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HSCNEWS *International*

The views of health and social campaigners worldwide



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Global Views

This issue of *HSCNews International* focuses on:

The future of medical research

and

Stem cell research

CORRECTION

On page 19, issue 11 (October 2004) of *Health and Social Campaigners' News International*, some parts of a statement provided by Khalil Elouardighi of ACT UP-Paris were misinterpreted. A letter submitted by Mr Elouardighi (page 70 of the present issue) explains these errors.

We extend our sincere apologies to Mr Elouardighi.

New approaches to health research and drug discovery

A pair of crucial meetings took place during the week beginning Monday November 15th 2004. The two proceedings discussed the strategic changes needed to improve the quality and quantity of health and medicines research. At one of the venues, the World Health Organization (WHO) and the government of Mexico organised a 'Ministerial Summit on Health Research', held in Mexico City. Across the Atlantic, at The Hague in the Netherlands, the WHO and the Dutch presidency of the European Union (EU) jointly convened a conference entitled 'Priority Medicines for Europe and the World'. Consumer and patient organisations were attendees on both occasions. This Health and Social Campaigners' News International article reviews the main outcomes of The Hague symposium (and briefly touches on the Mexico meeting), then concentrates on what health campaigners had to say about it. Included in the latter part of the article is a summary of a parallel satellite seminar organised in The Hague by Health Action International (HAI), a consumer-oriented group which is largely critical of the pharmaceutical industry. The HAI seminar was designed to be a response to the proposals put forward by the WHO and the EU on the important subject of health and medicines research.

The WHO issues the results of a year-long study in November 2004

The Priority Medicines report identifies means of encouraging research into vitally-needed medicines

The WHO/Dutch EU presidency initiative on priority medicines

On November 18th 2004, the World Health Organization (WHO) released a 134-page report, *Priority Medicines for Europe and the World* [WHO/EDM/PAR/2004/7]. The document was written by Warren Kaplan and Richard Laing of the WHO's Department of Essential Drugs and Medicines Policy. *Priority Medicines* was supported by 30 background papers prepared by eminent academics, medical professionals, health advocates, and the WHO's various Collaborating Centres around the world.

Priority Medicines was the end-product of a year-long investigation by the WHO into public health. The organisation hoped to identify which treatments are desperately needed on a global scale, yet which do not (or scarcely) exist. The report, though, went further than exposing the more important pharmaceutical 'gaps' in Europe and around the World. It also defined ways of encouraging innovation into the discovery and development of such drugs.

“On November 18th 2004, the WHO, with financial support from the Dutch government, released a ground-breaking report on the future of medical innovation”

The project is funded by the Netherlands

Priority Medicines is launched at a November 18th 2004 conference in The Hague

The Dutch government thinks that medicines R&D should be coordinated Europe-wide

The entire Priority Medicines project was funded by the government of the Netherlands, which wished to make a mark on the direction of pharmaceutical R&D in Europe during its presidency of the European Union (EU), between July 1st 2004 and December 31st 2004.

The role of the EU

On the launch day of *Priority Medicines*, the report's contents and applicability to the EU were discussed at a pivotal conference in The Hague, in the Netherlands. The Netherlands Ministry of Health, Welfare and Sport described the conference aim as the creation of "a shared vision that is politically and scientifically relevant, covering the nature of the problems, and on possible ways forward." The Dutch government put forward several compelling reasons why medicines R&D should be part of a Europe-wide agenda, including:

- The incorporation of ten more countries into the EU in 2004 has heaped extra responsibilities onto EU policymakers, who must now accommodate the disparate needs of the new Member Nations. Many of the 'ascendant' nations are only just experiencing the impact of demographic change and increases in their levels of chronic disease.
- The EU has required its Commissioners to investigate ways of bolstering the competitiveness of the European pharmaceutical industry, which, for more than a decade, has been lagging behind its American counterparts in R&D productivity and revenue growth. Europe's pharmaceutical industry believes that cost controls instituted by the continent's governments as a way of limiting national healthcare bills are to blame for its relative lack of inventiveness.
- The EU is well positioned to advise on the pharmaceutical 'gap', [medicines not yet discovered for important public health hazards]. EU national health systems aspire to providing all their citizens with a 'social safety net'. European health

Médecins sans Frontières on the meetings in Mexico City and The Hague

Underscoring the importance attached by health campaigners to the two November 2004 events, a November 11th 2004 press release issued by [Médecins sans Frontières \(MSF\)](#) stated: "Convening this month are two important conferences that will decide the future of patients suffering from neglected diseases in the poorer countries of the world—the 'Ministerial Summit on Health Research', November 16th-20th 2004 in Mexico City, and the WHO/Dutch Government 'Priority Medicines for Europe and the World' meeting, November 18th 2004 in The Hague. The lives of neglected patients hang in the balance. Will they be promised life, in the form of new drugs? Or will they be left to suffer their fate?"

MSF (the US arm is known as [Doctors Without Borders](#)) was founded in 1971 by a small band of French doctors who wanted a group that could respond rapidly to medical emergencies overseas. MSF's main virtue is that, since inception, it has attempted to undertake duties without reference to the economic or political backdrop in which it might be working. MSF is equally willing to function in war-zone hospitals, refugee camps, or remote health clinics. Even under the most extreme circumstances, MSF endeavours to supply food, medicines and healthcare to people in need of their support.

The submission on priority medicines made to the WHO by the International Osteoporosis Foundation

The mission of the Berne, Switzerland-headquartered [International Osteoporosis Foundation \(IOF\)](#) is the advancement of the understanding of osteoporosis, and the worldwide promotion of the prevention, diagnosis and treatment of the disease.

The IOF believes that a great crime exists in osteoporosis care today. The disease is preventable, diagnosable, and treatable. Yet the increasingly sedentary lifestyles of populations, allied to a lack of appropriate intervention from governments, has allowed osteoporosis to escalate. The total direct costs associated with the condition are forecast to double to 76.7 billion Euros (US\$100 billion) by 2050.

Greater awareness about the true scale of osteoporosis is needed, since the popular belief is that the condition strikes only older women. Osteoporosis affects men in substantial numbers, and they suffer a higher mortality rate than women. The widespread use of steroid therapy has increased the prevalence of the disease in children, too. Young women can acquire the condition as a result of steroid therapy, anorexia or chronic illness. Unfortunately, much of the current research into the treatment of osteoporosis has only been carried out on older female subjects. Little data exists about the effectiveness of osteoporosis medication on men, children and young women—or on patients with gastro-intestinal problems, who may have problems absorbing oral therapies.

Osteoporosis in Europe, 2000

Fractures: 3.7 million

Hip fractures: 0.7 million

Death rate after first hip fracture: 24% in women; 33% in men

Direct costs: 31.7 billion Euros

Source: IOF

The Netherlands government would like the EC to become more involved in encouraging research ...

systems are also run along principles of social solidarity, rather than market forces—as they are in the US. European health ministers are therefore well acquainted with the trade-offs that have to be made in order to encourage medical research which is aimed at the public good, rather than at industry's purse. In other words, the European Commission can be called upon to reduce the stultifying effect of cost controls on industry, while simultaneously promoting the concept of cost-effective pharmaceutical innovation.

- Developing and developed countries share a commonality of interest in receiving effective healthcare. Poorer countries have seen a radical increase in the incidence of certain cancers, diabetes, heart disease and mental illnesses—the main contributory factors to death and sickness in richer nations. Conversely, richer nations face the imminent threat of pandemic infections, which are a major cause of death in poorer countries. Across the globe, HIV/AIDS remains a persistent health problem.

Why the WHO/Dutch government *Priority Medicines* report is important

The WHO/Dutch government report and conference in The Hague could have the following ramifications for Europe and developing countries:

... and thinks that the Priority Medicines report could guide EU research spend

The report might help determine priorities in European health research

In particular, it could steer EU efforts to promote pharma's research

Dr Laing, one of the report's authors, points out that the study had to be conducted quickly

- The Dutch Ministry of Health, Welfare and Sport is proposing that the results of the WHO's analyses should guide EU spending on technology and research during 2006-2010 (the period of the EU's seventh technology 'framework'). To date, the EU has invested relatively small sums in medical research for the third world.
- The Dutch Ministry of Health, Welfare and Sport is also liaising with the WHO to determine top priorities for health research.
- The Dutch Medical Research Council (ZonMw) wishes to stimulate the formation of a European Research Area (ERANet), which would bring together principal national research programmes undertaken by various countries in Europe. The WHO documents will then help set the research agenda for the ERANet.
- Finally, the findings of the WHO report will be used by the EU to develop policies to promote the efforts of Europe's pharmaceutical industry in priority areas.

Dr Laing's comments

At The Hague conference, Dr Laing outlined the basic thinking behind the WHO/Dutch government report and the project's major findings.

