countries are to provide equitable health services for their populations, they need to develop more cost-effective solutions for these diseases than those deployed in the rich countries.

The bias away from the needs of poor populations is exacerbated by the structure of incentives within the international market for researchers. The vast majority of high-quality scientists are drawn away from the areas of greatest need in the low-income and middle-income countries by the attractions of good facilities, easier links with their colleagues and better rewards for their efforts in the established market economies.

In the Committee's view, obstacles such as these are hampering the effectiveness of the overall R&D effort. Yet certain limited changes could, we believe, greatly enhance the prospects for responding to global needs. This chapter sets out some of the key problems and puts forward a number of realistic and practical proposals which, we argue, could help to harness R&D for international public good in a climate of restricted resources. Before discussing these proposals, however, we begin with a brief descriptive background on the current structure of the international health R&D system.

7.1 The international health R&D system

Health researchers and those who fund them are a highly diverse group. In the simplest scheme, the major players in the health R&D community may be divided into those who *do* research—the operational level—and those who *finance* research—the resource allocation level. Within each of these two broad categories there are further groupings which we set out below. The system is shown graphically in Figure 7.1.

7.1.1 The operational level of R&D

This consists of:

- **The health service providers** which, while rarely conducting any R&D directly, are inextricably linked with health research because they are the source of information about R&D needs, the end users of R&D products and the focus of most clinical research involving human subjects;
- **The institutions**, both discrete and linked into functional networks, that conduct R&D. At national level, these include universities, private institutes, government institutes, health care settings and the pharmaceutical industry. At the international level, there are

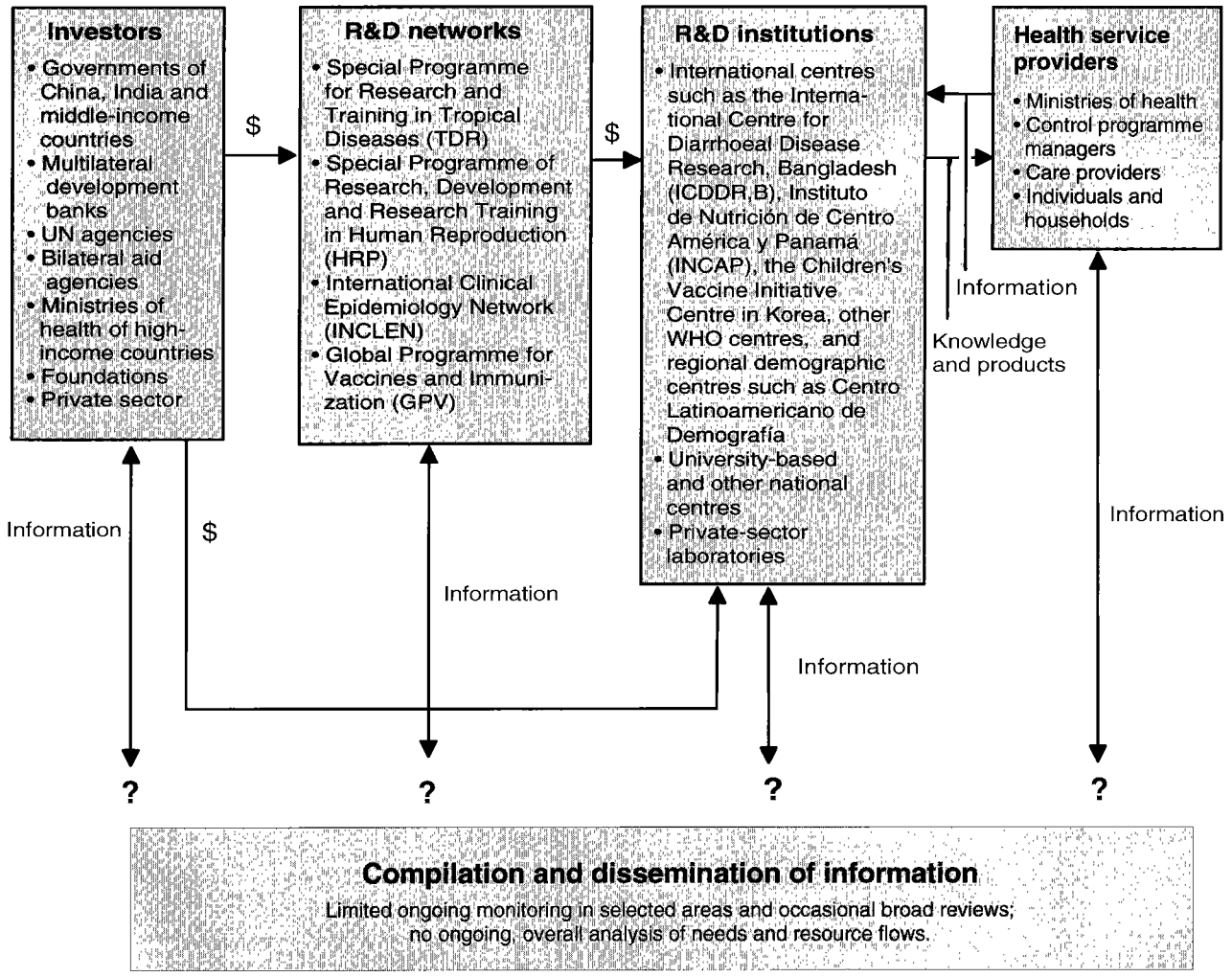
internationally supported institutions and operational networks such as WHO collaborating centres, the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), and the Instituto de Nutrición de Centro América y Panamá (INCAP). Annex 6 discusses the history and potential of international institutions (using ICDDR,B as an example), and points to how it is possible to gain high productivity in such a context.

7.1.2 The resource allocation level of R&D

This consists of two broad subgroups: R&D networks and other investors. These diverse groupings are summarized here; greater detail on individual bodies and programmes and their investment levels can be found in Annex 5. The main groupings are as follows:

- **Specific international R&D networks and programmes** that are charged with the responsibility of investing in focused R&D areas by their sponsors. These include certain special programmes of R&D located at WHO's headquarters in Geneva and supported by a number of international investors: the Special Programme for Research and Training in Tropical Diseases (TDR), and the Special Programme of Research, Development and Research Training in Human Reproduction (HRP), together with the Global Programme for Vaccines and Immunization (GPV). They also include the International Clinical Epidemiology

Figure 7.1 The international health R&D system: current structure



Network (INCLEN) and the International Health Policy Programme (IHPP).

