Opening Session

The Chair of the Commission invited Mr Claude Allen, Deputy Secretary of the Department of Health and Human Services to make the opening remarks. Mr Allen noted the high interest of many governments in the work of the Commission, including the USA, and the potential for making evidence-based recommendations. Ageing societies, increased global travel, and the continuing prevalence of infectious and chronic diseases meant shared global concerns on health. The issue was how to get innovative medicines to those who needed them. This required an input from governments, academia, and the pharmaceutical and biotechnology industries. He thought that the USA bore a disproportionate share of global investment in R&D. How could we all do more to encourage medical innovation, and spread the benefits more widely. Access to medicines needed to be promoted, but not at the expense of stifling innovation.

Dr Joxel Garcia, deputy director of PAHO, recounted his experience of patenting in the private sector, and the protective and competitive behaviour this tended to induce. After leaving the private sector, he now had a different perspective. In aggregate he felt that there was too much research on some diseases at the expense of others. He hoped the Commission would bring some clarity and wisdom to a field where opinions were very polarised. There was a great need for new medical innovations but there should also be greater attention paid to their equitable distribution.

Dr Tomris Türmen, Representative of the Director General of WHO, noted the importance to the Commission of understanding the situation in the USA. In the field of intellectual property rights (IPRs), US policy was influential, both directly and indirectly, in the rest of the world. Innovations similar to the Orphan Drug Act, or the Bayh-Dole Act, had been adopted in other countries, and debates in the USA on specific aspects of IP policy were relevant both to other developed countries, and also developing countries. Moreover, the US remained globally predominant in pharmaceutical and biotechnological research in both the public and private sectors. Probably more research was done on diseases that disproportionately affect developing countries in the USA, than the rest of the world put together. Moreover the Commission was interested in the impact of the drug regulatory system on the process of drug development, and in ways in which drug discovery could be accelerated and the cost reduced. The Commission needed to understand how the vast resources of the developed world, and growing capabilities in the developing world, could be brought together to meet the healthcare needs of the developing world.

Ruth Dreifuss, Chair of the Commission, noted that the member states of WHO wanted the Commission to produce a calm and clear analysis of issues that were very much contested within nations and between nations. The disparity between the developed world on the one hand, and the developing world on the other, posed great challenges for policymakers globally and nationally. It was the job of the Commission to consider how best to stimulate relevant innovation, while at the same time seeking to ensure that the products of innovation could be made available to those who need them in developing countries. The visit to the United States would be very helpful to the Commission in developing concrete proposals to advance this agenda.

Food and Drug Administration (FDA): Dr Murray Lumpkin, Teresa Mullin, Randall Lutter

Dr Lumpkin and his colleagues explained how the drug regulatory system in the USA functions and the complex issues that arose in the process of drug regulation. Particular aspects noted included:
• The process of priority review for products which represented a "significant improvement compared to marketed products"
• The promise offered by new technologies in research e.g. proteomics, nanotechnology
• But the number of products approved had declined in recent years while R&D expenditure has increased - the failure rate at each stage of development was very high
• Thus the cost of successfully marketed products was rising
• Commercial pressures tended therefore to favour "blockbuster drugs" for chronic conditions with less attention paid to curative and preventive interventions - "decreased focus on true innovation"
• Role of FDA is positive (facilitating "good" new products as well as keeping out "bad" products)
• The Critical Path Initiative seeks to promote innovation in the process of drug discovery by applying new techniques, methodologies and technologies to the process
• A key point is to increase the ability to predict probable failures at the earliest stage of development and to produce smarter trial designs and other new tools to improve the productivity of drug discovery
• The impact of measures such as the Orphan Drugs Act (and paediatric extension) as incentives for treatments where market forces are inadequate.