He explained that the study's short, single-year time frame permitted only a highly-focused approach. The report's authors therefore steered clear of attempting any comprehensive analyses of the following related subjects:

- Issues of equity or quality of healthcare, as brought about by logistical and/or societal barriers.
- Preventive health practice and risk factors that trigger disease.

“The EU has a role to play in defining pharmaceutical innovation. Its drug industry is declining, the new ascendant nations face significant health problems, and the disease profile across Europe is being replicated in other parts of the world”

The drug research system: a matter of serious concern?

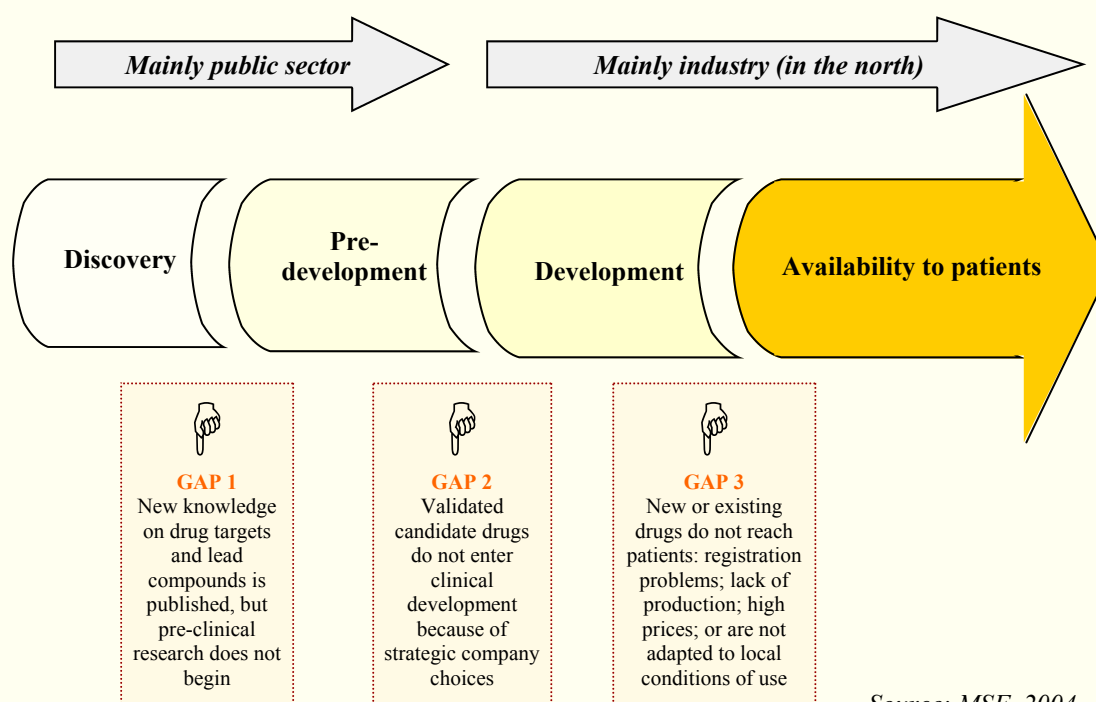
On October 4th 2004 in Brussels, Ellen t’Hoen, global coordinator of the [Access to Essential Medicines Campaign](#) (which was launched in 1999 by [Médecins sans Frontières \(MSF\)](#)), talked about the topic of neglected diseases to the WHO team dealing with priority medicines.

Ms t’Hoen stated that the market-driven nature of the drug research system was resulting in a dearth of medicines. This serious problem, she said, has expressed itself in the following developments:

- Between 1975 and 1999, 1,393 new chemical entities were marketed by the pharmaceutical industry. Of these, only 13 were directed at tropical diseases and three at tuberculosis.
- Since 1990, the private sector has emerged as the biggest investor in health research, outstripping the investments made by government.
- The pharmaceutical industry’s research productivity (although not its R&D spending) has declined since peaking in the late 1990s.
- The majority of medicines emerging from pharmaceutical company pipelines do not represent major therapeutic breakthroughs. Frequently, new products promise only limited additional value, or are, indeed, superfluous.
- Public policies toward pharmaceutical innovation have focused on stimulating private R&D investments by ensuring that returns are attractive. The approach has failed to provide “*effective, affordable and easy-to-use medicines for 75%-80% of the world population.*”

Ms t’Hoen told the WHO that new approaches to drug innovation are needed to address the pharmaceutical ‘gap’. She added that support for alternative methods of setting priorities and financing medicines research is required.

Filling the gaps in R&D for neglected diseases



Source: MSF, 2004

Footnote:

Ms t'Hoën's presentation on the previous page was based on a document supplied to the WHO on October 7th 2004, entitled *A Needs-Based Pharmaceutical R&D Agenda for Neglected Diseases*. This backgrounder was drafted by Els Torrele, Martine Usdin and Pierre Chirac of MSF and its sister campaigns, the [Campaign for Access to Essential Medicines](#) and the [Drugs for Neglected Diseases Initiative \(DNDi\)](#)—the latter founded in 2003 with the help of MSF. For more details about MSF and the two related projects, see *Health and Social Campaigners' News International*, issue 2, December 2003, pages 8-48).

- Medical devices and diagnostics.
- Intellectual property rights, pricing and pharmaceutical trade—which is currently being reviewed by the WHO Commission on Intellectual Property Rights, Innovation and Public Health [<http://www.who.int/intellectualproperty>].

Despite the above limitations, the authors of *Priority Medicines* felt that their report “offers a bold vision of a Europe that can invest, innovate, and cooperate to address the critical need for priority medicines for all citizens of the world.”

The pharmaceutical ‘gap’ ...

Dr Laing identified three types of pharmaceutical ‘gaps’:

1. No existing treatments, or treatments that are inadequate.
2. Existing treatments or preventive measures that are likely to become ineffective in the near future.
3. Treatments for which the formulations and methods of delivery need improving.

... is the result of market failures

Despite the existence of a vigorous global pharmaceutical industry, hundreds of millions of people are forced to survive without access to adequate medical treatments. Dr Laing blamed this state of affairs on market forces, which compel pharmaceutical companies to undertake research only in subject areas that generate profits. The *Priority Medicines* report stated that the approach has resulted in a massive shortfall in the types of medicines available to treat diseases endangering public health, including:

- **Rare and neglected diseases.** Treatments for these diseases do not generate sufficient revenue to be of interest to the pharmaceutical industry. Over 5,000 rare diseases exist, embracing conditions such as cystic fibrosis or cerebral palsy. Rare diseases are of particular concern to developed nations. Neglected diseases tend to be prevalent in poorer countries of Africa, Asia and the Middle East, which hold three quarters of the world's population. They are chiefly caused by parasitic organisms—such as Chagas, which is transmitted by a water-borne microscopic organism, or Leishmaniasis, communicated by a sandfly.
- **Diseases with complex aetiologies.** As the complexities of the biology involved in understanding the progression and onset of various diseases have escalated, so too has the investment

The threat of global pandemics

Bacterial infections account for less than 5% of the burden of disease in Europe. But a real and worrying danger exists that their prevalence is set to soar with the decline in availability of effective antibiotics (the latter being caused by over- and misuse). The UK, for instance, has witnessed a more than 60% increase in the incidence of methicillin-resistant staphylococcus aureus (MRSA) infections since 1992. MRSA is an organism which is unaffected by commonly-used antibiotics. The infection is lethal unless identified early and treated with an intravenous injection of one of the two antibiotics that work against it.

The submission on priority medicines made to the WHO by the EPPOSI

Formed in 1994, the [European Platform for Patients' Organisations, Science and Industry \(EPPOSI\)](#) is an alliance of patient organisations, technologists and industry. EPPOSI members work on health policies related to the treatment and prevention of serious diseases—notably rare conditions affecting no more than 5 in every 10,000 people. Though rare, the total number of the conditions is so great (some 5,000-8,000 different conditions fall into the category of rare, serious diseases), that, taken together, they afflict as many as 20-25 million people in the EU alone. The EPPOSI's activities include:

- Promoting R&D.
- Encouraging dialogue about ethical guidelines in innovative technologies.
- Determining factors that improve access to care.
- Sponsoring medical services and support for people affected by rare disorders.
- Advocating the appropriate use of genetic testing and counselling.
- And helping collaboration between patient organisations in the EU.

One coup for the EPPOSI was the December 1999 EU Orphan Medicinal Products Regulation [No 141/2000], providing financial incentives to pharmaceutical companies to conduct R&D in treatments for rare diseases. Previously, pharmaceutical companies would not usually develop treatments for these conditions, inhibited by the small number of patients affected and the uneconomically low revenues anticipated. Since the implementation of the 1999 regulation, however, 300 applications for approval of orphan medicines have been made via the European Agency for the Evaluation of Medicinal Products (EMA). Before 2000, the EMA had not processed any orphan medicinal products at all.