- **Investors in R&D.** This highly diverse group includes public bodies, private foundations and nongovernmental organizations and operates at both national and international level. Some key groups of investors are:
  - (i) the governments of the established market economies, through their research councils, national institutes, ministries of health and official development assistance programmes and, in the cases of a few countries such as Canada and Sweden, their specialized development research agencies; and regional bodies such as the European Commission;
  - (ii) the governments of the middle-income countries, such as Brazil, Mexico, South Africa and Thailand; and large low-income countries, notably China and India, as well as the governments of selected other low-income countries with an interest in health research. As with (i) above, decision-makers may be within national research councils and/or ministries of health;
  - (iii) the UN agencies. As a specialized agency for health, WHO has a mandate in its constitution "to promote and conduct research in the field of health". Other UN agencies and funds involved in health research to varying degrees include the UN Population Fund, the UN Development Programme, UNICEF, the Joint UN Programme on HIV/AIDS and the Subcommittee on Nutrition of the Administrative Committee on Coordination;
  - (iv) the World Bank and regional development banks, which have given increased attention to health in recent years, and which are also specialized agencies of the UN;
  - (v) private foundations such as the Carnegie Corporation, Rockefeller Foundation, the Wellcome Trust, the MacArthur Foundation, the Edna McConnell Clark Foundation, the Sasakawa Memorial Health Foundation, the Aga Khan Foundation, the Pew Charitable Trusts and the Ford Foundation;
  - (vi) nongovernmental organizations whose work relates to health research in various ways, including, for example, the International Planned Parenthood Federation, the Program for Applied Technology in Health, and the Council on Health Research for Development;
  - (vii) pharmaceutical and other companies, which are modest investors in health research and major investors in product development.

How do all these organizations at both levels talk to each other? Currently, most do so only through occasional or intermittent links that owe as much to informal networking as to a structured intent to share information. In health research there are only limited formalized review activities, most having either a particular focus or non-permanent resources. WHO's Advisory Committee on Health Research advises the WHO Director-General and the Organization on current trends and issues in science, particularly as they bear on the research activities of WHO itself. The Council on Health Research for Development facilitates individual countries' assessments of their national needs for health research and aims to increase the representation of low-income countries in setting international health research priorities. In addition, there have been periodic, intermittent reviews of health R&D needs, such as the present review and its forerunners. But there is no continuing, informed effort to provide analysis and to facilitate coordination for investors and researchers at international level. We shall return to this issue later.

Figure 7.1 sets out the existing system in schematic form, showing the health service providers, R&D institutions, R&D networks and investors that we have listed above. As the figure emphasizes, there are important flows of resources, information and products between these groups but relatively little analytic overview or monitoring of these flows.

With this descriptive background in mind, we now turn to a discussion of the potential solutions to some important current problems in the system for international health research. Since these problems are familiar to most of those who are involved in the field, the Report will not rehearse them in detail but will summarize them. It focuses first on the operational level, with discussion of the issues of capacity-building in low-income countries and a discussion of possible mechanisms to enhance cooperation between public and private sectors. It then moves on to the resource allocation level of R&D, to address the wider issues of funding, needs assessment and prioritization.

7.2 Building capacity for R&D

7.2.1 The problem: too few good scientists

A lack of resources has long handicapped R&D into the health problems of poor populations. Comparative data on human capital for different regions are difficult to obtain and are subject to bias and the effects of highly incomplete data. However, estimates from UNESCO suggest that about four-fifths of working scientists of *all disciplines, including health*, are concentrated in the Western industrialized nations, Japan and, to a much lesser extent, other large Asian countries. Africa, Latin America and the Middle East *together* have only some 13% of the world's scientists (UNESCO 1996). While Japan has one scientist for every 250 people, most low-in-

Table 7.1 R&D scientists (all disciplines) and engineers by region, 1992

Region/country	R&D scientists and engineers (thousands)	Population (millions)	R&D scientists per 1000 population
European Union	682.0	369.0	1.8
European Free Trade Association	32.6	11.9	2.7
Central and Eastern European countries	285.5	131.0	2.2
Israel	20.1	5.4	3.8
Commonwealth of Independent States	452.8	283.0	2.2
United States	683.7	257.5	2.7
Canada	64.6	27.8	2.3
Latin America	158.5	464.6	0.3
North Africa	81.6	219.7	0.4
Middle and Near East	117.4	465.9	0.3
Sub-Saharan Africa	176.8	482.6	0.4*
Japan	497.3	124.8	4.0
Newly industrialized Asian countries	136.7	92.5	1.5
China	391.1	1 205.0	0.3
India	106.0	887.7	0.1
Other Asian countries	60.3	513.5	0.1
Australia–New Zealand	48.5	21.2	2.3
World total	3 995.5	5 563.0	0.7

*Includes South Africa.

Note: the categorization of economic regions used in this analysis does not correspond with the system adopted elsewhere in this Report but general comparisons can be drawn.

Source: Observatoire des science et techniques (Paris) data in UNESCO 1996

come countries make do with one for several thousand people (see Table 7.1). The existing disparity is exacerbated by the brain drain, whose beneficiaries are principally the established market economies, but also the richer middle-income countries within each region. South Africa, for example, has obtained a substantial human resource from other southern African states.

While no one would argue that scientists from low-income countries should be denied rights to work where they have opportunities—rights long enjoyed by scientists from high-income countries—the globalization of labour markets for the highly skilled presents the low-income countries with serious policy challenges about how to prioritize scarce funds and, indeed, whether sufficient resources can be committed to create the environment for excellence and to retain and use capable scientists.

The conduct of research and development in low-income and middle-income countries is commonly hampered by this brain drain to the richer nations. For those who remain, there are considerable problems at the operational level. We summarize them here.

Just as the quality and productivity of research effort varies dramatically from one institution to another within the established market economies, it varies in the low-income and middle-income countries. Exemplary work is done in a number of institutions and countries; but in general, the obstacles to high quality are greater when countries' incomes are lower. Inadequate training, insufficient staff motivation and lack of competition prevent many institutions from attaining their potential. Lack of leadership, the instability of short-term funding, isolation from peers and poor access to the research literature all compound the problem and prevent researchers from responding rapidly to ever-changing demands. Salaries are generally very poor; rewards to productivity are hampered by non-merit considerations in the appointment and promotion of senior staff and by restrictive personnel policies. Core support for the maintenance of libraries, databases, equipment and buildings is inadequate; and communication between scientists at the regional and international level is difficult. Recent communications improvements resulting from electronic mail and distance learning programmes have tended so far to benefit those who are already internationally networked, not those who are most isolated.

The basic cell of research is a laboratory or unit headed by a senior scientist, with each research institute or university employing a number of senior scientists. A department or institute's interests will tend to be multidisciplinary, while each basic cell will focus on one discipline or a small set of closely related ones. Crucial to the success of research is the ability to respond quickly to change—both at the level of the individual cell and the institute as a whole. The basic cell must respond by acquiring new technologies and skills; the institute must respond by acquiring new or more developed disciplines. In the public sector at least, this ability to respond is continually compromised by the very nature of the mechanisms that fund R&D. Governments usually provide basic core funding for R&D institutes and their civil service personnel policies tend to push research institutions too heavily towards management structures that lack accountability, thereby creating institutions that become unproductive and unable to respond to new challenges. Over time, core budgets tend to be eaten up by salaries, reducing manoeuvrability still further. In order to overcome these structural weaknesses in institutions, network centres of the type described above have evolved in some countries.