The FDA presentations are at:

The Roles of Drug Regulatory Authorities in Enhancing Medical Science Innovation: Diseases that Disproportionately Affect Developing Countries [pdf 1.15Mb]

Commissioners asked a number of questions and made a number of comments. In reply Dr Lumpkin and colleagues made the following points:

• The Critical Path Initiative could have general applicability, including for products aimed primarily at developing countries
• FDA did have a network of relationships with other regulators in different parts of the developing world, and sought to collaborate actively with them
• FDA was talking to companies in India and South Africa about the new review process for products that might be included in the PEPFAR programme, which could apply also to generic copies of drugs patented in the USA.
• The issue of different risk benefit equations in different parts of the world was important. e.g. rotavirus
• Market exclusivities could be important where market incentives were deficient e.g. Congress wanted incentives for paediatric devices
• The capacity of FDA was necessarily limited but, within those resources, they tried to meet the demands put upon them including, for instance, in respect of drugs for TB where there was no recent history of regulatory involvement
• FDA could use the mass of data it has accumulated to analyse failures and the factors associated with them e.g. liver toxicity or carcinogenicity. Much could be learnt from failures
• A key issue in improving the process was the possibility of substituting in vitro or in silico models for animal and human testing.

United States Patent and Trademark Office (USPTO): Dominic Keating, Mary Critharis, Jeanne Clark

Dominic Keating gave a presentation on the benefits of the patent system. He explained how "limitations on some patent systems" with respect to the commercialisation of government funded research and incentives for R&D on rare diseases had been addressed in the USA through the Bayh-Dole Act and the Orphan Drug Act.

His presentation is at:
In response to questions from the Commission Mr Keating gave the following answers:

- He thought that government march-in rights under the Bayh-Dole Act were not used to control prices
- He questioned whether there was an issue about the patenting of research tools - treating them as trade secrets would be worse
- There was a high bar for patentability of gene sequences in the USA, requiring specification of a specific use
- He saw no need for research or similar exemptions
- Asked about how USPTO reconciled patent policy with wider government policy objectives (e.g. in health or agriculture), he said they followed the mandate provided to them by Congress, although there was a dynamic between different government departments
- The recommendations of the 2001 White Paper had not been pursued
- A global patent system would be a good thing, and there might be benefits for developing countries in the sphere of traditional knowledge.

Mary Crittharis then made a presentation on the patenting of new uses of known compounds available at:

"New Uses" [pdf 28kb]

**Lunchtime Speaker: Mark McClelland, Administrator, Medicare and Medicaid Services**

Mark McClelland discussed, amongst other things, the need to establish a global system where the pricing of drugs varied according to ability to pay. The big differences in policy in this area in developed countries were not sustainable, and could drive prices down globally at the expense of innovation. Current systems for setting prices in many developed countries tended to discourage innovation and delay the introduction of new treatments. 60% of new drugs first appeared on the US market because of its pricing policies. Countries were now moving away from compulsory licensing also. Pricing and spending policies should be guided by the need to reward innovation for branded drugs. On the other hand, in many countries there was too much reliance on branded generics, and the prices of unbranded generics were higher than in the US. Efforts should be made to redirect spending towards cheaper unbranded generics.

Apart from pricing policies, the new scientific advances in biomedical science had not yet delivered in terms of new products. Thus initiatives such as the Critical Path were very necessary. There was also a need to provide more incentives for specific purposes such as the Bioshield programme. In the field of regulation there was a need to work together internationally to reduce duplication and draw on global experience. In particular, there was a need to monitor how products, post-approval, behaved in real world situations with different groups of patients. Not enough was being done in this area.

In response to questions Dr McClelland said:

- There was a lot of research on the "push" side, but "pull" mechanisms such as Bioshield were a possible model to stimulate research on neglected diseases
- In general, reducing risk and uncertainty (e.g. through the Critical Path) was important to stimulate private investment
- In the Bioshield model, the first inventor should be rewarded, but this did not exclude the possibility of rewarding a second innovator
• There was a danger of pricing in the developed world being depressed at the expense of innovation
• Pricing according to ability to pay is threatened by failure to tackle smuggling effectively
• There should be uniform standards for regulation globally
• On the question of the balance between the $9 billion for Bioshield and $2 billion for the Global Fund for AIDS, TB and Malaria, both objectives were important
• The issues before the Commission were the most important challenge of the century and global leadership was required.