The EPPOSI on the WHO/Dutch government *Priority Medicines* report

The EPPOSI submitted a number of criticisms about a draft, pre-publication version of the WHO/Dutch government report. The organisation's comments included:

1. The report was unclear about whether the whole exercise was conducted to encourage the development of new medicines.
2. Although the report mentioned prevention and diagnosis, the document's main emphasis fell on drug treatment.
3. The report failed to clarify how the health of the EU population compared with that of the rest of the world.
4. The report claimed to provide solutions as to how public intervention can promote research into the development of priority medicines in the presence of market failure. But the published recommendations were entirely lacking in detail. In addition, the report did not acknowledge the significant role of legislation in altering the direction of medical research (the EU's own 1999 Orphan Medicinal Products Regulation, for example, has promoted the rapid development of treatments for rare diseases).
5. The methodology for prioritising research areas was poorly described in the report. According to the EPPOSI, the usual criteria for selecting top-priority diseases are: prevalence; severity of the condition (for the patient, society and the economy); and the contribution to the rate of premature deaths. The report also failed to take into account drugs currently under development in the R&D pipelines of pharmaceutical companies. Given the WHO's unique ability to consider the evaluation of priority medicines without reference to national economic circumstances, the EPPOSI believes that "*the WHO should be looking at these issues from a primarily humanitarian and societal standpoint.*"
6. The report did not separate the healthcare issues that affect developing countries from those which are important for developed nations. Such a distinction must be made when looking at the criteria for prioritising medicines.

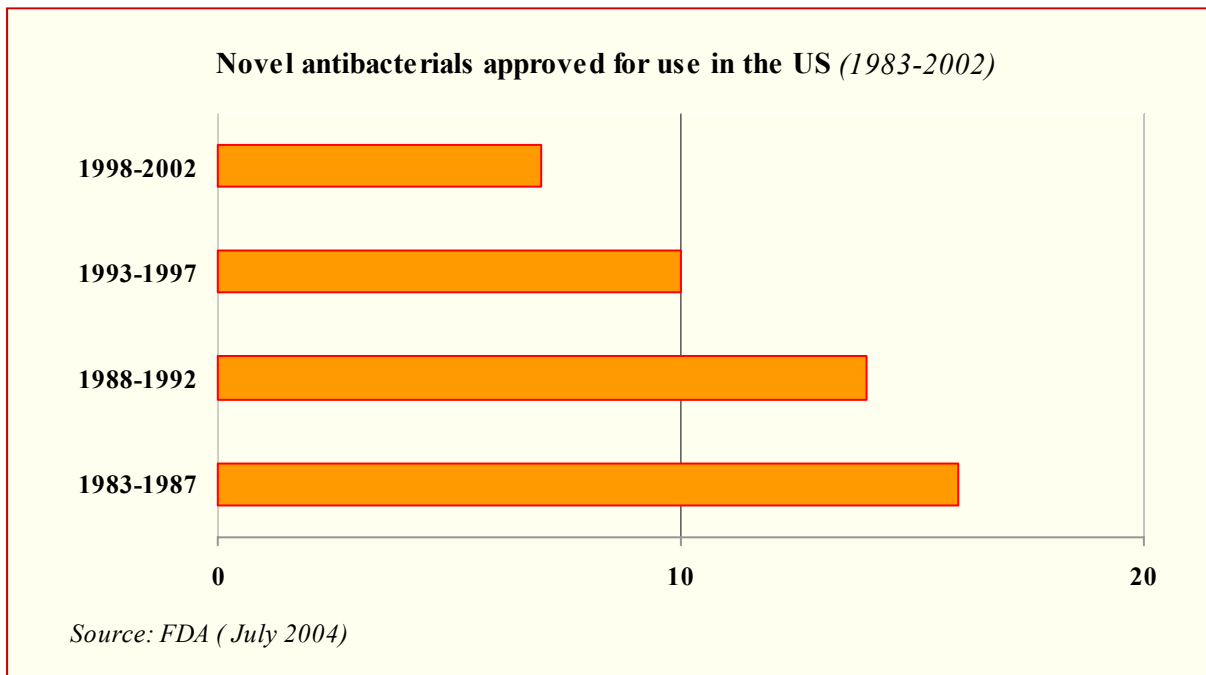
In a market-forces system, says Dr Laing, complex diseases discourage research

Pharma is developing fewer antibiotics

The industry also finds most vaccines uneconomic to produce, states Dr Laing

required to develop treatments. Hence, some pharmaceutical companies have decelerated their research into medicines for Alzheimer’s disease, osteoarthritis, acute stroke and certain cancers. One of the problems with Alzheimer’s disease in particular, said *Priority Medicines*, is that medical science cannot diagnose the condition in its early stages. The report therefore argued that far more should be done to develop accurate tests.

- **The vanishing antibiotic.** Deterred by the relatively low incidence of bacterial infections in the US, Europe and the richer parts of Asia and the Pacific Rim, the pharmaceutical industry has little reason to invest in the development of new antibiotics. Over the past decade, the US Food and Drug Administration (FDA) has recorded a halving of the number of new molecular entities approved to combat bacteria [see figure below]. But dangerous strains of bacteria continue to evolve and acquire resistance to medicines. Dr Laing feared that future generations may well have to live “*in a world without antibiotics*”.
- **Vaccines for communicable diseases.** The 1919 influenza pandemic counted millions as its victims. Most were elderly. Recent outbreaks of avian influenza in east Asia have set alarm bells ringing in international and national healthcare bodies (such as the WHO). The WHO is convinced that the world will face a new influenza pandemic sooner, rather than later. The pharmaceutical industry, meanwhile, has curtailed its research into vaccines. The economic benefits resulting from the development of vaccines are insufficient for almost any company with an eye on the bottom line. Compounding the damage, said Dr Laing, is the five years needed for factories to set up to produce vaccines. *Priority Medicines* made a special mention of the need for HIV/AIDS vaccines. However, the industry’s very success at creating drug therapy to halt the progression of HIV/AIDS in developed countries has also stunted its interest in developing vaccines for the disease.



Press release on the Priority Medicines conference by the International Alliance of Patients' Organizations

Founded in 1999, the [International Alliance of Patients' Organizations \(IAPO\)](#) is a UK-based, Netherlands-registered international umbrella patient organisation. IAPO is concerned with promoting patient-centred healthcare throughout the world. The organisation believes in the importance of cross-border cooperation between patient groups. IAPO counts some 100 patient groups as members.

Support for the WHO/Netherlands government report

IAPO was invited by the WHO to comment on a draft version of *Priority Medicines*. The group also issued a press release after the November 18th 2004 conference in The Hague [*Priority Medicines Project: IAPO Makes Urgent Plea for Patient Involvement*, November 19th 2004].

The press release made clear that IAPO supports the general framework proposed by the WHO for identifying areas worthy of important new research. The organisation also approves of the WHO's attempts to encourage the pharmaceutical industry into reducing the dearth of medical innovation in important disease areas (particularly in rare diseases). The WHO's call for an increase in the public funds available for R&D is in sympathy with IAPO's own thinking, too. But the group expressed caveats, as well.

Research priorities should involve patients and patients' representatives

IAPO has consistently campaigned for patient involvement in all major aspects of healthcare decision-making. The assessment of priority areas for medical research should be no exception, it said. The patient view is important, according to IAPO. The organisation offers the example of risk perception: "*While the report says that the risk people want to take is different depending on the severity of the disease and the availability of other options, it should also point out that is different depending on the patients' own individual personality and the perception of how each level of risk could affect their lives.*" The patient, argues IAPO, is the only person who can decide what level of risk is acceptable to them—something that *Priority Medicines* does not make explicit.

The main reason why patients should be involved "*is that healthcare affects patients' lives, and they therefore have a right to equal involvement. In addition, shaping these processes and policies with the patient at the centre will improve patient satisfaction, patients' lives overall, and health outcomes.*" IAPO's November 19th 2004 press release specified that patients and their representatives will, of course, need to be trained and supported if they are to participate fully in healthcare decision-making.

IAPO were dismayed that patient representation at The Hague conference (the launch venue for the WHO report) was limited to a brief question-and-answer session at the end. The minimal patient involvement sat oddly with the recognition by the WHO and the Dutch government that consumer input was critical to the successful implementation of the report's recommendations on drug innovation. IAPO's press release concluded: "*Patients with long-term chronic conditions, and the organisations that effectively represent them—patients' organisations—must be involved in every step of the process. Not just in treatment guidelines, but in all health policy—including regulatory processes—because, ultimately, the decisions that will be made affect patients' lives.*"

- **Too few drugs for women, children and older people.** Medicines differ widely in their effects according to the age, gender and genetic profiles of individual patients. The pharmaceutical industry, however, finds that the cost of developing medicines for consumption by certain categories of the population—especially children, older people, and pregnant and breast-feeding women—is too prohibitive to be worthwhile. A case in

Combination therapies are another element in the medicines ‘gap’

‘Head-to-head’ clinical trials are on the decrease

Heat-stable medicines are needed, too

The *Priority Medicines* report suggests methods for establishing a list of vital medicines

point is the recent discovery of suicidal tendencies as a side-effect in teenagers (but not in adults) prescribed medicines from among a class of well-known antidepressants. *Priority Medicines* emphasised the need for paediatric formulations of HIV/AIDS treatments.