Yet in many countries, even the scientists and institutions who overcome these structural barriers to productivity face another hurdle: the international invisibility of their work. Because of typical publication in English and, arguably, a mainstream "core" of prestigious publications whose interest is restricted largely to North America, Europe, Australasia and Japan, researchers from less favoured regions often find it difficult to share their findings with wider audiences. Estimates vary but one assessment of the papers *for all disciplines* published in 1994 in 3 300 journals included in the database of the Institute for Scientific Information, the Science Citation Index, found that 31% of all papers came from the United States, 8% each from Japan and the United Kingdom, and the vast majority of the remainder from the other established market economies and the former socialist economies. Among the low-income countries, only India and China produced more than 1% of the world total, and most produced much less than 0.1% (Gibbs 1995). The Science Citation Index, which accepts only journals that produce English-language abstracts and fulfil various other conditions, heavily underestimates the numbers of papers published in large middle-income countries such as Argentina, Brazil, Chile, and low-income countries such as China.

It is also possible to assess the more specific areas of biomedical and clinical research (though not other health research disciplines) using bibliometric methods. The regional patterns for biomedical and clinical research are shown in Table 7.2. Once again, they emphasize an orientation toward English-speaking and northern industrialized regions.

Of course, bibliometric analyses are of only limited value even when they are representative of all regions. One of their drawbacks is that they cannot measure the quality of work, but only the volume and the impact, as measured by the number of citations received. Another important drawback is their failure to capture the importance of turning R&D results into products and interventions, from drugs, vaccines and equipment to clinical algorithms, packages of services and essential drugs lists. Future assessment of international R&D activity should be augmented to incorporate indicators of the degree to which findings are put to use by health service providers.

The data and discussion above have demonstrated the unevenness of human resources and visible output in R&D between regions, emphasizing the relatively impoverished resources of the low-income and middle-income regions. Given that scientists operate in an international market, it might be argued that the relative share of the total pool of scientists and the visible productivity in any particular region is irrelevant to the conduct of good research worldwide, provided equal attention is paid to all region-specific health problems. Yet, however true this might be for certain other domains of science, the practice of health research relies heavily on close contact with other areas of the health sector, on the local epidemiological environment, and on clinical, behavioural and social sciences that are tied to national frameworks as well as global ones. Many of the needed solutions to the health problems of people in low-income countries are more likely to be found by researchers working closely with those populations than by researchers who remain remote from them. In addition, the development of research capacity depends on good training and teaching, and the establishment of an (often expensive) critical mass. These are more likely to be achieved by strong leaders within local structures and by concentrating resources on productive institutions while freeing the resources committed to nonproductive ones.

7.2.2 Proposed solutions

The Committee is convinced that health R&D effort and capacity in low-income and middle-income countries must be significantly increased and strengthened if the emerging challenges to global health are to be tackled effectively. We summarize here some of the conditions that, in our view, would facilitate productive R&D efforts and competitive research capacity creation. We then suggest some practical proposals for realizing these conditions, proposals that rely, for the most part, on *national* policies and commitments. Our emphasis is on developing mechanisms to focus resources on productive institutions. Since resources are limited, these proposals will inevitably lead to geographical unevenness in the distribution of effort within each developing region.

Table 7.2 Percentage share of published papers in health R&D accessible on international databases, 1993

Country/region	Clinical medicine	Biomedical research
Europe	41.0	36.8
Commonwealth of Independent States	1.4	2.9
North America	41.3	44.9
Latin America	1.3	1.3
Middle Eastern crescent	0.9	0.4
Sub-Saharan Africa	1.2	0.5
Industrial Asia	8.1	9.5
Other Asian countries	1.6	1.4
Australia–New Zealand	3.2	2.3
TOTAL	100.0	100.0

Note: data on other health research disciplines not available.

Source: Observatoire des science et techniques (Paris) data in UNESCO 1996

Individual teams, institutions and programmes have demonstrated that it is possible to do first-rate research in low-income and middle-income countries. Their experience and advice have been well documented elsewhere (see, for example, the interviews with individual leading researchers in TDR 1995). Certain factors apparently help to ensure the success of institutions and programmes, and the Committee highlights them here. They include:

- autonomous management;
- appropriate compensation policies that will attract young and talented scientists;
- the capacity to train a large number of individuals from whom subsequent leaders can emerge. The number must be large enough to allow for transfer to other sectors and other losses;
- stable core funding;
- a significant element of competitive funding which might be allocated to research projects, or to individual development, or to institutional development;
- internationalization, and collaboration not only with institutions in the North but also with other institutions in the South;
- increased use of electronic media for peer review and publication as a first step towards reducing the regional bias in established publishing formats.

Investors and institutions could take a number of steps to make these factors more widespread. More institutions in low-income and middle-income countries should be freed from civil service management procedures, as is happening already in other government-funded institutions worldwide. This step would enable institutions to offer salary scales that will give them a competitive advantage and begin to combat the brain drain. To secure good staff, institutions should be enabled to recruit by active search and on the basis of peer-reviewed competition. Some—and possibly many—national governments will conclude that the financial, administrative and even political costs of these steps exceed their benefits. This may be a reasonable choice, but it creates an environment where science is unlikely to flourish and where competition for support is unlikely to be effective.

In the Committee's view, institutions are more likely to succeed if they receive stable core funding, but also if a proportion of their work is funded competitively. They may decide to support some extramural work, set up collaborative networks with an element of competition, or develop internal competition mechanisms. Some institutions, such as the Oswaldo Cruz Foundation in Brazil, have already moved in these directions with great success, for example by freeing up intramural resources for competitive allocation between groups and within the institution, with assessments being made by an external review group. There have also been notable successes with the formation of networks such as the International Clinical Epidemiology Network (see Box 7.1).

High-quality research increasingly depends on international collaboration, and almost no institution can now perform effectively without an international element. Institutions should therefore expect that some of their staff will be foreign nationals, although restrictive policies in some countries may, at present, prevent this. Where foreigners may not be employed, it is at least preferable for the scientific advisory board of the institution to contain some international representation. Staff should be enabled to participate in international fellowship schemes, exchanges and other mechanisms that foster long-term links and enhance the capacity of reciprocating institutions.

7.3 Accessing the power of the private sector

The contribution of the private sector to health research, in the traditional pharmaceuticals (drugs, vaccines, diagnostics, devices) industries and in a growing list of other health products such as health education materials, has been highly significant in recent decades. Public sector requirements for new product development are dependent on industry for many reasons, including the industry's expertise in development, its efficiency as a manufacturer and distributor, its knowledge and skills in market research and, not least, its financial power. Officials in a number of countries are exploring the ethics and potential of new collaborative ventures between the private and public sectors (Yach 1995), and their efforts may bring significant new funding sources to address unmet health needs. For the present, however, both private and public sectors recognize that the health problems of the world's poorest are neglected by industry. The problem is most acute in relation to pharmaceutical products, and we shall focus on them here.

