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Medical research:

# Science in the public interest

## "Equitable licenses" for the results of publicly sponsored medical research

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# I Why this brochure?

Drugs may be essential for survival: According to the information of the World Health Organization (WHO), several millions of people die every year of diseases which could be treated with medication or prevented by vaccinations.[1]

There are a lot of reasons why life-saving drugs are inaccessible for many people: infrastructural problems in poor countries, lack of personnel in the healthcare system, high customs and tax duties on medical products, but also high prices for the drugs themselves.

Especially in the case of newly developed drugs, monopolies cause high prices due to patent protection. In terms of the economy, patents are an instrument to increase prices. However, this is how drugs become unaffordable, particularly for poor people. How can access to low-priced drugs be ensured? This question is not only important to people in poor countries, because even in Germany expensive drugs already contribute significantly to the crisis in healthcare systems.

Pursuant to the conventions of the United Nations, health is one of the human rights, as well as access to healthcare supply.[2] This is why the World Health Assembly 2008 endorsed an action plan to enhance medical supply for people in poor countries.

Publicly sponsored research plays a decisive role in the solution of this problem. 41 per cent of medical research and development worldwide are sponsored by public funds.[3] Research and development of new vaccines, drugs and diagnostic instruments are often performed in universities and other public research institutions. Many Aids drugs, for example, were developed in public laboratories (see p. 11). You might think that this would ensure wide access to innovations. Unfortunately, this is not the case. What is the use of innovative drugs if most people cannot afford them?

This is where the role of patents and license agreements between public institutions and companies comes into play. There are various perceptions regarding patents. On the one hand, patents are considered the basis of an "efficient collaboration between universities and companies",[4] for others they are a symbol "of science in the private (industrial) interest".[5] Nobel Laureate Joseph Stiglitz complains, intellectual property rights "close down access to knowledge."[6] He explicitly includes access to medication. The German Federal Government wants to use the **Utilization Initiative** to specifically support commercial usage of public research.

Similarly, in recent years, another new phenomenon has found its way into public research: alongside publications, patents have become second yardstick for the success of scientific research.

"Life sciences is not like managing other technologies [...] as there is a basic public interest that brings a strong ethical aspect since this technology meets fundamental human needs that bring public expectations and a distinct ethical framework." [7]
*Anthony Taubman, Director World Intellectual Property Office*

*Photo: Marko Kokic, WHO*

This development goes hand in hand with the boom of the biotechnology sector, where new companies have often been developed from public research projects.

*Photo: Torgrim Halvari, WHO*

Global access to innovative medical research products, however, has hardly been made the subject of discussion yet — although medical progress has almost always been the result of worldwide research in the last decades, and public funds have been used for these purposes in a target-oriented manner. This is why developed products should reach as many people as possible – also and in particular in poorer countries. Not only is this the place where they are needed most to cope with the high burden of disease, appropriate healthcare is a human right and demands public responsibility. How does cooperation between science and industry look, how are patents granted to universities or when will rights of use be assigned? At present these are central issues of research policy – with global effects.

How can it be ensured that as many people as possible have health benefits from new research results? There are already modern approaches worldwide, trying to meet this demand. New license models under the **Equitable Licensing** concept are being discussed in the United States between public institutions and commercial enterprises. These aim to allow access to the products and technologies of publicly sponsored research.

We want to use this brochure to present the Equitable Licensing concept and thus contribute to a solution of the problems of drug supply in poor countries.

**The right to health**

International Covenant on Economic, Social and Cultural Rights (article 12)[8]

1. The States Parties to the present Covenant recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health.
2. The steps to be taken by the States Parties to the present Covenant to achieve the full realization of this right shall include those necessary for:

   (a) The provision for the reduction of the stillbirth-rate and of infant mortality and for the healthy development of the child;

   (b) The improvement of all aspects of environmental and industrial hygiene;

   (c) The prevention, treatment and control of epidemic, endemic, occupational and other diseases;

   (d) The creation of conditions which would assure to all medical service and medical attention in the event of sickness

# II The Problem

## Drug supply in developing countries

Worldwide healthcare is in a dilemma: Although there has been enormous technological progress, with new drugs and diagnostics available, this progress remains unachievable for most people. In 2003, over 80 per cent of the world population lived in developing countries.[9] Apart from a small upper and middle class, most people there are often not able to afford medical treatment.