- **Combination therapies, or fixed-dose combinations (FDCs).** Clinical trials have shown that heart attack or stroke patients can greatly benefit from treatment with a combination of four drugs. The WHO insists that a ‘polypill’ of four different statins would reduce by 66% the chances of a repeat incidence among these patients. Because the four drugs in question are off-patent, no pharmaceutical company has been willing to shoulder the cost of developing the appropriate FDCs. “*Time for some serious research,*” said Dr Laing.
- **Comparative clinical trials.** Scientists have a rough idea of what new medicines can do. True capabilities, though, remain unknown. Doctors thus need guidance if they are to discern what to prescribe. Clinical trials act as a yardstick by which medicines can be assessed against each other. The pharmaceutical industry is required to attain product market approval by testing for safety and efficacy. However, companies are not required to undertake trials that compare their own inventions with that of their competitors. Such ‘head-to-head trials’ are usually performed by academics. But the rising cost of clinical practice has forced non-commercial organisations to scale back their clinical trials activities.
- **Heat-stable formulations.** The WHO has said that no heat-stable version of the hormone insulin is available to treat diabetes. Refrigerators abound in richer countries—the main markets of pharmaceutical companies—and demand there for a heat-stable version of insulin is consequently almost non-existent. The hot climates and lack of refrigerators in many poorer countries, however, preclude home storage of insulin. A similar story can be told for oxytocin, which is used in the treatment of postpartum haemorrhaging after childbirth.

A list of priority medicines

The preamble in the WHO/Dutch government report said: “*Priority-setting is a real challenge for every healthcare system in the world. As yet, it is safe to say that there are no widely-accepted methods for legitimate and fair priority-setting in healthcare.*” The WHO’s methodology considers several parameters useful for determining areas of need:

- Evidence-based analyses which compare the European and global burdens of diseases with available information on the clinical efficacy of existing medicines.
- Past and future demographic and epidemiological trends.
- Identification of diseases that represent a high burden on society and for which no market incentives to develop treatments currently exist. The priority areas may include rare (also known as ‘orphan’) diseases, which particularly affect people living in Europe. Other important diseases may include neglected conditions, which mainly strike at the poor in developing countries.

The WHO's list of conditions requiring priority medicines
Acute stroke
Alcohol-use disorders
Alzheimer's disease
Cancer
Cardiovascular disease (secondary prevention)
Chronic obstructive pulmonary disease
Depression in older people and teenagers
Diabetes
HIV/AIDS
Infections caused by antibiotic-resistant bacteria
Influenza (potential pandemic)
Malaria
Neglected diseases
Osteoarthritis
Postpartum haemorrhage
Smoking cessation
Tuberculosis
<i>Source: WHO, 2004</i>

Working through various databases, the WHO identified 17 public health hazards for which priority medicines were needed [see table, left]. The WHO pointed out that the preferred intervention for some diseases (such as alcoholic liver disease, chronic obstructive pulmonary disease [COPD], heart attack and stroke) is prevention through changes in lifestyle. Nonetheless, help should be at hand for individuals who have difficulty altering their behaviour or who already have the condition. For most other conditions on the list, medicinal innovation remains the only possible hope, stated the WHO.

Getting the drug industry on board

To promote research into drug innovation in the priority areas, and to encourage greater commercial involvement in the process, four different stimuli should be instituted, argued the WHO:

- Deregulation—reducing barriers to innovation.** The chain of actions that comprises drug development—from invention to prescription—are estimated to exceed US\$800 million per product. If bureaucracy was slashed and regulatory and other obstacles condensed, pharmaceutical companies might be more inclined to undertake R&D in the priority disease areas identified by the WHO. The European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) are both examining tactics for wringing time and cost savings out of the medicinal discovery-and-development process.
- Public-private partnerships (PPPs).** The past decade has seen PPPs assume an important role in bridging the gap between basic and applied R&D. Most of the funding for PPPs has flowed from philanthropic organisations (such as the Bill and Melinda Gates Foundation). National governments (especially those of northern Europe) are also big donors. However, the amount of money raised for PPPs is still nowhere near enough. This is why the *Priority Medicines* report considered the possibility that multinational bodies (such as the EU) should supplement public funding of R&D within PPPs. The idea of developing anti-malarial drugs with less than US\$10 million in the kitty is unrealistic, said Dr Laing. Yet that is precisely what PPPs are being asked to do. In 2003, the EU funded the European and Developing Countries Clinical Trials Partnership (EDCTP), an alliance of European and developing countries that provides clinical services to test vaccines and drugs for use against malaria, tuberculosis and HIV/AIDS. But, to achieve meaningful goals, the EDCTP needs far more money than the EU grants it. Another candidate for investment might be the New Medicines Faster Initiative of the European Federation for Pharmaceutical Sciences (EUFEPS), a partnership of industry, academic and regulatory agencies that was founded in 1991.
- Valuing innovation for the purposes of setting the prices of medicines.** Governments should—in principle—pay what a medicine is worth, not how much it costs to develop, said Dr Laing. The process by which reimbursement levels are set for medicines varies significantly from country to country. The WHO has called for the establishment of a common means of valuing medicines—a method that rewards the innovative. But whatever price is set, the value should reflect the destination

Across the Atlantic: the WHO ‘Ministerial Summit on Health Research’

Delegates at The Hague November 18th 2004 conference on Priority Medicines were given a videoconference link to the WHO ‘Ministerial Summit on Health Research’ (Mexico City, November 16th-20th 2004). The Summit was organised by the WHO and the Mexican government, and was run simultaneously to the event in The Hague. The Mexico City conference was attended by 30 national Ministers of Health, as well as by a delegation from Europe. Over 1,000 participants from 75 countries were also present.

Julio Frenk, Secretary of Health in Mexico (who once worked in Geneva as the WHO’s ‘Executive Director of Evidence and Information for Policy’), used the videolink to outline to the Netherlands assembly the aspirations of the Mexico meeting. He emphasised that the Dutch government-backed initiative on priority medicines neatly dovetailed with the WHO’s agenda in health research, as currently being discussed in Mexico.

Health research has been a concern of the WHO since the early 1990s, explained Dr Frenk. The specific goal of the Mexican Summit, he added, was to address “*the vital role of research in the improvement and sustainable development of population health, with specific emphasis on how to translate knowledge into action—the ‘know-do gap’—to improve health.*” Dr Frenk spoke of several important challenges that must be met to achieve that aim, including:

- ➔ **The overall budget for health research needs to increase.** In 2001, global private and public expenditure on health research reached US\$100 billion. But even this huge sum remains insufficient, since the majority of the funds are used to serve the needs of only a few [see next bullet point for explanation].
- ➔ **The current imbalance in research investment.** The needs of 90% of the population are served by only one tenth of total health research expenditure. This situation is not acceptable and should be addressed, said Dr Frenk.
- ➔ **Greater understanding of the way that health systems operate.** Another WHO publication, the 2004 *World Report on Knowledge for Better Health*, was highlighted at the Mexico City forum. The *World Report* said that half of the world’s death rates are preventable with simple and cost-effective interventions. But not enough is known about the logistics of getting these treatments to the people who need them. The report concluded: “*A stronger emphasis should be placed on translating knowledge into action to improve health.*”

Can the EU help? According to Dr Frenk, Europe has a role to play in lessening the global burden of disease. The WHO/Dutch government-commissioned *Priority Medicines* report agrees, and has contributed some suggestions as to how:

- ➔ Europe’s experience with tax-based and insurance-based social healthcare systems is of value to, and can be adapted for use in, developing countries.
- ➔ Most of the priority medicines identified in the WHO/Dutch government report are also of paramount need in poorer nations—notably HIV vaccines; better treatments for diabetes; drugs to combat antibiotic resistance; and drugs for neglected diseases.
- ➔ The WHO/Dutch government report suggests ways of making the transition from basic to applied research, and considers interventions for promoting public-private partnerships.
- ➔ The WHO supports the view that regulatory processes for the approval of drugs need to be reviewed, so that innovative medicines can be made available more quickly for patients in need.
- ➔ The WHO concurs with the notion that the design and implementation of any healthcare policies require the involvement of all stakeholders.
- ➔ ERaNet [see page 9] is an idea that should be replicated worldwide.

The WHO argues for country-specific pricing and labelling

Specialised medicines for children and older people are vital, too

About Janet Voûte

Janet Voûte has been chief executive officer of the [World Heart Federation \(WHF\)](#) since 1991.

Ms Voûte is responsible for strategic planning, corporate partnerships, marketing, communications, finance and information technology. She is also active in global advocacy efforts.

