John Griffin revisits north/south drug inequalities.

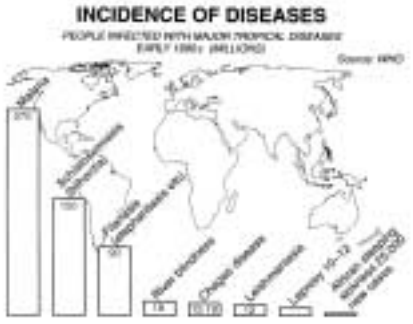
Developing World Drugs

THE BULK OF NEW CHEMICAL ENTITIES LICENSED HAVE BEEN LIMITED TO... CONDITIONS WHICH ARE LARGELY CHRONIC AND OCCUR PRINCIPALLY IN THE AFFLUENT WESTERN COUNTRIES.

The recent publication by *Medicines sans Frontiers* entitled 'Fatal imbalance: the crisis in research and development for drugs for neglected diseases' has caused considerable interest in the press.[1] The report describes the research and development activities of eleven major pharmaceutical companies, representing combined sales of nearly $117bn (£78bn). In the last financial year, eight of the eleven companies spent nothing on research and development into sleeping sickness, leishmaniasis or Chagas' disease. One company did not answer the question. Two reported spending on malaria and five reported spending on tuberculosis, but seven reported spending less than 1% of their research and development budget on any of the five diseases highlighted. The authors commented, 'Drugs are not developed according to public health need but according to profitability'.

In fact, not much has changed in the last twenty years. In 1979 Prof Franz Gross wrote, 'the concentration of research efforts on a relatively small number of fields, which look promising from a commercial point of view, has had the consequence of a crowding in some areas of research and a neglect of others'.[2] Similar views were expressed in 1981 by Griffin and Diggle[3] who wrote, 'The bulk of new chemical entities licensed have been limited to a relatively small number of therapeutic groups...in fact conditions which are largely chronic and occur principally in the affluent Western Society. Innovation is therefore directed towards commercial returns rather than therapeutic need. The pharmaceutical industry like any other major industry is of necessity motivated by the need to be profitable'. Diana Melrose of Oxfam[4] reported in 1983 that only one to three per cent of the international pharmaceutical industry's total research and development allocations is devoted specifically to tropical diseases.

One has to be careful of taking these comments as an outright condemnation of the research based pharmaceutical industry - this would be naive.



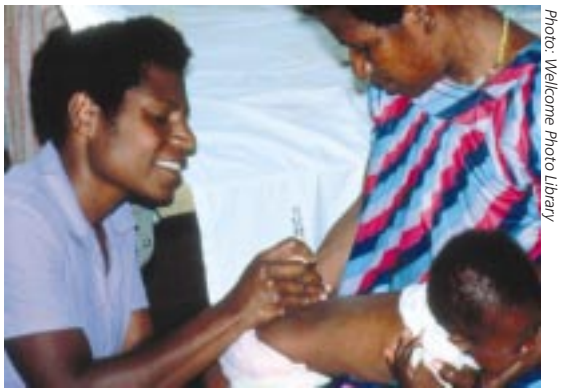
Incidence of diseases. People infected with major tropical diseases (millions). World Health Organization.

Type	Orphan	Definition
I	diseases	rare diseases for which treatment would be very expensive to research
II	medicines	medicines that are not developed as their target populations are too poor to afford them
III	patients	Patients who are too poor or isolated to afford existing treatments

Taylor and Griffin[5] writing on the subject of '*Orphan Diseases, Orphan Medicines and Orphan Patients*' in 1985 dissected the issue into three categories of orphan. First, those cases in which the condition to be treated is prevalent only in a very small section of the global population. Type I orphans suffer from rare diseases. In such instances, the ratio of the costs of research, development and production against projected market earnings and the overall levels of welfare to be generated may be so high as to discourage investment in the area.