7.3.1 The problem: too few incentives to invest

The poor lack buying power in the world's markets and there are thus few or no incentives for industry to engage its expertise with their problems. The costs of bringing a new pharmaceutical product from laboratory bench to market have been estimated at as high as US$ 359 million and the process may take 10 years or more. These costs must be recovered through pricing the resulting product at levels far above the (often quite small) marginal cost of production and packaging. The short-term monopoly over a product that the near-global patent system confers—through the power of government—allows these high prices and the consequent underuse of the product in its first few years on the market. As a result of this system, there is little incentive for investing in markets where the possibility of recovering costs is perceived to be poor. The industry is also deterred by the perceived greater risk of investing in products for low-income markets, and a number of

Box 7.1 Capacity-building: the INCLEN experience

The International Clinical Epidemiology Network (INCLEN) began life in the early 1980s. Started by the Rockefeller Foundation, its aims are to strengthen research in health institutions, to improve medical education and training, and to encourage evidence-based clinical practice around the world. It seeks to do so by building up a critical mass of researchers to form clinical epidemiology units, each staffed by epidemiologists, health economists, social scientists and biostatisticians. There are now 35 such units in 18 countries: each one conducts health services research to support rational decision-making by service providers and provides research consultation and teaching.

During the first 10 years of the programme, INCLEN has trained more than 300 people in six centres in Australia, Canada and the United States. During the last three years, the training programme's emphasis has moved to the middle-income and low-income regions, and training centres have been established or are under development in Brazil, Chile, China, Colombia, India, Indonesia, the Philippines and Thailand.

INCLEN graduates have published more than 500 articles in peer-reviewed journals. Equally important, the network's research has already influenced health policy in several countries. For example, research on the effectiveness and efficiency of immunization against hepatitis B virus in the Philippines resulted in the addition of hepatitis B vaccine to the country's immunization programme. And research on the cost-effectiveness of short-course chemotherapy for tuberculosis led to a change in the national treatment policies of Brazil, the Philippines and Thailand.

INCLEN strengthens local capacity by providing support for initial training and encourages continuing education through start-up research grants, annual scientific meetings, peer teaching and site visits by staff from the training centres. INCLEN participants have also formed regional networks for regular meetings and collaboration. The network also provides a small amount of core support for computers, teaching materials, communications and administrative staff.

The network's success is due to two key factors: first, INCLEN has a long-term vision and has been working with its participating institutions for more than a decade, recognizing that capacity-building can take time. Second, it has adopted a strategy of changing the health system by changing the perspective of its stakeholders. INCLEN targets academic physicians in major teaching centres who have established their careers and hold positions of influence within the medical system. Deans of medical schools, for example, are involved to ensure institutional support, including the protection of members' time for research and training. The network has maximized the opportunities for sharing experience, resources and skills—and its work is starting to bear fruit.

companies have withdrawn products from these markets after experiencing extremely low sales. Although many products can be brought to the market for much less than the sums that are widely quoted, there are clearly strong disincentives for investment in markets where purchasing power is perceived to be extremely limited.

This may be illustrated by several recent cases of vaccines developed for the prevention of diseases prevalent in low-income countries. Several highly promising candidate vaccines against diseases of major importance, such as diarrhoea caused by rotavirus, have reached an advanced stage of development. However, the lack of suitable funding to proceed to essential clinical trials and the lack of incentive for industry have proved to be serious hurdles in the final stages.

It is possible that some markets in the middle-income countries will grow extensively in coming decades and that this will encourage the pharmaceutical companies to invest in them. However, this prospect seems unlikely for the poorest regions, particularly sub-Saharan Africa, whose health needs are currently greatest and projected to remain so for the foreseeable future, and where pharmaceutical production is currently low (see Table 7.3). Market growth is also likely to be concentrated in the middle and upper classes whose health needs more closely resemble those of the high-income countries than of the poor in their own countries. Only to the extent that their governments act as purchasing agents for the poor—facilitated by overall national economic growth—can purchasing power become significant; we shall return to this point.

As a result of these constraints on the private sector, national and international research programmes in the public sector, and with support from the private foundations, have increasingly accepted that they must take some responsibility for researching and developing products themselves, through new mechanisms of collaboration with industry. At the same time, the pharmaceutical industry is itself adapting to recession and other factors to turn itself more into an integrated organizational framework that is comparable to some of the international R&D programmes financed by the public sector. This is partly because of the growing interdependence of different types of skill and capacity in the industry, as, for example, in the relationships between the small biotechnology companies and the larger, more stably resourced, pharmaceutical companies. The industry increasingly contracts out its research and manufacturing components, locating each component in the most

Table 7.3 Production and consumption of pharmaceutical preparations, 1990 (in billions of 1980 U.S. dollars)

	Production	Consumption	Imports as % of consumption[a]
Developed market economies	109.7	107.8	8.2
North America	34.1	34.6	2.7
Western Europe	40.4	36.5	20.3
Japan	33.5	34.6	2.1
Others	1.7	2.1	30.5
Former socialist economies	12.9	14.0	NA
Developing countries	27.7	28.4	19.8
Latin America and Caribbean	11.9	9.0	10.6
North Africa	0.6	1.4	58.5
Other Africa	0.6	1.5	61.2
South and South-East Asia	7.4	8.4	15.1
China	5.3	5.4	3.7
Others	1.9	2.7	48.2
Total	**150.3**	**150.3**	–

[a]These figures are for 1989 and include intraregional trade.

Source: Ballance, Pogany & Forstner 1992: tables 2.1, 2.3, 2.10

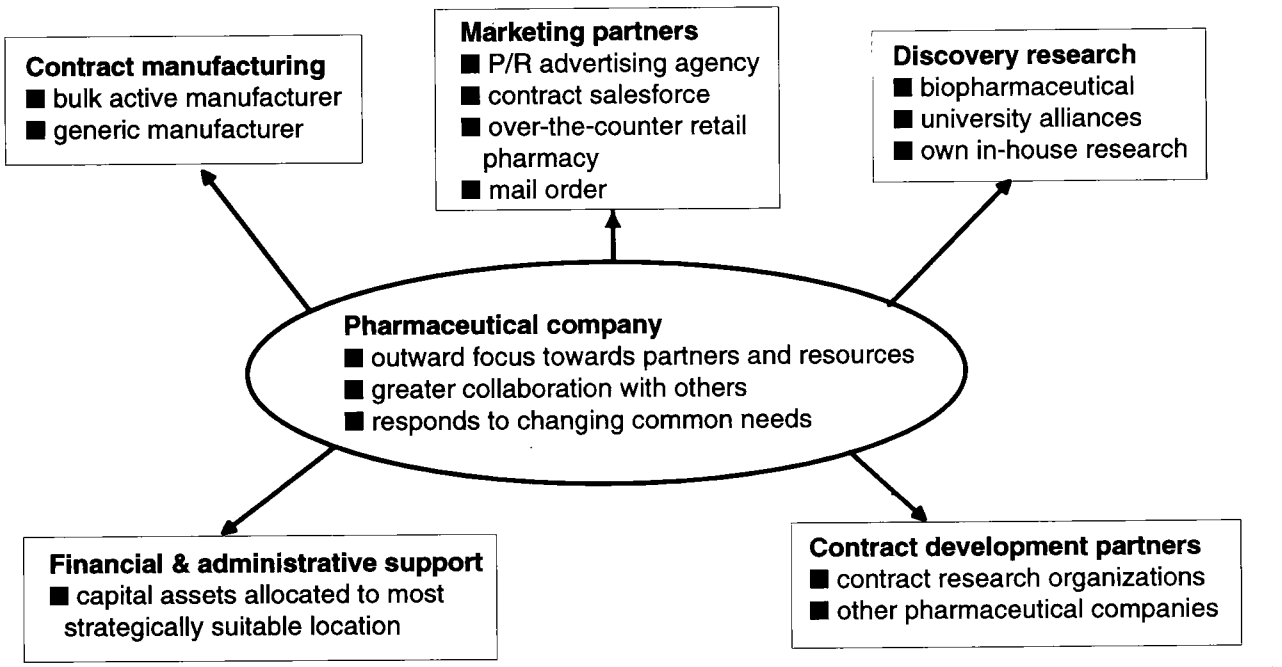
economically and technically suitable location rather like an assembly industry. The increasing integration has been described as a move towards an "extended family" network (see Figure 7.2).