The WHF, which is based in Geneva, has a mission to prevent and control heart disease, particularly in low- to middle-income countries. The WHF is the only NGO recognised by the WHO as a partner in heart disease treatment and control.

country's ability to pay. To make the system attractive to industry, regulators will need to impose country-specific labelling and packaging measures. These would hopefully handicap attempts at parallel trade, and prevent wholesalers from taking unfair advantage of differential country-to-country medicines prices. Another consequence of differential pricing is that richer countries will have to bear the brunt of the development costs of medicines.

- **Legislating for change**—in particular, for the approval of medicines for children and older people. The US already has regulations for children's medicines, and new rules are to be passed in the EU in 2005. On the other hand, governments are unlikely to legislate for the regulation of medicines consumed by the elderly for some years yet, Dr Laing recognised. In addition, he considered that better systems for detecting the adverse effects of drugs should be initiated, once they are available to patients.

The role of patients

Dr Laing said that the role of patients as contributors to the WHO/Netherlands government report was not properly considered when the study commenced in 2003. But as the project progressed, the value of public and patient perspectives became more apparent. Patient advocates, Dr Laing noted, have shown themselves capable of moving innovation forward.

The WHO has been encouraged in this regard by the experience of the National Institute for Clinical Excellence (NICE), which is charged with developing clinical protocols and scientifically-based guidelines on cost-effective treatments for use in England and Wales. Since 2003, NICE has been actively embracing organisations that represent patients and people with a disability. Patient advocates play an active, rather than a passive, role within NICE assessment teams—even though the teams are mainly staffed by specialists and senior doctors. NICE also provides training to people who participate in their assessments. Other regulatory bodies, insisted Dr Laing, should follow suit.

At the close of The Hague conference

The Hague conference closed by using a panel discussion (panel members included an ethicist, a politician, an expert in public health, and a representative of the pharmaceutical industry as well as Dr Laing) to develop recommendations on the following subjects:

- The selection of priority research areas.
- The types of populations most at need.
- The methods by which research could be delivered, and the types of research required.
- And the role that public-private partnerships, small-to-medium enterprises, the European Investment Bank (the EU's financing institution), and the EU's own R&D framework might play in bolstering research in priority areas.

Ms Janet Voûte, chief executive officer of the World Heart

The pharmaceutical industry's impressions of the *Priority Medicines* report

Andrew Witty, President of GSK Europe, explained the pharmaceutical industry's points of views regarding the WHO/Netherlands government report on priority medicines.

- ➔ Mr Witty believed that pharmaceutical companies were generally pleased with the *Priority Medicines* report. He thought that the entire exercise was based on sound mechanisms capable of stimulating industry to conduct research in areas where profits are difficult to attain.
- ➔ Mr Witty said that drug pricing schemes are unlikely to be harmonised across Europe. The customers in European markets are governments. Governments also provide perverse incentives to encourage pharmaceutical investment without regard to the R&D agenda—which could explain market distortions.
- ➔ The proliferation of 'me-too'-type drugs was related to the competitive nature of pharmaceutical R&D, observed Mr Witty. In effect, the R&D process is a form of horse-race in which a number of rival firms run neck-and-neck towards a distant finishing line. First past the post—the swiftest company to make market—sweeps up most of the winnings. In such races, as many as six or seven 'also-rans' may trail in behind the leader.

The debate at the end of The Hague conference concentrates on recognising potential flaws in the *Priority Medicines* report

Federation of Geneva, was given the task of moderating the stakeholder discussion. She ensured that the patient and consumer standpoint received adequate attention in the debate.

The debate exposed a number of possible flaws in the WHO/Dutch government report:

- The databases used by the WHO were not as robust as they could be.
- Patient compliance (when taking medicines) and the distribution of medicines in difficult national infrastructures were subjects that the report mostly overlooked.
- Important disease areas (such as renal failure) were omitted.
- The huge differences in health priorities between the first and third world were not properly considered.
- Too great an emphasis was placed on pharmaceutical interventions, and little consideration was given to other types of treatments.
- Methods for improving procedures for the reporting of adverse side-effects of prescribed drugs were not taken on board.

The panel also argued, however, that many of the misgivings about the report stemmed more from the limitations that the authors themselves imposed on the research agenda at the outset, than from any fundamental weaknesses in the completed analyses.

“Some shortcomings of the WHO report were highlighted by various stakeholders”

**But
conference
attendees are
generally in
favour of the
report**

Thus, conference attendees applauded the WHO and the Netherlands government on the back for their well-timed report, and for throwing down the gauntlet and asking policymakers to correct what is a clear and evident pharmaceutical ‘gap’.

Health campaigners’ perspectives

Health campaigners were among the many groups consulted as part of the WHO’s endeavour. The Netherlands government regarded these soundings as an absolute pre-requisite for developing any schema about medical R&D. A December 22nd 2003 resolution of the EU Council of Ministers (the main decision-making body of the EU concerning pharmaceutical and public health challenges) mentioned that *“Patients must be the focus of pharmaceutical policies, and that, therefore, emphasis should, in particular, be on providing medicines needed to treat otherwise incurable diseases—as well as on more efficacious, safer, and higher-quality medicines.”*

**The EU
regards
patients as a
crucial part
of medicines
policy**

**But patient
groups at The
Hague venue
say that
patient
consultation
has been poor**

But, despite the effort to include public and patient sentiment within both the WHO/Netherlands government report and the venue at The Hague, many of the health-based NGOs attending the event felt that the consultation was still too limited. They were also certain that the WHO and the Netherlands government failed to exploit the report and the occasion as potential means of embracing some of the more crucial issues of importance to health advocates.

Boxes scattered throughout the pages of this article have provided the comments of various health advocates, including the [Access to Essential Medicines Campaign](#), the [European Platform for Patients’ Organisations, Science and Industry \(EPPOSI\)](#), the [International Alliance of Patients’ Organizations \(IAPO\)](#), and the [International Osteoporosis Foundation \(IOF\)](#).

***“Nonetheless,
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and evident
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Health Action International holds an alternative meeting at The Hague

Attendees at the HAI's alternative meeting are less pleased with the Priority Medicines report than the audience at the official conference

Professor Graham Dukes speaks at the alternative meeting

He says the report should have looked more at prevention

Health Action International's satellite seminar

The next few pages summarise the presentations made at a satellite seminar entitled 'Setting Priorities and Missing the Point', organised by [Health Action International \(HAI\)](#), and also held in The Hague on November 18th 2004. The HAI roundtable took place in the morning, across the road from the venue for the main WHO/Dutch government conference that occurred in the afternoon. In attendance at the HAI meeting were 50 representatives of consumer, patient and aid-development organisations.

HAI is a consumer-oriented group that largely disapproves of the pharmaceutical industry and its activities—a fact reflected in the tone of the seminar. Several criticisms of the WHO proposal were announced at the HAI meeting. Contributors especially disputed the value of the WHO's suggestion that pharmaceutical companies should be encouraged to conduct the important medical research that would fill the pharmaceutical 'gaps'.

Dr Laing was present at the HAI satellite seminar, too. He opened proceedings by giving a talk based on his presentation at the WHO/Netherlands government conference. Three other scheduled speakers then indicated that they were opposed to the WHO model. In summary their objections amounted to the following:

- The WHO's blueprint for change did not guarantee patient safety.
- It failed to represent value for money.
- And it condemned millions of people to continue suffering from diseases for which medicines will not be developed.

Professor Graham Dukes

The first of the three commentators to address the HAI seminar after Dr Laing was Graham Dukes, Professor of Pharmacotherapy at the University of Oslo, and co-founder of the [International Society of Drug Bulletins \(ISDB\)](#). The ISDB was formed in 1986 with support from the WHO.

Professor Dukes opened his remarks by congratulating Dr Laing and his team on producing such an "excellent piece of work." After passing the compliment, though, Professor Dukes proceeded to admonish the *Priority Medicines* report on the following counts:

- **On prevention versus treatment.** The *Priority Medicines* study was large and complex, and conducted at great speed. As a result, the published report was forced to omit areas of analysis that affect drug innovation. Professor Dukes felt that more recognition of preventive health practices should have been incorporated in the report's findings. He stated: "After all, prevention is the most efficient and cost-effective way of bringing improvements in health."
- **On fixed-dose combinations for the treatment of secondary heart attacks and strokes.** Professor Dukes contested the wisdom of prescribing a 'polypill' of four different statins. Long-term consumption of these drugs, he noted, has been associated with side-effects. [According to [DiPex](#), a highly-

He disagrees with the report's stance on fixed-dose combinations, and thinks the document is Western-focused

Professor Dukes insists that suffering should be considered, as well as death

He is opposed to the WHO's contention that pharma companies form much of the future for research into priority medicines

He says that industry has a record of under-achievement and is too market-oriented

respected NGO that chronicles patient experiences, statins are effective in the prevention of heart attacks among those people who are at high risk of a cardiovascular event. However, these drugs also cause harm, and, in some instances, kill—see http://www.dipex.org/community/topic.asp?TOPIC_ID=87].