**Federal Trade Commission (FTC): Susan DeSanti, Bill Cohen, Suzanne Michel, Tom Mays**

Susan DeSanti and Bill Cohen made a presentation on the FTC’s 2003 report “Balancing Competition and Patent Law and Policy”. The main points were:

• Both competition and patents can promote innovation, if properly balanced
• Patents have costs as a means to foster innovation but so do other means of protecting appropriability
• Competition policy suggests that patents should be awarded when an invention would not arrive in the same time frame “but for” a patent
• Patents are most effective in drugs, medical equipment and chemicals
• Patents can help structure and enhance the efficiency of technology transfer
• Patents most effective in industries characterised by large R&D costs and discrete, rather than incremental, innovation where the final product is protected by only a few patents
• Incrementally modified drugs (IMDs) versus new chemical entities (NCEs) - is the same degree of patent protection necessary to elicit IMDs as NCEs?
• Invalid or overbroad patents can hinder innovation and competition resulting in unjustified market power and unnecessary transactions costs which may raise prices and potentially interfere with follow-on innovation
• Perfection at the examination stage is impossible, but mechanisms are needed to reduce the impact of questionable patents
• Cross-licensing and patent pools are ways to mitigate costs of the system
• Developing countries need rules to stimulate price competition amongst generics and to govern dominant firm conduct.

The presentation is at:


Suzanne Michel and Matthew Bye gave a presentation on competition in the pharmaceutical industry based on the 2002 FTC Report “Generic Drug Entry Prior to Patent Restoration”. The main points were:

• The 1984 Hatch-Waxman Act sought to increase availability of lower-priced generic drugs while also promoting innovation through patent term restoration
• Hatch-Waxman provided an 180 day exclusivity for the first generic to enter the market after patent expiry
• This provides an incentive for the brand and generic companies to collude by retaining monopoly and sharing proceeds in some way
• Generics may also have an incentive to collude
• The Act also provided for a 30 month stay on approval of a generic where brand name company sues generic entrant for infringement
• More patents per drug are now listed in the FDA's Orange Book, and more patents per infringement suit
• This can lead to successive 30 month stays (for instance, there were five successive overlapping stays in the case of Paxil)
• This leads to significant litigation and uncertainty and entangles the drug approval process with patent issues
• As a result of the Medicare Act 2003, there can now be only one 30 month stay per generic application and the rules governing listing of patents in the Orange book have been revised.

The presentation is at:

**Competition in the Pharmaceutical Industry [pdf 252kb]**

In the discussion, it was noted that more information on patent issues in biotechnology was available from Steve Merrill's presentation in Geneva on the National Academies' report "A Patent System for the 21st Century":


FTC noted that there was no particular economic rationale in either the 180 day exclusivity or the 30 month stay, which were determined politically. It was not clear that either of these mechanisms were necessary to achieve the goals of Hatch-Waxman, but they had added to the complexities of the system and provided opportunities for extracting rents ("gaming").

**Industry**

Presentations were made by:

- The R&D Guide – P. Corr
- The Biotechnology Perspective - U. Ryan
- Incremental Innovation – K. Kaitin
- Research on Neglected Diseases – L. Marks
- TRIPS, TRIPS plus and Beyond - H. Bale

Dr Corr introduced the R&D guide commissioned by the industry for the Commission which is available at: URL. This seeks to explain the nature of biomedical innovation in a way accessible to non-scientists. Dr Corr concluded that industry and the Commission were each looking at the same problem. The solution was innovation. The current system was not perfect but IP incentives for innovation had to be preserved to meet the needs of the developing world. Other elements of access and affordability had to be addressed in parallel and across sectors. This could only be achieved in partnership and through communication. IP, Public Health and Innovation must be looked at comprehensively. He hoped this event would begin a continuing dialogue.