7.3.2 Proposed solutions

The failure of current incentive structures to produce health products for the lowest income groups demands remedial action, and this Committee can merely add its voice to several more specialized reviews of need and opportunity in this area. In essence, the public sector must either harness the skills, energy and capacity of the private sector to develop *and bring promptly to market* products for the lowest income groups, or it must take responsibility for doing so itself. In reality, a combination of the two is likely. After some consultations between representatives of both sectors, the Committee has concluded that a number of actions may be taken to enhance cooperation between them, based on existing experience where successes have been achieved. The public sector may engage the private sector in each of the following ways:

- by supporting the costs of the early stages of product development, from compound screening right through to phase II trials if necessary, and offering to support post-marketing surveillance;
- by providing the industry with detailed analyses of the potential market and of the risks and benefits of introducing a product;
- by providing the industry with guaranteed markets for new products such as vaccines. In such schemes, national governments agree to purchase a known quantity of a specified product, raising the financing either from their national budget or through special loans. The up-front investments needed for successful collaborations of this type must be large;
- by streamlining the regulatory controls imposed by the public sector on the industry to the minimum necessary for good standards, in order to cut the industry's costs;
- by carefully designed tax relief schemes;
- by financial incentives within the patents system. A number of attempts to modify the patent system have been attempted, such as the Orphan Drug Act of 1983 in the United States. This gives companies tax breaks and lengthened exclusivity rights for drugs with small markets, creating strong incentives where there are third-party reimbursement mechanisms that are relatively insensitive to cost. However, the act has not reversed the downward trend in R&D on drugs for diseases that are prevalent in demographically developing countries and further extension of the period of patent protection—beyond the 20 years recently internationally agreed in the Uruguay round—is unlikely to substantially affect incentives, pointing to the need for additional mechanisms;
- by making the best use of the extraordinary commitment of individuals and particular companies within the private sector. Some have already demonstrated themselves willing to undertake research and development, production and supply of drugs on a break-even or defined-profit basis; more may be encouraged to do so. The example of some individuals is clear. For example, Jonas Salk, when asked who owned the patent on his polio vaccine, answered: "Well, the people, I guess. There is no patent. Could you patent the sun?" Salk believed that public goods should be common property for all time. The Committee certainly feels that there is a major role for patents among the instruments of government policy designed to stimulate innovation. Yet the spirit that Salk conveys—of personal or corporate commitment—represents an important additional resource to draw upon. Likewise innovation at public expense, even if in the private sector, requires an important reduction in

Figure 7.2 The virtually integrated pharmaceutical group model



Source: Scrip 1994

unrestricted patent rights, as, for example, through guaranteeing relatively low prices to public-sector buyers.

As a practical step towards putting some of these mechanisms in place, the Committee proposes a specific new initiative: a Health Product Development Facility or Alliance. The proposed facility or alliance would aim to enable private–public sector collaboration to develop cost-effective products for important health problems of people with very low incomes. Its work should be tightly focused on a limited number of products for major causes of disease burden that are currently neglected by existing efforts—such as many of those needed to address the R&D agenda identified in response to the threat from continually changing microbes. The facility or alliance should have a clear strategy to enable, and in some cases directly manage, the speedy development and deployment of those products; a professional management team with expertise from the pharmaceutical industry; adequate financial and human resources; and regular scientific review. It should facilitate, where appropriate, collaborations between large multinational pharmaceutical companies and small emerging companies in middle-income and low-income countries. Its expertise should include staff with skills and experience in the international regulatory systems. While public sector support will be essential, the facility's roles should include catalysing new and non-traditional funding sources and it should make full use of any resources made available to it by the pharmaceutical industry, such as laboratory facilities or staff.

7.4 Investment in health R&D: trends, prospects and proposed solutions

This section discusses global health research at the level of resource allocation, beginning with an overview of overall investment trends, and moving on to discuss the gaps in research needed to meet the challenges identified in earlier chapters.

7.4.1 Problem 1: health investments are not being directed at global health challenges

R&D has a low claim on the health expenditure of all but a few nations. As a share of the world's total expenditure on health, research claimed just 3.4% in 1992 (see Figure 7.3). No government, whether in developed or developing regions, accords research more than about 5% of its total domestic health spending, and for most the share is much lower. In 1992, the United States spent

5.1% of its total publicly funded health expenditure on R&D, Denmark spent 3.8% and Germany 3.3%. Most countries spent less than 2% (Annex 5). Available data from middle-income countries suggest that R&D is seen as an equally low priority. For example, South Africa spends no more than 1.7% of its total health budget on R&D, while for Mexico the figure is no more than 0.5%.

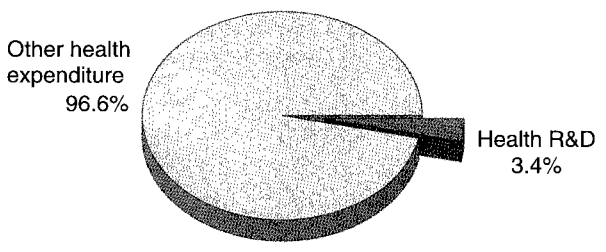
The health problems of low-income countries are the first casualties of this relative neglect of R&D. Even though 90% of disease burden is in low-income and middle-income countries, only about 5% of R&D funds are spent on health problems that are overwhelmingly found in poor populations. Defining those health problems is a complex task, but several different definitions yield broadly similar figures (Annex 5). If, for example, we take a traditional definition of these health problems that is limited to parasitic diseases, the childhood infections and maternal and perinatal conditions, then about US$ 2.4 billion or 4.3% of the total global R&D investment can be said to be spent on these problems. This definition, while clearly providing an incomplete picture of low-income and middle-income countries' health needs at the end of the 20th century, does reflect the current priorities within the system for international health R&D. We find that of this US$ 2.4 billion, approximately half comes from the governments of middle-income and low-income countries. Of the remainder, about US$ 683 million came from the governments of the established market economies, US$ 400 million from the pharmaceuticals industry, and about US$ 80 million from private foundations.