Drug supply is associated with two basic problems:

**Supply gap:**

On the one hand, there is deficient infrastructure in healthcare. On the other hand, the prices for drugs are high. Patent protection for drugs is the cause why important new drugs are unaffordable for poor people. The prices for patent-protected Aids drugs were only reduced in developing countries when exemptions from patent protection* created competition from manufacturers of generic medicines: in 2001 the lowest price for an annual therapy of HIV infections was 10,439 USD; by 2008 this had fallen to only 87 USD.[10]

**Research gap:**

Diseases which mainly affect poor people are of no interest to commercial drug research. This is why tropical and poverty-related diseases are called neglected diseases. Only twenty-one out of 1556 new active substances which have been developed in pharmaceutical research in the last three decades were suitable for poverty-related and tropical diseases.[11] This research gap is gradually being closed by non-commercial research networks, so-called Product Development Partnerships.[12] Commercially oriented research plays only a limited role in this field. Research and development for neglected diseases is supported, in particular, by public institutions and sponsored by private foundations.

The global drug market clearly reflects the distribution of social wealth. In 2007, worldwide drug sales amounted to 664 billion USD. Profit is mainly made in developed countries: North America, Europe, and Japan represent 86 % of the world market.[13] China, Brazil, Russia, and India are considered emerging markets – countries with increasing industrialisation and a burgeoning middle class who can afford expensive medical treatment.

** Patent protection was globalised by the TRIPS agreements of the World Trade Organization (WTO). Exceptions of patent protection were safeguarded to a certain degree only by the Doha statement of the WTO in the year 2001.*

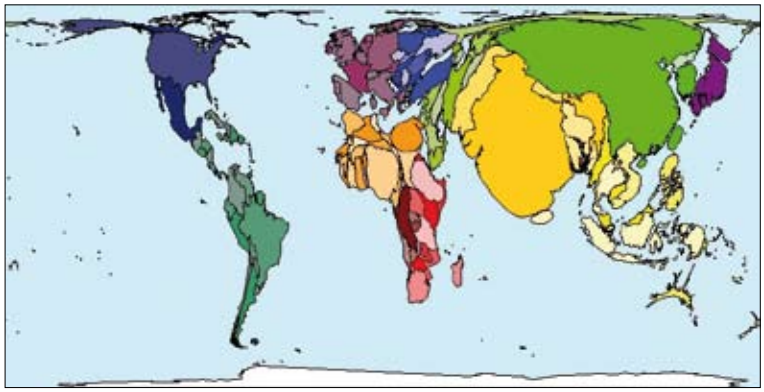
*Photo: Christopher Black, WHO*

Poor and rich countries have different disease patterns. Poverty-related diseases are the main cause for half of the disease burden in developing countries.[14] They include the effects of malnutrition, infectious diseases, and high mortality of infants, children and young mothers. These diseases must be tackled at the roots by

**Affordable medicines**

*The size of the countries shows the share of people who have access to affordable vital drugs. Pursuant to the definition of the World Health Organization vital drugs are what the population needs most.*

*Source: http://www.worldmapper.org/display.php?selected=222*

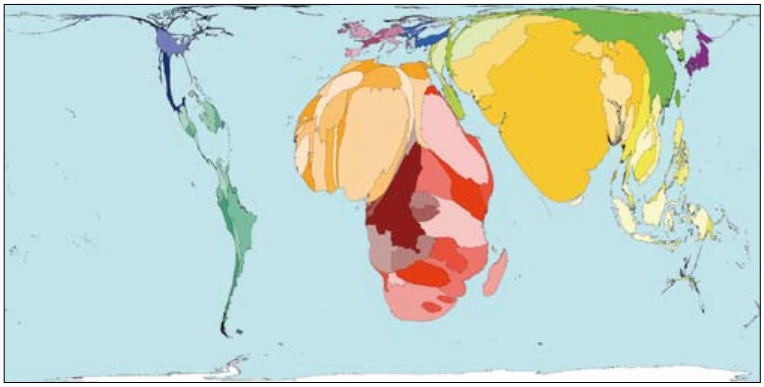


improving the living conditions, but also by providing improved medical care. Another important global health problem is HIV/Aids. 22.5 million HIV infected people out of a total of 33 million worldwide live in Africa.[15] The infection threatens the people on the poorest continent and deprives them of any hope for a better future. Affordable drugs are vital for these people.