- **A too-Western perspective.** Europeans are obsessed with the health implications of an ageing population, emphasised Professor Dukes. Changing demographics is indeed triggering a rising incidence of chronic disease. But, while heart disease, diabetes and cancer contribute to ever-higher death rates in poorer nations, infection is prevalent in first and third worlds alike, and is a constant concern to all nations. The WHO's own data indicates that five out of every thousand people in the 25 countries of the EU die of some sort of infection. The world average is far higher, at 74 per 1,000 population. Professor Dukes contended that the WHO/Netherlands government report on priority medicines sets aside these facts, and overly focused on the implications of the range of diseases that afflict Westerners.
- **Suffering, as well as death.** Death and sickness are the main yardsticks by which the WHO measures the impact of specific diseases on public health. Yet, said Professor Dukes, levels of suffering ought to be taken into account, too. "*Sympathy*", he said, "*should weigh more heavily than statistics.*"
- **Is pharma the answer?** For Professor Dukes, the most contentious theme in the report was the WHO's belief that pharmaceutical companies represent a major part of the solution to the world's public health difficulties. "*Perhaps they do*", he conceded, and then added reflectively: "*but not without radical change in that industry.*" Professor Dukes went on to cite three problems that he thought bedevilled the pharmaceutical industry:

⇒ **Low output, and of questionable quality**

Pharmaceutical companies publicise their contributions to society, stated Professor Dukes. But their actual performance, he argued, has not lived up to expectations. For instance, only 1% of the industry's innovations have been directed at tuberculosis and other tropical diseases during the past 25 years. Or again, Professor Dukes pointed out that a new class of drugs called cox-2 inhibitors were heralded as breakthroughs for the treatment of arthritis in the 1980s and 1990s. Despite their high price, the cox-2s were thought to be worthy because they were free from the side-effects caused when relieving the symptoms of arthritis with aspirin or ibuprofen. But, by 2000, the cox-2s were no longer seen as a triumphant medical advance. Indeed, they were found to have side-effects of their own. One of the cox-2s, Merck Sharp & Dohme's Vioxx, was withdrawn from the market in late 2004 on account of its side-effects. The decline in pharmaceutical industry productivity, Professor Dukes insisted, can be blamed on an obsession with being market-driven. He referenced a book by Jürgen Drews, *In Quest of Tomorrow's Medicines* [published by Springer in 1999]. Dr Drews is an eminent scientist and former president of global R&D at Roche. His volume reasoned that pharmaceutical industry R&D is too disease-focused, and

**Professor
Dukes notes
that
innovation
sometimes
comes from
outside
industry ...**

**... and
medicines are
often
expensive**

**He believes
that
deregulating
to encourage
pharma
would not
produce
results of
value**

**He is in
favour of
parallel
importing**

that companies thereby end up subordinating research to market requirements.

⇒ **Genuine innovation is often sourced outside the pharmaceutical company itself**

Pharmaceutical companies cannot take all the credit for discovering the existing small handful of truly innovative medicines, considered Professor Dukes. For example, the anti-cancer treatment Taxol, currently marketed by Bristol-Myers Squibb, was originally discovered in the early 1960s by scientists from the US National Cancer Institute as a chemical extract in the bark of the Pacific yew tree, *Taxus brevifolia*.

⇒ **Inappropriate pricing practices**

Most EU nations are worried that the prices of patented medicines may be reaching intolerable levels—which is why many countries have introduced mechanisms to reduce the cost of their medicines. Professor Dukes calculated that less than one tenth of the price of a drug is channelled into continued research. Much of the rest is absorbed by marketing budgets.

For all these reasons, warned Professor Dukes, multinational pharmaceutical companies should not play a major role in debates on the future of research and medicines policy. The WHO recognised some of the problems he had outlined, said Professor Dukes. Yet the *Priority Medicines* report remains over-reliant on the pharmaceutical industry for solutions.

Incentive schemes for pharmaceutical companies

Professor Dukes then continued his talk by discussing the mechanisms by which WHO wishes to deploy to encourage large pharmaceutical companies to take on R&D in priority areas of medicine. He felt these tools were inappropriate, especially in three areas:

- **Deregulation**

Professor Dukes pointed out that the European Medicines Agency (EMA) already rejects one third of the drugs submitted to it for approval—which begs the question why the agency should lower its regulatory barriers. In the US, Professor Dukes alleged, regulations governing drug approvals have been relaxed so that patients can get quicker access to medicines. But the outcome has been of questionable worth, he said.

- **Differential pricing**

Although indicating that he recognised the value of incentives to reward therapeutic innovations, Professor Dukes added that pharmaceutical companies have, in the end, managed to sabotage these schemes (though how the industry achieved this, he did not specify). Parallel importing will occur if differential pricing exists between countries. But, said Professor Dukes, such trade is an “*excellent and acceptable way of levelling the huge disparities that exist in prices—as witnessed in the EU. There is really no reason why a medicine should cost twice as much in one country than in another,*” he insisted.

Formed in March 2002 in Paris, the [Medicines in Europe Forum \(MEF\)](#) is a partnership of patients, family and consumer bodies, mutual insurance groups, health professional organisations, and the International Society of Drug Bulletins (which is independent of the pharmaceutical industry). The group was created at the start of the EU legislative review on pharmaceuticals, to lobby on behalf of the organisations it now represents in Brussels. The MEF has 60 members based in 12 different European countries. The Forum seeks European pharmaceutical policies that serve the public interest.

Danielle Bardelay, a pharmacist, also argues that pharma companies have performed poorly

- **Public-private partnerships (PPPs)**

Professor Dukes felt that PPPs ought to be encouraged, but only on the understanding that industry does not usurp the lead role in the partnerships. Any public funding of PPPs should not be allowed to subsidise pharmaceutical companies.

If the WHO is looking for industrial partners, concluded Professor Dukes, better to rely on small companies—which at least hold the advantage of not yet having developed the bureaucratic and management problems that can sometimes beset big pharma. The smaller-sized outfits could then be encouraged to take on the important responsibility of filling the pharmaceutical slot created by their much-larger peers.

Danielle Bardelay

The second of the HAI satellite seminar's speakers to follow Dr Laing was Danielle Bardelay. Ms Bardelay is editor of La Revue Prescrier, a journal that was founded by a group of French physicians and pharmacists in 1981. She is a representative of the [Medicines in Europe Forum](#), and of the International Society of Drug Bulletins. Ms Bardelay is a pharmacist by training.

Ms Bardelay opened her presentation by also praising the WHO for its initiative on priority medicines. But, as with Professor Dukes, she found several faults with the report. Her main message seemed to be that pharmaceutical companies are not the organisations best suited to produce medical innovation.