As earlier chapters have shown, analysis of spending by specific health topics also shows a neglect of the problems that currently dominate low-income and middle-income countries. For example, pneumonia, diarrhoeal disease and tuberculosis, which together made up more than 18% of *global* disease burden in 1990, collectively receive no more than US$ 133 million in R&D funds each year—or *0.2% of the US$ 56 billion spent on health research worldwide* (Annex 5). This is equivalent to just US$ 0.51 per DALY for pneumonia, US$ 0.32 per DALY for diarrhoeal disease, and US$ 0.68 per DALY for tuberculosis. By contrast, asthma—which is currently, if not permanently, a health problem mainly of the industrialized countries—received more than US$ 13 in R&D funds for each DALY.

Funding for R&D on the emerging problems of poorer populations also appears to be neglected, though assessments are inherently more complex for these problems because the distinctions between regions are becoming increasingly blurred. There is massive investment in cardiovascular disease, neuroscience, and oncology in the established market economies, but much of this is directed at the development of therapies that are not likely to be cost-effective in the resource-poor nations whose need for them is increasing most rapidly. The Committee has attempted to assess investment on a few of these health problems. R&D on the health impact of tobacco was found to receive no more than US$ 164 million per year, equivalent to less than US$ 4.50 per DALY. If, however, that level of investment does not rise in real terms as the smoking epidemic takes its toll, by 2020 only about US$ 1.25 will be spent on R&D for each DALY arising from this massive health problem. And studies of the health impact of road-traffic accidents, at least that research funded by the public sector rather than by the motor industry, show an even greater neglect. Current investment is estimated to be no more than US$ 34 million a year, equivalent to US$ 0.83 per DALY. By 2020, without real increase, the projected burden expected from road-traffic accidents would mean that just US$ 0.40 was spent for each DALY.

Although there are many factors to consider when judging priorities for R&D, there is little doubt that better information on the balance between investment and disease burden would prove a highly provocative aid to decision-makers. Our own analyses are clearly only a very partial beginning; more systematic assessments will be needed to provide a fuller picture.

Figure 7.3 Per cent of global health spending on health R&D, 1992



Source: Annex 5

7.4.2 Problem 2: investment in the health needs of poorer populations is falling

Through the late 1980s, investment in health R&D rose sharply in real terms worldwide, from US$ 38 billion in 1986 to US$ 56 billion in 1992, measured in constant 1992 dollars. But the rate of growth has now declined in both the public and private sectors (Annex 5). The pharmaceutical industry, which during the 1980s expanded its investment in R&D more rapidly than the public sector in the United States, has recently sharply contracted its investment because of the soaring costs of health care, which have led the industry to project a decrease in its profit margins. Because of the projected decrease, the rate of growth in R&D investment in the pharmaceutical industry has tumbled from an average of 12.7% in real dollars in the early 1980s to 5.6% by the beginning of the current decade. There is some evidence that this contraction has disproportionately affected work on antimicrobials—a shift that is likely to affect low-income populations most acutely.

However, it is the sharp decline in investment in offi-

cial development assistance (ODA)—also called development cooperation assistance—from the governments of the established market economies to the rest of the world that is most likely to impact upon health research for poorer populations. On average, the governments of the rich nations are now allocating just 0.36% of their GDP to their ODA budgets, half the target set by the OECD. The share of this total allocated to health has declined too, and within the health budget less than one-tenth is allocated to R&D.

Official development assistance is given in two ways—as bilateral assistance directly from one government to another; or as multilateral assistance, from a government to an international agency which acts as an intermediary and passes it on to a recipient country. About 44% of ODA for health R&D is given as bilateral funds, the rest as multilateral funds. Bilateral funding for health R&D as a part of all ODA has declined sharply in real terms since 1992. The decline has been sharpest in the United States, Canada and Sweden, which between them in 1992 provided about four-fifths of the total bilateral ODA for health R&D. The United States Agency for International Development, which had rapidly increased its funding for health R&D in the late 1980s, cut its commitment by 30% between 1992 and 1994 and further reductions are expected. Overall, bilateral commitments to the health sector dropped 37% between 1988 and 1993.

Trends in multilateral funds for health R&D are more difficult to assess because of the accounting systems of the donors and recipients of these funds. The principal agencies that receive multilateral funds are the UN organizations, but multinational, nongovernmental organizations such as the Council on Health Research for Development (COHRED) and the International Health Policy Programme (IHPP) also receive some multilateral support. As well as providing regular, budgetary support to international organizations, many governments choose to provide additional discretionary (or extrabudgetary) funds to specific research programmes. These extrabudgetary funds are classified as multilateral aid and it is possible to get a partial picture of multilateral investment trends by examining extrabudgetary contributions to particular research programmes.

Two such programmes, the Special Programme of Research, Development and Research Training in Human Reproduction (HRP) and the Special Programme for Research and Training in Tropical Diseases (TDR), have been regarded as excellent investments by many donors and have been frequently cited as models for the effective support of R&D. Box 7.2 summarizes some of the key achievements of these programmes and shows the cumulative investments of a number of countries, including relatively small nations such as Denmark, Norway and Sweden, that have been critical in bringing these high returns for global health. Yet even for these two special programmes, the trends are disturbing. Investment has begun to show some downward trends, with the contributions of many donors declining in the early 1990s (Annex 5).

As the discussion in this section has shown, finance for R&D is not reaching the health problems that need it most—those that are responsible for the greatest disease burden worldwide. The sharp downward trend in official development assistance and the slowing growth in overall R&D investment are both likely to exacerbate already gross imbalances between the needs of the majority and the efforts of the scientific community. In the Committee's view, these imbalances, and the downward trends in investment, point to two failures of the international health system: first, a failure to monitor broad trends and allocate resources in a rational manner; and second, a failure to convince those at the highest political levels of the enormous human and economic payoff from R&D that, we believe, demonstrably justifies greater investment. The fragmented nature of health R&D may have contributed to this second failure, by preventing the development of strong and coherent international advocacy. In our view, the major challenges that governments face in the next 25 years in dealing with health problems will not be met without serious efforts to overcome these failures.

7.4.3 Proposed solutions

In the Committee's view, there is a need for a mechanism to enable the review of global health needs, the assessment of R&D opportunities and the monitoring of resource flows. There is also a need for advocacy for health research to convince governments and other investors, including non-traditional sources, of its benefits in improving health and enhancing economic development among the poorest populations. The Committee considers that such a mechanism could be created out of existing health research structures. A new collaboration, which might be called the Forum for Investors in International Health R&D, could bring governments, other investors and scientists together to perform these functions. Such a forum would base its reviews on analytic data on the health needs of countries and regions. Its aims would be to identify existing effort and fill important gaps in global health research, particularly those that affect poor populations, and to help reduce overlap and waste. To perform its function effectively, it would need access to high-quality analytic capacity to supply it with data on disease burden, reasons for the persistence of that burden, measurements of the cost-effectiveness of potential interventions, current patterns of spending on R&D, and assessments of national health system performance.

Such a forum would take advice from existing scientific advisory groups already involved in enabling health research at national and international levels, such as the WHO's Advisory Committee on Health Research system, scientific and advisory groups of existing international research programmes, and bodies such as the Council on Health Research for Development (see Box 7.3), the International Clinical Epidemiology Network and the International Health Policy Programme. Its rec-

ommendations and conclusions would be presented to existing programmes for consideration and implementation.