**Often preventable deaths**

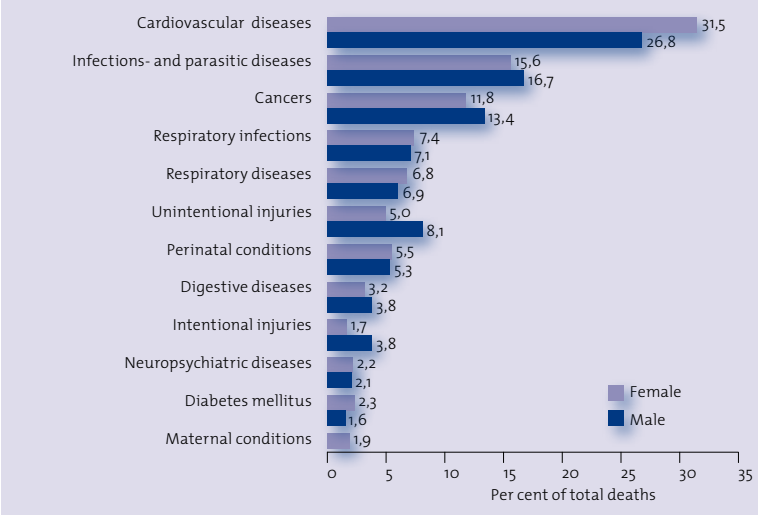
The size of the countries is in direct proportion to the number of cases of death by diseases which could be avoided by prevention and medical treatment.

*Source: http://www.worldmapper.org/display.php?selected=371*



A frequent concomitant disease of HIV infection is tuberculosis. It is a typical poverty-related disease which spreads particularly when people's immune system is severely weakened by living in poverty or by a disease. Tuberculosis requires prolonged treatment which can hardly be carried out under the living conditions of many patients. New, simple and effective drugs and vaccines are required.

**Distribution of deaths by leading cause groups**




*Source: WHO 2004* [17]

But chronic diseases are also causing comprehensive economic and social burdens worldwide. The most important of these are non-infectious diseases such as cancer, cardiovascular disease or diabetes mellitus. Poor people are also increasingly affected by chronic diseases. Although good drugs are available for these diseases, often they are not affordable.

This is why the World Health Organization has been coordinating the preparation of an action plan over recent years to improve the catastrophic drug supply of developing countries. The framework programme was resolved in May 2008 by the World Health Assembly. Now all governments are requested to contribute their share towards the implementation.

On 29 May 2008, the Bundestag emphasised "Germany's global responsibility to fight neglected diseases"[16] in a resolution. New license models (equitable licensing, page 21) may be a contribution which Germany could easily implement.

**WHO Plan of Action:**
**drug supply for poor countries** [18]

**Target:**

- Support of research in accordance with the requirements of poor countries.
- Improvement in the supply of low-price drugs.
- Extension of production in developing countries.
- Development of new financing instruments.

**Steps (selection):**

- Assumption of public responsibility where the commercial sector has failed.
- Providing new research incentives, as patents are no sufficient research incentive without a market.
- Supporting fair access to research results, for example, open access publications, open licenses, equitable licensing (see page 21).

**"Generic competition and differential pricing can contribute substantially to the affordability of medicines in low-income countries."** [19]

*World Health Organization 2004*

## How patents can close down access to drugs

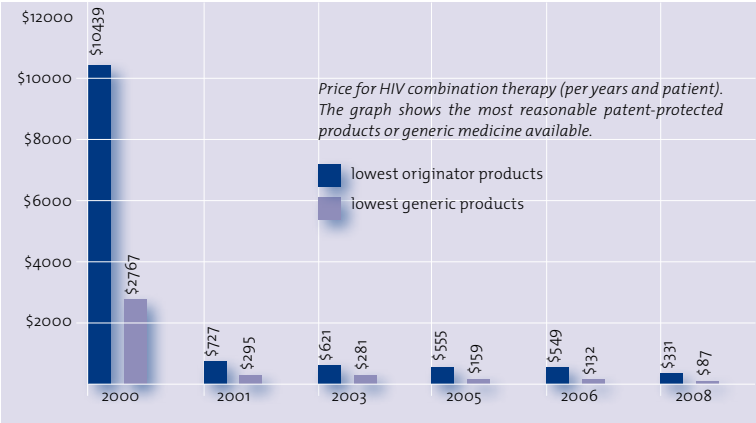
As long as drugs are under patent protection, they are expensive. And this, of course, is deliberate, because development costs have to pay off in this time. Production itself is comparatively low-cost. For comparison: A pack of the HIV drug Stavudine costs 296 Euros in Germany (56 tablets with 20 mg active ingredient each); purchased in bulk, the price of the active ingredient required amounts to 50 cents.[20]

The consequence of high prices ensured by patents is that drugs are unaffordable for a majority of people. They become reasonably priced (and thus affordable for more people) only if generic medicine is available. Experience shows that drug competition results in strong price reductions.