**Overview of Basic Science, Discovery and Development for Therapeutics: Brief Synopsis of the R&D Guide [pdf 928kb]**

Dr Ryan, CEO of Avant Therapeutics explained how her company developed and sold vaccines and immunotherapeutics for high-value large markets. With GSK they were also developing a rotavirus vaccine for global use. They had also developed a technology platform for bacterial vaccines which combined low cost, the possibility for combination vaccines and room temperature storage. Funding sources had included three different government programmes including the Department of Defense. The technology offered a lower cost of goods, a lower distribution cost (by reducing the cold chain) and development costs had been offset by government funding for R&D and Foundation funding for clinical development.

Professor Kaitin reported the results of research on incremental innovation. He reported that the development of follow-on drugs often occurs contemporaneously with that of the first-in-class. Market exclusivity for first-in-class drugs has been shrinking, fostering price competition. The therapeutic value of follow-on drugs is reflected in the percentage of (FDA) priority designations, inclusion in clinical practice guidelines, and coverage in major formularies.

Incremental Innovation R&D and Follow-on Drug Development: Economic and Therapeutic Considerations [pdf 1.21Mb]

Dr Marks reviewed the lack of access to existing treatments for many common diseases. IP was not a reason for neglect of R&D on diseases but nor was it sufficient - new incentives and approaches were needed. Financial, scientific and regulatory hurdles existed as also poor infrastructure and weak IP protection. Industry had responded by establishing dedicated research centres and there was a proliferation of R&D players in the public and private sectors, including in developing countries as well as the development of product development PPPs. Partnership between different actors was a key to unlocking barriers, and industry had specific expertise to offer in research, clinical development and manufacturing. There were already promising candidates in development for several diseases. Several critical gaps should be addressed to facilitate R&D efforts for neglected diseases which required the mobilisation of the entire global health community.

http://www.who.int/intellectualproperty/events/en/LynnMarks.pdf

Dr Bale proposed that implementing IP rights beyond those required by TRIPS would contribute to economic growth and development. Many countries were doing so including Singapore, Morocco, Jordan and Australia. It could help stem the brain drain, encourage local and foreign investment and promote technology transfer. He concluded that many countries seek to expand health care access through freer trade and IP protection and nurturing knowledge-based industries.

Enhanced IP Rights for Economic Growth and Development [pdf 80kb]

In discussion the following points were made:

- Could industry provide constructive and practical proposals on what would stimulate more research?
- Dr Marks thought that standards of regulatory assessment should be harmonised. The issue of varying risk-benefit ratios in different countries could be dealt with separately through treatment guidelines. But rejection by one country of a product raised serious issues for those proceeding with development elsewhere
- The issue of follow-on innovation was not confined to the patent system- a prize system would have to grapple with similar issues
- Procurement mechanisms (e.g. as in defence) might me considered as possibilities.
- Dr Corr did not think there were a lot of compounds in company libraries whose possible use in developing countries had not been ascertained.
- Dr Bale made a series of concrete proposals: that governments should do more, including for PPPs; that public research institutions should do more; and that governments should bear more responsibility for facilitating take-up of new innovations.