The proposed forum should have certain key characteristics. It should be inclusive, with all partners having an equal footing. It should be informal, should respect the mandates of its partners and should strengthen rather than diminish each partner. It should not be a legal entity nor the creature of any specific organization; its conclusions should be made widely available to all who might be interested in them to inform decision-making by others (see Figure 7.4).

One important function of the forum would be to demonstrate at national and international levels the benefits of health research, and, through the data on resource flows and performance that it could generate and monitor, to convince investors—including, perhaps, new and non-traditional sources—of the high payoffs that research can bring. Another critical function would be to establish (and update) a *short* list of key R&D products to be realized in a specified time frame, to monitor progress on items on the list, and to remove items from the list as they reached completion or if progress faltered excessively. If WHO were to take the lead in the establishment of such a forum with the help of other key players, the advantages would be many, including a speedy aggregation of dispersed international R&D activities.

In order to strengthen resources for research on the major challenges to global health, the Committee concludes that additional specific initiatives are needed in four areas. Three of these have been identified already in the Recommendations sections of Chapters 4, 5 and 6 and the need for the fourth initiative has been discussed in greater detail in section 7.3 above. *All of these initiatives can be achieved through the consolidation and enhancement of existing institutions and structures.* To summarize, the initiatives are:

- A Special Programme for Research and Training on Noncommunicable Diseases and Healthy Aging;
- A Special Programme or Initiative for Research, Training and Capacity-Building on Injuries;

Box 7.2 High returns: the outcomes of investment in two R&D programmes

The parasitic diseases and poor reproductive health that plague so many people in low-income countries are now under sustained attack from two highly effective programmes, the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) and the Special Programme of Research, Development and Research Training in Human Reproduction (HRP).

Some key achievements of TDR include:

- success in treating leprosy using multidrug therapy in combinations tested and monitored by the programme. Leprosy is due for elimination as a public health problem by the end of the decade;
- the control of onchocerciasis (river blindness) now promises to be sustainable. Success has been achieved through treatment with the drug ivermectin combined with rapid epidemiological mapping, monitoring and distribution methods;
- the expected interruption of the transmission of Chagas disease by the end of the decade in the southern cone of Latin America as a result of control using fumigant cans, insecticidal paint and techniques to screen donated blood in blood banks;
- the development, through multicentre trials, of effective control programmes for lymphatic filariasis based on the use of dietylcarbamazine, ivermectin and soap and water.

Some key achievements of HRP include:

- the development of new or improved methods for regulating fertility, including: new monthly injectables, extension of the duration of effectiveness of copper IUDs to 11 years and confirmation of their safety in women at low risk for STDs, the evaluation of the potential of antiprogestins for fertility regulation, and ongoing clinical trials of antifertility vaccines and hormonal methods for males;
- the assessment of the long-term safety of existing methods of family planning including reassurance on the relationship between oral contraceptives and cancer, and updated information on the relationships between oral contraceptives and cardiovascular disease;
- the assessment of the behavioural determinants of choice of family planning methods, including understanding of the reasons why women resort to unsafe abortions, as a means to inform intervention development.

Both programmes have contributed strongly to strengthening research capability in low-income and middle-income countries. Through TDR support, for example, 17 institutions in disease-endemic countries have now reached an international standard and regularly compete with laboratories in non-endemic countries.

The countries and international organizations that have supported this work over two decades have been repeatedly persuaded of the value of their investment in improving human health. In many cases, small countries have played key roles (see Box Table 7.2.1).

(Box 7.2 continued)

Box Table 7.2.1 Cumulative voluntary contributions to two international research programmes, 1970–95 (millions of U.S. dollars)

UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR), 1974–95		Special Programme of Research, Development and Research Training in Human Reproduction (HRP), 1970–95	
Source	**Amount**	**Source**	**Amount**
Denmark	53.1	Sweden	92.1
World Bank	48.3	UK	60.2
USA	46.0	UNFPA	48.0
Sweden	45.8	Norway	43.4
Norway	46,6	Denmark	29.5
UNDP	42.3	World Bank	19.3
The Netherlands	23.5	Germany	13.1
WHO	23.4	WHO (regular budget)	12.8
Germany	21.6	USA	11.2
Canada	21.4	Canada	10.0
UK	19.2	The Netherlands	5.1
Switzerland	18.3	Australia	3.5
Belgium	10.4	Rockefeller Foundation	3.2
Australia	8.7	Finland	2.8
Italy	6.3	Switzerland	2.7
MacArthur Foundation	6.1		
Japan Shipbuilding Industry Foundation	5.9		
France	5.8		
IRDC	3.3		
Finland	2.8		
African Development Bank Group	2.3		
Others	12.9	Others	40.6
Total contributions to each programme*	**474.0**		**398.0**

*Only contributions greater than US$ 2 million are itemized.

- A Special Programme for Research and Training on Health Systems and Policy; and
- A Health Product Development Facility or Alliance.

It is not for the Committee to specify exactly how such initiatives might best be organized. The essential requirement is to enhance and expand effort in these areas without delay by whatever means should be considered most effective.

7.5 Chapter summary and recommendations

The current system for the conduct and financing of international health research is unable to respond adequately to the world's current and changing health needs. In particular, a lack of capacity at national and regional level is holding back high-quality research, while inadequate collaboration between private and public sectors is directly affecting the health of poorer populations. At the resource allocation level, there is neglect for health R&D overall, a severe imbalance of resources away from the needs of low-income populations, and a lack of mechanisms to facilitate coordination between investors. The result is fragmentation, some duplication, some gaps and a dispersion of resources. At a time when research has more than ever to give, this suggests two failures of the international health research community: first, to allocate its effort in a rational manner to improving health; and second, to convince investors and potential investors of the benefits of investing in research for health.

The following recommendations are addressed to investors: some are more particularly the concern of governments in middle-income and low-income countries, and some the concern of governments in the established market economies and other traditional "donors" to health R&D. The recommendations outline some steps that might be taken to proceed, first in terms of the operation of research at national and international levels, and finally in terms of resources and international coordination.

Recommendations

1. Governments have much to gain from the development of national agendas for health research, with the active involvement of all relevant actors, including scientists, service providers, policy-makers and community leaders. Such agendas are likely to be most useful if their focus includes both population health needs and available R&D capacity. Investors may increase the efficiency of R&D by strengthening national and regional research capacity, through, for example, focusing efforts on areas of comparative advantage, on improvements in the quality of training, on explicit initiatives to translate results into relevant policies and interventions; by offering incentives to reverse the brain drain, by promoting policies that require research posts to be competitive and based on the peer-reviewed allocation of funds, and by making core support for institutions competitive. Additionally, supporting national institutions with a strong international orientation—in funding, staffing and mandate—might have a high payoff. The returns on investment in good standards are likely to be significant, while poor-quality or repetitive research is wasteful and may have adverse consequences for health.