If patents are owned by a public research institution, it has its share of responsibility to enable the people to have access to the final product. The examples of HPV vaccination and the Aids drug d4T (see box) illustrate these connections.

Photo: Evelyn Hockstein, WHO

*Within a few months in 2001 Indian and Brazilian generic medicine caused a dramatic price reduction of HIV drugs for developing countries.[22] This was only possible because there was no or only weak patent protection on drugs in these countries.*




### Case study: d4T – Aids medication from public laboratories[21]

*The active ingredient d4T was invented in the 1960s in the USA at the Detroit Institute of Cancer Research in the search for cancer medicine. When Aids was detected in the 1980s, a feverish search for appropriate drugs for the therapy of HIV infection began. The Yale University focused on d4T and continued studies which were sponsored by the US National Institutes of Health. In 1986, the Yale University applied for a d4T patent for the treatment of Aids. The pharmaceutical company Bristol-Myers Squibb (BMS) was granted an exclusive license for further product development and finally marketed the drug as Zerit® in 1994. As patent holder the Yale University shared profits.*

*It soon became obvious that Aids was turning into a catastrophe of dramatic scale, particularly in southern Africa. The costs for Aids*

*medication were so high that medical aid organizations were hardly able to pay them, not to mention the people concerned themselves. This was why, in February 2001, Doctors Without Borders (MSF) requested the university whether it was possible to grant a voluntary license on d4T to allow for the production and import of low-priced generic medicine for South Africa. The university management referred to the contractual commitment to the exclusive license for BMS and refused. This reaction caused discontent at the university. Students and scientists rebelled. How could a life-saving drug owned by the university be withheld from the people in need? Petitions, press releases, public debates followed. In June 2001, the licensee BMS relented and signed a waiver of its exclusive rights in Africa. This was an important contribution to the enormous price reduction of Aids therapy (see illustration).*

Comprehensive patenting of scientific knowledge and inventions may also impede research itself. Known examples are breast cancer genes BRCA1 and BRCA2 and a comprehensive patent of the US group Chiron on the Hepatitis-C virus.[23] In the end, this also impedes access to required healthcare.

**Case study HPV vaccination: many inventors, many patents**

*Vaccination against the human papilloma virus (HPV) is supposed to protect against cervical cancer. Although its efficacy is controversial,[24] it illustrates some basic relationships:*

- *It is the result of extensive international and publicly sponsored research.*
- *It is exclusively marketed worldwide (Gardasil® by Sanofi Pasteur MSD and Cervarix® by GlaxoSmithKline).*
- *At 480 Euros it is the most expensive vaccination available.[25]*

*The basic principles were created at the German Cancer Research Centre in Heidelberg, for which Prof. Dr. Harald zur Hausen was granted the Nobel Prize in medicine in 2008.[26] The L1-protein which is effective in the vaccine has been studied at the Georgetown University in Washington DC, the University of Louisville (Kentucky)[27] and the Queensland University (Brisbane, Australia). Important patents are owned by the universities of Rochester (New York), Queensland and Georgetown, the National Cancer Institute as well as the National Institutes of Health. The key patent was granted to the Georgetown University after 10 years of legal disputes. The pharmaceutical companies Merck Sharpe & Dome (USA) and GlaxoSmithKline agreed on mutual licenses with all patent owners.[28]*

**The World Health Organization (WHO) concludes:**

*"An emphasis on patenting and licensing as the chief means by which technology transfer takes place, as compared to publication and open knowledge sharing, may have negative implications for research in the area of public health."[29]*

**This is why a commission recommends:**

*"Public research institutions and universities in developed countries should seriously consider initiatives designed to ensure that access to R&D outputs relevant to the health concerns of developing countries and to products derived therefrom, are facilitated through appropriate licensing policies and practices."[30]*