Non-governmental Organizations:

- Viji Rangaswami, Congressional Staff - Bilateral trade agreements
- Amy Kapczynski, Yale University - Access to government and donor funded research
- James Love, Consumer Project on Technology - R&D Treaty
Ms Rangaswami delineated the ways in which bilateral or plurilateral trade agreements might disadvantage developing countries by requiring "TRIPS plus" arrangements. She gave as examples: the prohibition of parallel imports, test data requirements similar to the USA and limitations on the use of compulsory licences. Even where countries had adopted these measures prior to an agreement with the US (e.g. parallel imports in Morocco) she argued that it constrained their future freedom of action contrary to the intent of the Doha Declaration. Applying US test data regulations might be appropriate in the US, but not in developing countries with no R&D base, and where poor consumers paid directly for their medicines. Similarly limitations on the grounds for compulsory licensing were contrary to the Doha Declaration. She noted that the 2002 Trade Act, governing US international trade agreements, laid down that agreements must respect the Doha Declaration. Although countries entered into these agreements voluntarily, political pressures existed to oblige them to adopt provisions not necessarily in their interest.

Ms Kapczynski emphasised the importance of the US public sector in research, especially for neglected diseases. The Bayh-Dole Act permitted licensing, including exclusive licensing, by universities if necessary to promote the commercial application of an invention. The growth of patenting and licensing by universities limited the public domain and, particularly for early stage research, might inhibit innovation. There needed to be new policies to promote R&D, preserve access to data, reintroduce a research exemption and facilitate access to end products in developing countries. New models for equitable access licensing and an Open Research Licence were required.

Access to Government and Donor Funded Research [pdf 49kb]

Mr Love noted the significance of the resolution recently passed at WIPO (http://www.cptech.org/ip/wipo/wipo10042004.html) which commits WIPO to incorporate a development agenda into its activities and to consider the development impact of intellectual property. He considered the current IP system was flawed. It encouraged too much innovation of me-too drugs and could prevent the development of required treatments (e.g. heat-stable Ritonavir). The pharmaceutical industry was not really very innovative, but good at the final stage of drug development and marketing. Only 10% of its turnover went R&D. We needed an alternative to the current system. He was proposing a treaty to encourage R&D though non-patent incentives including, for instance, prizes.

The following points were made in discussion:

• So-called me-too drugs included a range of treatments for malaria and HIV/AIDS which are surely desirable
• There needs to be cooperation between the public and private sectors, not competition
• More information and empirical data was needed to assess the implications of what was being proposed
• Radical reforms of the IP system were unlikely to work but incremental reforms might - there was a tension between the proposals for incremental and radical reform
• Extreme views might "frighten industry" with counterproductive results
• Me-too drugs were not so much a product of the patent system but more of reimbursement mechanisms
• TRIPS plus was, of course, consistent with TRIPS
• Parallel imports might in fact not be in the best interests of developing countries
• Rules on data exclusivity might not be in the best interests of developing countries

In responding Mr Love said they would submit more evidence on me-too drugs. He thought that ideas that seemed radical now would not seem so in a few years. Both short term and longer term strategies were required. It was necessary to have a vision, and the ideas put forward were not utopian. The big pharma business model was broke. Were we getting value for money from
the amount currently invested in R&D? Comparisons with the experience of the Soviet Union were not appropriate. A prize system should be seen as a complement not a threat to the patent system. He also agreed that parallel trade between the developed and developing world should not be allowed.

5TH OCTOBER: NATIONAL INSTITUTES OF HEALTH (NIH)

The Chair of the Commission, Ruth Dreifuss, introduced the session. She noted that much of the work done by NIH was relevant to the Commission - both in terms of the science and in seeking to develop policies for the patenting and licensing of the research.

The Commission was interested in how the IP system can best be used to promote R&D and the application of new biomedical technologies for diseases that disproportionately affect developing countries. As regards the scientific aspects, the Commission had high on its agenda how research on vaccines and treatments for HIV/AIDS, malaria and TB (but not just them) could be promoted and accelerated. The Commission had also identified traditional medicine as an area of study to see if it can be used more effectively in its own right to address diseases. Finally, the Commission assigned importance to the development of innovative capacity in developing countries themselves so that they can better address their own priorities. How NIH helps to build this capacity through technology transfer and collaboration in research and development was therefore of great interest.

She then passed the chair to Dr Mashelkar, vice-chair of the Commission.