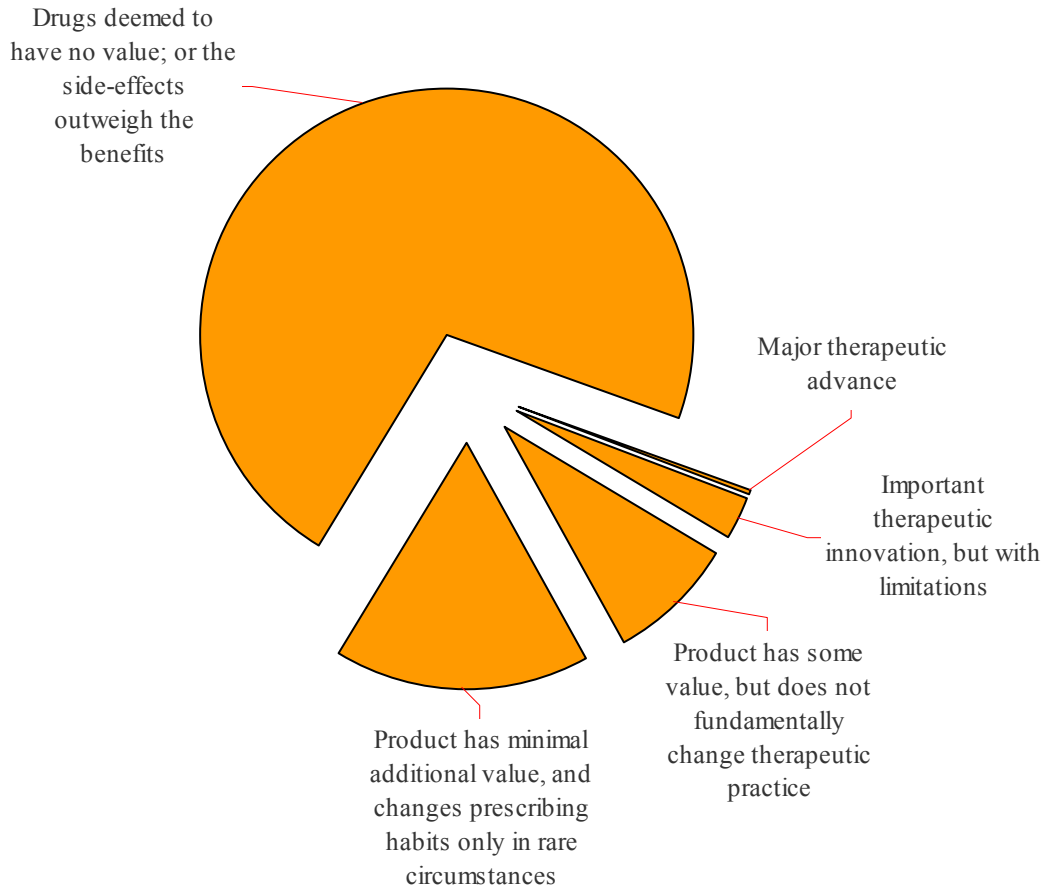
Prevention rather than cure

Like Professor Dukes, Ms Bardelay felt that the *Priority Medicines* report ought to have paid more attention to the value of preventive measures in avoiding disease, rather than merely concentrating on encouraging the development of new drugs. “*We don't want more drugs for diabetes and smoking-cessation,*” she said. “*Instead, we want interventions that prevent people from developing these conditions in the first place.*” In France during the summer of 2004, food manufacturers tried to obstruct the government proposal to ban the drinking of coke in schools. Although health experts won the day and the drink was banned, the experience illustrates the importance of the need for more research in the area of prevention, said Ms Bardelay. She specifically called for more research into the economic merits of prevention as compared with paying for medicines.

A poor innovative performance by industry

Ms Bardelay emphasised the importance of distinguishing between newly-marketed drugs that may offer little new advantages, and true therapeutic advances that provide patients with benefits unavailable through existing therapies. One of the main tasks of *La Revue Prescrier* is to assess in terms of clinical performance all novel drugs that reach the French market. The assessment is made by analysis of published and unpublished data. To date, *La Revue Prescrier* has looked at 3,000 drugs launched on the French market between 1981 and 2001. Each of the drugs is awarded a rating. Top notch is “Bravo”, indicating the best-possible clinical performance—a truly valuable contribution to medicinal treatment.

Therapeutic value of new drugs launched in the French market, 1981-2001



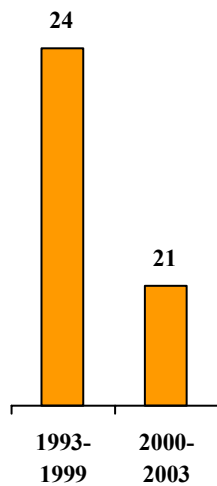
Source: *La Revue Prescrierer* (HAI satellite seminar, November 2004)

La Revue Prescrierer reckons only 0.2% of medicines on the French market are truly valuable

According to *La Revue Prescrierer's* calculations:

- 0.2% of pharmaceuticals looked at fall into the 'Bravo' category.
- 2.6% were classified as a "Real Advance", but possessing some limitations.
- 8.2% of products had some value, but did not fundamentally change therapeutic practice.
- Just over 16% had minimal therapeutic value, and only changed therapeutic practice in rare circumstances.
- The remaining 72.2% of new drugs launched on the market were considered unimpressive—either because they represented no medical advance at all, or because the side-effects outweighed benefits (or because the authors felt unable to make a judgement).

Percentage of new drug approvals allocated "priority status" by the US Food and Drug Administration, 1993-2003



Source: FDA

Given well-publicised cases of side effects, Ms Bardelay queries the WHO's tactic of reducing regulation

Similar results have been reported in other parts of the world. During 1993 to 1999 (inclusive), the US Food and Drug Administration awarded "priority status" (drugs that hold the potential to save lives) to under one quarter of all New Drug Approvals (NDAs). The remaining 75%-plus were earmarked for "standard status"—which meant that the FDA believed they offered little or no therapeutic value over existing therapies.

Canada's drug regulator, Health Canada—like the FDA—awards 'priority status' to products it considers embody a true medical breakthrough. For the years 1999 through to 2003, the percentage of new drug submissions granted such status ranged from just 7% to 14% for each of the five years.

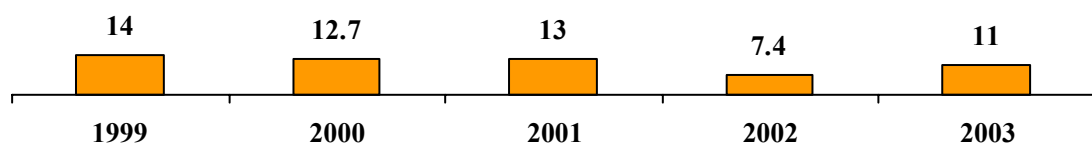
Prices of medicines do not reflect their clinical value

A 2002 article in the *British Medical Journal* by Silvio Garattini and Vittorio Bertele of Milan's Mario Negri Institute for Pharmacological Research ['Efficacy, Safety and Cost of New Anticancer Drugs,' *British Medical Journal*, August 3rd 2002, pages 260-271] estimated that the prices of twelve new anti-cancer treatments introduced into the EU from January 1995 to December 2000 ranged from three times to 350 times more than the nearest equivalent existing treatment. These sorts of premiums, said Ms Bardelay, might make patients and the public assume that the new products must be substantial therapeutic advances. But, as the authors of the *BMJ* article pointed out, such is not always the case.

Approved drugs can be unsafe

Ms Bardelay drew attention to the fact that cases of intolerable pharmaceutical-induced side-effects have been regularly and widely publicised since the 1950s. The medicines concerned have been approved by regulators. Some will have been on the market for years. One of the most recent disclosures involves a class of anti-depressants known as Serotonin Selective Inhibitors (SSRIs). A number of the drugs falling into this chemical category have been shown to cause suicidal tendencies in teenagers. Similarly, arthritis treatment Vioxx was withdrawn from the global market after the drug's potential to increase the risk of heart attack and stroke was made known. The Vioxx record was of eight years of widespread usage. Each of these incidents has led to stricter drug regulations. Today, the talk is of introducing new rules to make post-marketing surveillance of pharmaceuticals compulsory. "Why then reduce the regulatory barriers for pharma?", Ms Bardelay asked.

Percentage of new drug submissions granted "priority status" in Canada, 1999-2003



Source: Health Canada

Ms Bardelay believes that pharma companies have exploited EU orphan drugs regulations

Perverse incentives

Ms Bardelay spoke about the WHO's proposal that the pharmaceutical industry should be given financial incentives to conduct research into priority medicines. The 1999 EU initiative on orphan drugs law is an example of what the WHO has in mind, she noted. The regulation stipulates that, once approved, orphan drugs (which are used to treat rare diseases) should be guaranteed 10 years of market exclusivity. In addition, their manufacturers should pay smaller fees during the steps that lead to market authorisation. Pharmaceutical companies have been quick to take advantage of these inducements, claimed Ms Bardelay. Privileges have been abused, she said. Some of the products attaining orphan drug status, for instance, have gained approval for other uses—thus increasing the size of their markets and the financial rewards for the producers.

She says that several factors support the idea that pharma's output is of questionable value

Ms Bardelay summarised why she believed the contributions made by the pharmaceutical industry to medicine have often been of questionable value:

- A lack of comparative evaluation of medicines means doctors have no idea of the therapeutic value of pharmaceuticals.
- Opaqueness in the regulatory affairs of the drug industry allows products to continue to be prescribed, even when clinical evidence known to the company and its regulators suggests that they might be harmful.
- An inadequate supply of information to the public on medical errors leads to inappropriate use of medicines.
- The lack of research into the clinical value of primary prevention has resulted in a continued and growing burden of chronic disease.

She advises careful application of stricter regulations and more attention to prevention

Ms Bardelay recommended the following actions:

- Regulations should be stricter, not more relaxed. Drug approval requirements—before a product is marketed—should include proof of clinical worth against existing therapies. The US has tried to control the distribution of approved medicines by offering conditional approvals to manufacturers, on the understanding that they track the performance of their product as prescribed. The FDA's intention is to provide patients with speedier access to potentially worthwhile medicines, while ensuring that, if a product is harmful, not too many people are damaged by it. However, according to Ms Bardelay, from FDA data: only half of the pharmaceutical manufacturers have complied with the provisos of the conditional approval.
- Therefore, existing drug regulations should be properly implemented.
- Attention should be paid to creating a system that permits patients to report adverse reactions to medicines.
- Drug regulatory processes and activities should be more transparent.
- Research should look at the economic merits of preventing the occurrence of disease, versus drug reimbursement.