*Photo: advertisement by German Association of Research-Based Pharmaceutical Companies. Text: “Research is the best medicine.“*

*“We want to become world's pharmacy again.“*

*Anette Schavan,German Federal Minister for Education and Research* [36]

## Importance of public drug research

51 per cent of the worldwide 160.3 billion USD for health research (in 2005) originates from the pharmaceutical industry and 8 per cent from foundations. These are important investments. We must not forget, however, the 41 per cent which comes from public funds.[31] This is often the basis for the actual innovations. For the field of neglected diseases the share of public funding is even higher at 69 per cent.[32]

The record of success of public research is impressive. A public institution holds the key patent for every fifth drug which was granted marketing authorization by the US Food and Drug Administration (FDA) as a particularly innovative drug by means of an accelerated approval. In terms of HIV drugs, it is actually every fourth patent. All in all, US institutions own key patents on every tenth newly approved active substance.[33] Since 1980, more than one hundred and thirty drugs, vaccines and diagnostic agents have been developed fully or partially in public institutions in the United States.[34] Leaders are the National Institutes of Health (twenty-one drugs), University of California (nine drugs) and the University of Missouri (four drugs). Most new developments relate to infectious diseases, oncology and metabolic disorders.[35] Important Aids drugs are patented by US universities (see table).

**Drugs with academic patents (selection)[37]**

| Active agent | Application | Patent holder |
|---|---|---|
| *Adenosin* | *Heart* | *University of Virginia* |
| *Busulfan* | *Leukaemia* | *University of Texas* |
| *Carboplatin* | *Cancer* | *Research Cooperation* [38] |
| *Fentanylcitrat* | *Pain* | *University of Utah* |
| *Fomivirsen* | *Viruses* | *US government, HHS* |
| *Ganciclovir* | *Viruses* | *University of Kentucky* |
| *Levonorgestrel* | *Contraception* | *Medical College of Hampton Roads* |
| *Lovastatin* | *Cardiovascular* | *Children's Hospital Boston* |
| *Omeprazol (with sodium Hydrogen carbonate)* | *Gastric disorders* | *University of Missouri* |
| *Paclitaxel (Taxol)* | *Cancer* | *US government, HHS* |

*(HHS = US Department of Health and Human Services)*

| Publicly developed Aids drugs [39] | |
|---|---|
| **Active agent** | **Patent holder** |
| *Abacavir* | *University of Minnesota* |
| *Enfuvirtid* | *Duke University* |
| *Lamivudin* | *Emory University* |
| *Emtricitabin* | *Emory University* |
| *Stavudine* | *Yale University* |

## From the idea to the drug

It is a long process from the idea to the finished drug. Many actors participate in research and development in universities, industry and authorities. On average, 16.5 years will pass from the development of a potential active agent to the final proof of efficacy by clinical studies.[42] The costs for the development of a drug until market maturity amount to 150-250 million USD – including failures in research.[43] Which individual development steps are required on the way to the finished drug, and where do they take place? Even if there may be different ways, the following general approach applies.

**Basic medical research:** A disease is best curable if you know it well. What is the cause of the disease, how does the pathogenic agent react, how does the body of the person concerned fight against it? Basic medical research which is carried out almost exclusively in public institutions such as universities attempts to answer these questions.