The session was introduced by Bill Steiger, Director, Office of Global Health Affairs, Office of the Director, DHHS. He said the Commission's work was of great importance. It was not just about intellectual property - other incentives and financing mechanisms were also important. NIH had a budget of some $27 billion of which $415 million was allocated to international research and training. Consideration should be given to the Wisconsin (or Stanford) models for getting new products to the market based on university research. Apart from the development of products, attention should also be paid to overcoming delivery bottlenecks. In respect of tiered pricing, there must also be effective ways to prevent backflow of products from developing countries.

Mark Rohrbaugh, Director, Office of Technology Transfer, NIH

"Technology Transfer Capacity Building and Product Commercialization in the Developing World"

Dr Rohrbaugh gave a detailed overview of NIH's goals with respect to technology transfer and the mechanisms used by NIH to achieve them. He noted that NIH had 254 patents, issued or pending, in six major developing country disease areas. He discussed general principles of licensing, public policy issues (such as White Knight clauses) and natural products licensing, including the example Calanolide A, an antiretroviral undergoing clinical trials in Malaysia. With regards to technology transfer, he noted NIH agreements or negotiations with many developing countries. Partnership and strategic alliances were important for success. The developing country partner needed to have some level of R&D capability, and it was important to work with both the public and the private sector. Gaps in capacity building included a cadre of scientists and managers, and insufficient knowledge about IP management.

The presentation is at:

Technology Transfer with Institutions in Lesser Developed Countries [pdf 586kb]

In discussion, it was noted that US provisions for US manufacture of licensed products were not in practice a barrier to technology transfer.

John Barton, Emeritus Law Professor, Stanford University
"Technology Transfer"

Professor Barton characterised technology transfer as principally a human process, only secondly an IP or legal issue. He presented a typology of potential transfers between four sectors (the public and private sectors in the developed and developing world). He discussed the pros and cons of Bayh.Dole arrangements and appropriate standards for the use of IP for the public sector, and how developing countries might be affected directly and indirectly. He discussed also the private sector process of technology transfer and the debates about it. Finally he proposed a new paradigm where public-private partnerships became central to technology transfer and the issues that needed to be addressed.

His presentation is at:

[Technology Transfer](#)

In discussion the following points were raised:

- Data exclusivity could be an alternative to a patent but, if, in most cases, the period of exclusivity fell within the patent period it was the length of the latter that was relevant
- There are two kinds of technology transfer often confused - a license to produce or sell and mechanisms for enhancing learning and technological capabilities
- The patent system is plastic which raises the question of whether we rely on that plasticity, or undertake formal reforms e.g. in respect of research exemptions or research tool patenting
- Although the system is plastic, biotechnology had placed a great stain on it.
- The Bayh-Dole Act itself was not necessarily the cause of problems identified, but it formalized a process that was already beginning to happen
- Was there a real alternative to the current system?

Audrey Chapman, Co-Director of Science and Intellectual Property in the Public Interest (SIPPI), American Association for the Advancement of Science (AAAS)

"The humanitarian use exemption and the research exemption"

Dr Chapman described SIPPI's aims which were to examine the effect of IPRs on science and innovation, promote equity in accessing the benefits of science, promote broad participation in public policy and develop models that facilitate open access and cooperative uses of scientific information. It is specifically looking at the humanitarian use exemption, research exemption, the effects of IP on research internationally, and monitoring IP policy and practice, including the implications of the Madey vs Duke decision. The humanitarian use exemption proposal is based on the premise that IP protection can hinder the development of pharmaceutical and agricultural products and restrict their transfer to developing countries. This could be done through a clause in negotiated agreements or more formal public policy changes. A working group is considering how this might best be achieved. Another group is looking at the research exemption, post Madey vs Duke. The goal is to define an appropriate scope for a research exemption, to determine principles and components for successful application and increase access to scientific data.

The presentation is at:

[Science and Intellectual Property in the Public Interest (SIPPI)](#)