[*Editorial note:* Speaking on November 18th 2004 before the US Senate Committee on Finance on Vioxx, David Graham, a senior

**A new US
Office of
Drug Safety
(post-
approval) is
mentioned in
November
2004**

**Ron
Hendricks, an
insurer, is the
third critic of
the *Priority
Medicines*
report to
speak after
Dr Laing**

**Mr
Hendricks
talks of the
importance of
prevention,
regulation,
and pricing
that reflects
therapeutic
value**

reviewer with the FDA, questioned the ability of the Agency to police drugs after their approval—since doing so calls into doubt the FDA’s ability to vet medicines in the first place. Dr Graham called for the creation of a new Office of Drug Safety, accountable for post-approval safety. The Office would be separate from the FDA (which would continue to maintain responsibility for originally approving drugs). Opponents of Dr Graham’s suggestion argue that the extra bureaucracy involved in approval would make pharmaceutical companies much more adverse to taking commercial risks, and would inevitably add to the costs of medicines.]

Ron Hendricks

The final of the three speakers to follow Dr Laing was Ron Hendricks, president of the Brussels-based Association Internationales de Mutualites (AIM). AIM represents the interests of 44 national non-commercial insurers drawn from across Europe. Its mission is to:

- *Defend and promote the social and political agenda of its member insurance companies.*
- *Increase levels of access and other healthcare rights for patients.*
- *And foster the principle that healthcare is for all.*

AIM is also concerned with the process of drug innovation. The organisation wants a political agenda in medicines R&D, so that new products are created to fulfil the real health needs of the public, rather than just generate profits for the pharmaceutical industry.

Mr Hendricks mentioned a number of his own criticisms of the WHO/Netherlands-government *Priority Medicines* report:

- **On prevention.** Although the report did consider the benefits of prevention, its focus was chiefly on the role that medicines could play in that approach. Mr Hendricks drew attention to the significant efforts made by Finland to reduce mortality rates among its citizens through comprehensive programmes that aim to promote healthy lifestyles.
- **On regulation.** Mr Hendricks opposed moves to reduce the regulatory barriers for the approval of medicines. He wondered why the *Priority Medicines* report made no mention of the recent EU Clinical Trial Directive, passed in 2004. The Directive stipulates that pharmaceutical manufacturers can challenge what they might perceive as unfair regulatory practice in the European Court of Justice.
- **Differential pricing.** Mr Hendricks affirmed that AIM does not support differential pricing as advocated in the report. Medicines prices should reflect their therapeutic value, he said. If pharmaceutical companies do not perform tests to evaluate the worth of one of their medicines against other similar remedies on the market, then that fact should be reflected in the product price.

Mr Hendricks proposed that unmet public health priorities could be tackled by the following suggestions:

- More emphasis on health education and prevention of disease.

**Mr
Hendricks
recommends
several
changes in
government
policy**

- A focus on infections and neglected diseases.
- Reflection on ways of rewarding organisations that produce ‘breakthrough’ innovations.
- Realise the effectiveness of medicines and add therapeutic value to them by conducting head-to-head clinical trials among pharmaceuticals in similar therapeutic areas.

**Dr Laing
replies to the
many
criticisms
made at the
HAI
alternative
meeting**

Dr Laing responds to the report’s critics

After the three follow-up speakers had their say, Dr Laing was bombarded with a series of wide-ranging questions from the floor. The queries focused on the role of intellectual property rights as an important lever for controlling innovation; on greater citizen participation in global and national policy-making in the area of medicines R&D; and on anti-trust and medical-liability issues.

Dr Laing responded with good grace to the numerous disparaging assessments of the *Priority Medicines* report. With only one year available to complete the report, many factors had to unfortunately be set aside during the analyses, he admitted. The subject of intellectual property rights, he said, was being studied by other parts of the WHO. Dr Laing agreed with the idea that the public and patients and their representatives should be welcomed as working participants in all areas highlighted by his report. However, he strongly defended the main recommendations of the report:

**He defends
the report’s
conclusions
on priorities,
regulation,
differential
pricing and
pharma’s
record of
innovation**

- **The choice of priorities.** Dr Laing pointed out that deaths from lung cancer in China are forecast to reach 4 million per year by 2020. The research and development of smoking-cessation products will be valuable to people who are addicted to tobacco and who find present anti-smoking aids ineffective. “*Just because someone is addicted, why give up on them, too?*”, he asked. Neglected diseases, he granted, are a very important area in need of further research.
- **Drug regulation.** Dr Laing informed the audience that the WHO is behind moves to expand the surveillance of approved drugs in the market [but unlike HAI, the WHO does not seem to support new regulatory structures prior to a product’s approval].
- **Differential pricing and parallel importing.** The former is a valid way of rewarding innovation, stated Dr Laing—it offers incentives for risk-taking. Parallel importing, however, increases prices in source countries (from which drugs are exported), and thereby hurts the poor of those nations. This is why such trading practices need to be inhibited, he reasoned.
- **The pharmaceutical industry’s record on innovation.** Dr Laing emphasised that pharmaceutical companies do not plan from the outset to spend lots of money producing ‘me-too’ products. But, once a medicine has gone through the lengthy and expensive process of clinical testing, abandoning it entirely after a competitor reaches the market first with a similar product seems nonsensical. If a differential pricing system was introduced in the manner indicated in the *Priority Medicines* report, ‘me-too’ products would not be remunerated with high price tags.

Conclusion

Health campaigners were united on several fronts in their response to the WHO/Dutch government proposals to boost health and medicines research in disease areas of great priority. For instance, conversations that *HSCNews* had with health advocates at The Hague indicated that all campaigners agreed on the following:

- The WHO/Netherlands government *Priority Medicines for Europe and the World* report was clearly a bold attempt to propose radical solutions to an intractable problem—the increasing paucity of research into what the WHO has termed ‘priority’ medicines.
- The report performed excellent service in identifying many of the areas most in need around the world—including the neglected diseases of poor, tropical countries; novel antibiotics; and vaccines to fend off potentially forthcoming influenza pandemics.
- *Priority Medicines* was correct in determining that commercial markets, when left to their own devices, had failed to deliver important medicines. And that the public sector could do a lot more in supporting health R&D.
- But the groups also felt that the WHO should have made greater efforts to develop different approaches to often widely-varying third- and first-world health problems. Also WHO should taken a more humanitarian approach in its assessment of priority disease in need of attention—rather than concentrating on stark statistics.
- Health campaigners believed that a greater emphasis should have been placed on preventive medical practices, even though this was not the immediate remit of the report.
- Finally, all groups publicly or privately rounded on the WHO for insufficiently representing citizen and patient viewpoints in the *Priority Medicines* consultation process—a failing that campaigners insist should be rectified in any implementation plans.

That, however, is where the accord among campaigners ended. Many of the patient groups at the meetings in The Hague were disgruntled that their own specific disease areas and treatments had been left off the WHO’s ‘priority’ list. The lowering of cholesterol as a method of prevention for heart disease was one such example. Other advocates lamented the WHO’s emphasis on promoting interventions to control diabetes or smoking—which are, anyway, manageable through changes in lifestyle, they said.

Patient and consumer groups were divided on the best means of promoting the R&D of medicines for the WHO’s priority disease areas. The EPPOSI and a number of other patient groups backed the introduction of financial incentives to encourage pharmaceutical companies to find ways of plugging the medicines ‘gaps’—albeit acknowledging that these schemes were certainly imperfect and may also be fragile. By contrast, HAI, MSF and Medicines in Europe Forum seemed to regard the *Priority Medicines* report as a vehicle for advancing the interests of the pharmaceutical industry. Consumer groups attending the meetings argued for a far more complete overhaul in thinking toward medical R&D than that provided by the November 2004 *Priority Medicines* report.

Where now?

In reality, the Mexico City conference and the meetings in The Hague form just a foretaste of things to come. Discussions about whether commercial organisations are a force for good in the public health arena are likely to continue as a major theme during 2005. Debate will stray well beyond the present topic of medicines innovation, though, and may embrace the following: the pharmaceutical funding of patient organisations; the mandatory registration of clinical trials; access to affordable medicines; intellectual property rights of medicines; transparency of patient information on prescription medicines; and under-achieving drug regulators. Most are matters of concern to health campaigners of all genres. If these subjects have not yet topped the agenda in December 2004, they certainly promise to rise high next year.

Issue 13/14 of *HSCNews International* (January 2005) will publish the results of an *HSCNews* global survey into health campaigners' most significant issues during 2004 and their predictions for the major themes of 2005.

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- ✓ Stem cell research splits the world of patient advocacy.
- ✓ Campaigners in the US, Canada and New Zealand take opposing sides on the DTCA issue.
- ✓ Three overarching patient umbrella groups are created in Europe.

Issue 2 (December 2003)

- ✓ Campaigners for affordable medicines scored huge successes.
- ✓ The men's health movement has moved beyond issues of sexual health, and is now a global force.
- ✓ Interview article: the Men's Health Forum—a model for campaigning groups?

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- ✓ Interview article: Active Citizenship Network's 'European Charter of Patients' Rights'.

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