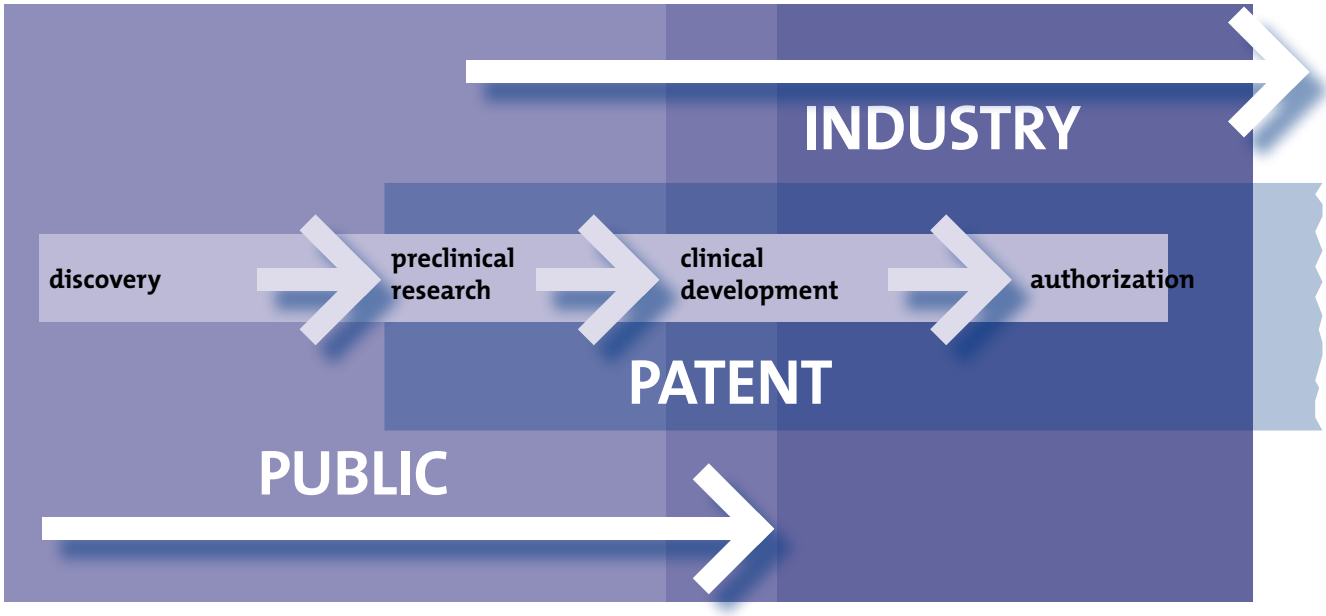
**Search for active ingredients:** Knowledge about a disease is used to test the effects of various substances. Promising candidates are tested in animal experiments and their chemical structure is optimised. This research phase takes place both in public laboratories and in private companies. Promising agents are usually patented so that they can be used commercially later.

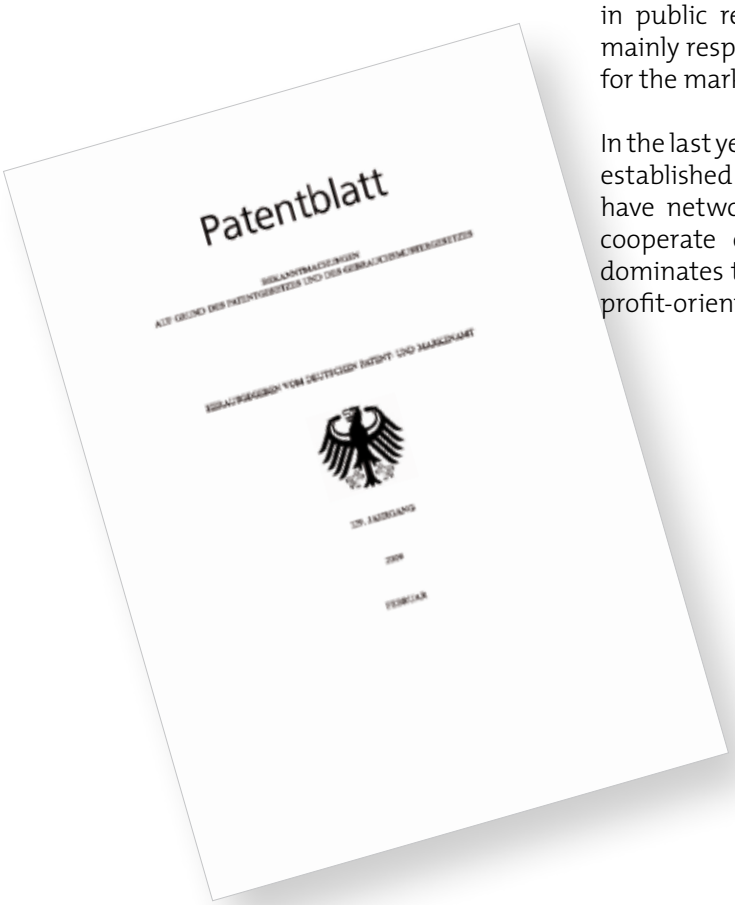
**Clinical studies:** If an agent has proven its efficacy in an animal test, tests in humans will follow. These so-called clinical studies comprise three phases. They are partially sponsored and carried out publicly, in most cases, however, by pharmaceutical companies.