The second group, type II orphans, describes the category where medicines likely to benefit very large numbers of people are not being developed because the people who suffer from these diseases are very poor and are not usually served by adequate health care systems. Here the conditions most likely to be involved are tropical diseases. In

In Rwanda only 500 patients are receiving AIDs drugs because the cost of $140 per month is half the average yearly income.[7]



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some environments, type III therapeutic orphans exist where effective remedies are freely available on the world market, but for economic or other distribution reasons they are simply not available to those who need them.

Dealing with type I and type II orphans requires considerable research and development expenditure. The development of a new chemical entity costs between £500 - £800 million. Pharmaceutical companies cannot invest sums of money of this magnitude without any possibility of recouping these costs. It has been calculated that in the current economic climate only one out of five new chemical entities recoup their research costs so 'block-buster products' fund the companies' overall research and development expenditures.

In the developed world, type I orphan drugs which are able to exploit American, European and other 'orphan drug' provisions can fund their research and development costs by charging health authorities a premium price for such products. However, no such opportunity exists for type II orphans. Pharmaceutical companies have a responsibility to their shareholders to provide return on investment. If there is an inadequate return on investment, a company's share price falls and this could be catastrophic for the future of the company, and any research and development it might undertake; this would inevitably lead to job losses.

The suggestion by *Medicines sans Frontiers* that governments should become involved in tackling the problem of type II orphans is not new and was advanced by Taylor and Griffin who stated: 'Governments should be encouraged to support ongoing initiatives like UNDP/World Bank and WHO special programme'. However, it has to be remembered that several western governments including that of the UK have reduced their funding of academic tropical research, and some nations have been slow in paying their contributions to the UNDP/World Bank/WHO programme. *Medicines sans Frontiers* also makes recommendations for technology transfer and increased research and development in developing countries, a proposal similar to that made by Sir John Vane (Nobel Prize Winner) as long ago as 1985.[6]

Future circumstances are likely to change. The re-emergence of tuberculosis in the western world and the appearance of malaria outside areas conventionally regarded as malarial risk areas, are serving as stimuli to increase government sponsored research in these areas. The increased resistance of the malarial parasite to existing anti-malarial agents, and increased travel for military, business and pleasure are also raising the demand for new anti-malarials and other treatments for tropical diseases. These demands by the developed world will have consequent beneficial effects for the citizens of developing countries.

In theory, the problem of type III orphans should be easier to deal with given good will. In recent months, a number of pharmaceutical companies have made considerable price reductions for their products for HIV/AIDs treatment, albeit under pressure. They have done this despite understanding from past experience that such dual pricing can lead to the re-export of low priced products back from recipient developing world countries into the markets of the developed world by unscrupulous governments or wholesale dealers seeking windfall profits. Furthermore, for nearly two decades, Merck Sharp & Dohme have provided generous and unlimited free supplies of ivermectin for the treatment of onchocerciasis in Africa, but this altruism of pharmaceutical companies is frequently ignored by activist groups. Attempts by developing countries to import from other developing countries products that do not conform to the patent agreements of TRIPS (trade related aspects of intellectual property rights) has resulted in the supply of defective rather than cheap drugs.

For many countries even cheaply priced HIV/AIDs treatment is not an option since they cannot afford to buy any treatment at all. For these type III orphans the only chance is free medicines and they will benefit from UN Secretary General Kofi Annan's initiative in setting up a Global AIDs and Health Fund with a $1.4 billion capital and a target spend of $7-10 billion per annum.

In conclusion, the situation as identified by Medicines sans Frontiers is neither satisfactory nor new. Realistic solutions have to be sought, but it has to be tackled by governments, the UN and WHO, not by charity from individual pharmaceutical companies. The developed countries must be made to realise that they are stewards but not the owners of the resources they have, and that these should be used responsibly.

John Griffin is an Independent Consultant to the Pharmaceutical Industry

KEY POINTS

A recent report on 'neglected diseases' by Medicines Sans Frontiers has concluded that 'drugs are not developed according to public health need but according to profitability'. Orphan diseases, orphan medicines and orphan patients still exist. Developed countries are stewards, not owners of their resources and, whilst there have been some encouraging developments, there is still much to be done which will require Western governments, the UN, WHO and pharmaceutical companies to work together.

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