2. Investors may profitably explore the development of new instruments—beyond the current patents system—for engaging the skills and energy of the private sector in the development of vaccines, antimicrobials and other drugs, diagnostic tests, devices and prostheses and equipment for the use of low-income populations. These incentives could include development subsidies, extended patent protection, guaranteed markets, streamlined regulatory requirements, improved market information (including certification of product quality) and contracting for specific tasks. The Health Product Development Facility or Alliance recommended by this Committee is a potentially effective mechanism to focus and synergise efforts—not only for products to combat the major microbial threats, but also for maternal and child health and for the coming epidemics of noncommunicable diseases and injury.

3. A Forum for Investors in International Health R&D should be formed to provide a mechanism for the review of needs and opportunities for global health R&D—making use of analytic data on disease burden, R&D opportunities and the level of ongoing efforts. The forum would bring together the governments of low-income and middle-income countries, the major traditional "donors", and the research community. Analytic work undertaken by and for the forum would provide improved information for decentralized decisions on funding and resource allocation. This in turn should help to focus resources more sharply on completing the highest priority tasks before moving on to others.

4. Given the high returns to R&D in health improvement, a reallocation of health sector resources to

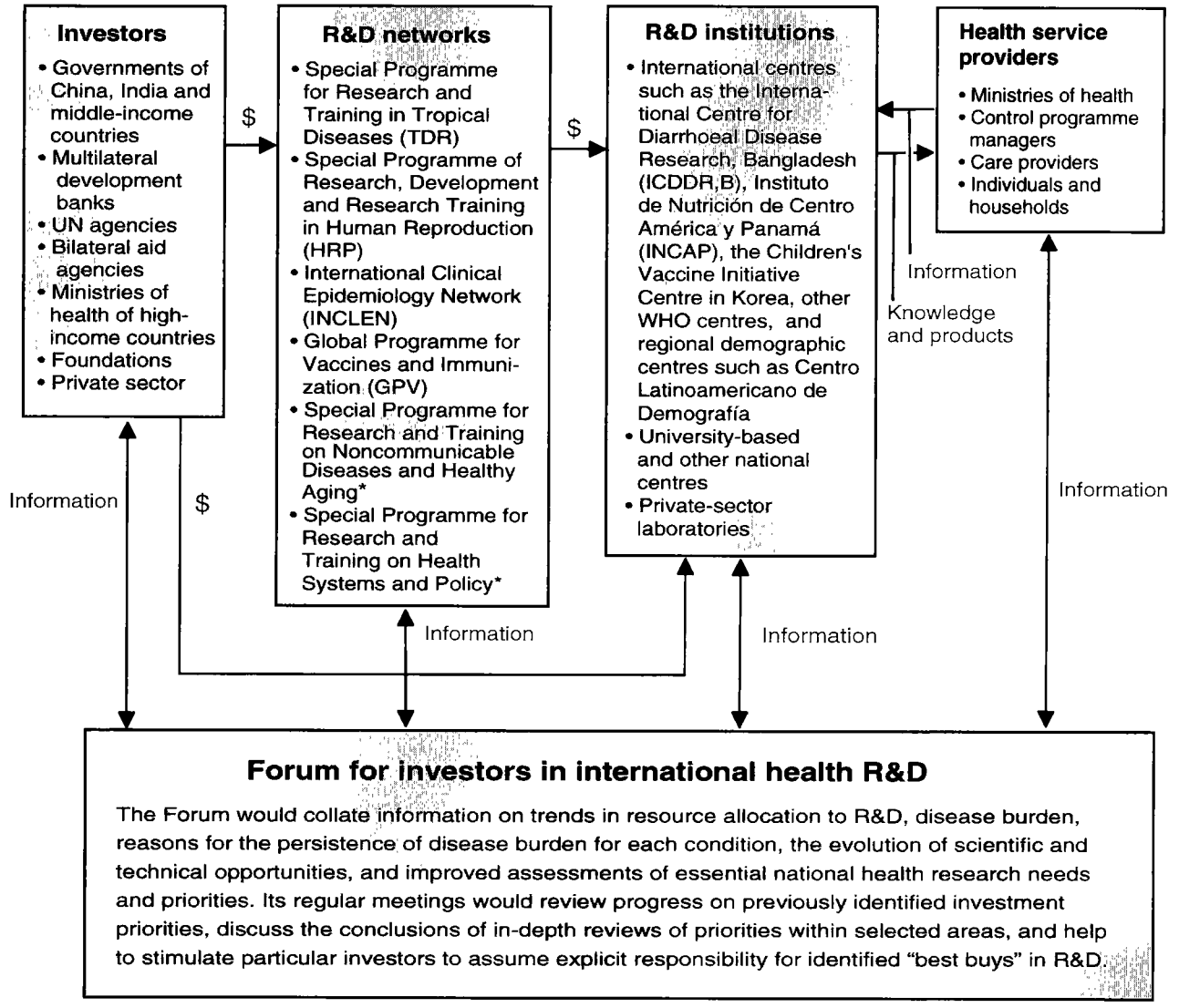
Box 7.3 The Council on Health Research for Development

The concept of Essential National Health Research grew out of the work of the Commission on Health Research for Development, whose purpose was to recommend how R&D could improve the health and well-being of the peoples of low-income and middle-income countries. The Commission argued that every country, no matter how poor, should have a health research base that will enable it to understand its own problems and enhance the impact of limited resources to improve health. Scientists, decision-makers and representatives of the people should all be involved as equal partners in the process of setting priorities for national health research and determining an agenda for action.

Towards this goal, the Council on Health Research for Development (COHRED) was set up following a resolution at the Second International Conference on Health Research for Development in March 1993. COHRED was to promote, facilitate, support and evaluate the Essential National Health Research strategy and other health issues of international priority. It took over from the task force formed to implement the Commission's recommendations.

Today more than 40 countries are collaborating with COHRED in implementing a strategy. Research agendas cover a broad range of problems but reflect common key concerns, ranging from sanitation and water safety to the need for research to inform health policy at local and national levels. The Council enables countries, agencies and organizations, both governmental and nongovernmental, to work together to promote, facilitate and support Essential National Health Research and to address health issues of international priority that require joint action. It works with countries to build links between researchers, health care providers, decision-makers and community representatives at all levels of the health system. These links are crucial if research is to help inform intelligent decisions and result in relevant action. The Council also works closely with international research programmes, UN agencies and other international organizations pursuing health and equity.

Figure 7.4 The international health R&D system: proposed enhancement



*Proposed new programme

R&D is recommended as a means to bring substantial net gains in health, particularly the health of poor populations. Given that much of R&D provides an *international* public good, there is a particularly strong case for public sector investors in the established market economies to reallocate their health portfolios to increase R&D funds. The institutional capacity for supporting health R&D that many traditional donors possess strengthens the case for them to increase this form of assistance. The globalization of health problems suggests that sources of investment in international health R&D should be diversified in order to enhance the likelihood of finding appropriate solutions to them. The ministries of health and research councils of high-income countries have much to gain from participating. Governments of low-income and middle-income countries are likely to find increased allocations to appropriate health R&D to be both a cost-effective way of improving health in their populations and, potentially, an investment in the infrastructure for productive national industries.