**Approval:** In Germany all drugs require marketing authorisation by the *Federal Institute for Drugs and Medical Devices (BfArM)*.[44] In the meantime, Europe-wide approval is applied for an increasing number of new drugs at the *European Medicines Agency (EMEA)*. European approval is obligatory for biotechnologically produced medicines.

**Case study Insulin – Production on behalf of the public**

*Insulin was isolated in 1921 by Canadian researchers. The development of production was advanced as far as possible at the University of Toronto and finally assigned to several Canadian and European pharmaceutical companies with non-exclusive licenses. The patent remained at the University.[40] In Canada insulin was produced on a quasi-state basis. The University of Toronto set quality standards worldwide for production and limited the price.[41]*




While basic medical research is almost exclusively carried out in public research institutions, pharmaceutical companies are mainly responsible for the development of a drug until it is ready for the market.

In the last years, so-called Product Development Partnerships have established themselves as a new form of organisation. Often they have network character: academic institutions and companies cooperate on a worldwide basis. This form of organisation dominates the research for neglected diseases and is usually not profit-oriented.

## Public drug research in Germany

### Research institutions:

The German research environment is diverse: Apart from universities and university hospitals, Max-Planck Institutes, institutions of the Leibniz Community and Helmholtz Centres as well as the Fraunhofer Institutes play an important role in publicly sponsored medical research. There are also some Federal and State research institutions (e.g. Robert-Koch Institute).

### Research policy

The *Federal Ministry for Education and Research (BMBF)* is responsible for the political parameters of public research in Germany. The Federal and Länder Governments provide the budget. The research framework programme of the European Commission is also important. As the Commission and the home country of the sponsored scientists share the costs for projects equally, the standards of European research framework programmes have a significant impact on national research policy.

In the medical field, mainly basic research and preclinical development are sponsored publicly. The closer clinical studies come to product development, the less public support is provided. There is no specific limit. On the one hand, clinical studies are defined as the responsibility of the pharmaceutical industry: "The BMBF does not support any clinical studies; this would be a distortion of competition." [45] On the other hand, the BMBF created important capacities for clinical studies in public research by sponsoring the development of the *Competence Network Clinical Studies*.[46] Public sponsoring of the clinical study phases I and partially also II is even considered a requirement, at least in vaccine development, for pharmaceutical companies to be willing to participate (see box VPM). Even the German Research Foundation (Deutsche Forschungsgemeinschaft DFG), who are traditionally active in basic research, are now supporting clinical studies.[47]

### Finance

The most important sponsor of medical research is the BMBF with the *Department of Life Sciences* (in 2008 over 400 million Euros).[48] The *Federal Ministry of Health (BMG)* also provides limited funding. The *Federal Ministry for Economic Cooperation and Development (BMZ)* funds development-relevant projects (e.g. *Special Programme for Research and Training in Tropical Diseases (TDR)* with 0.81 million Euros in 2007).[49] The Länder also play an important role in financing many public research institutions.

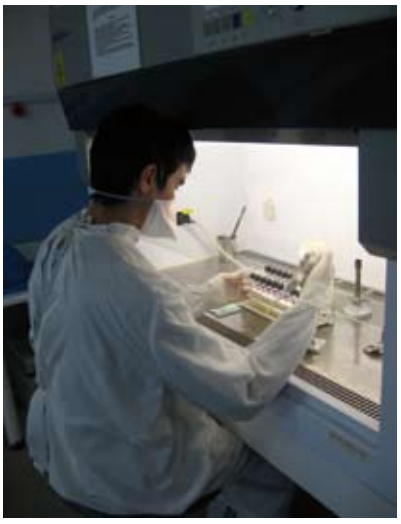


*Photo: Oliver Moldenhauer, MSF*

*"The work required for drug research as well as the various phases of clinical studies are the exclusive responsibility of the pharmaceutical industry."*

*Ulrich Kasparick, former German Parliamentary State Secretary at the Federal Ministry for Education and Research.*[53]

*Photo: Marko Kokic, WHO*

**Vakzine Projekt Management GmbH: Preparatory work for the pharmaceutical industry**

*To support the development of new vaccines in Germany, the Vakzine Projekt Management GmbH (VPM) was founded on behalf of the Federal Ministry for Education and Research in 2002.[54] Its task is to take up promising approaches of basic research and continue development until industrial buyers can be found. For this purpose VPM has sponsorship of 25.6 million Euros until 2010. "With this support, the Federal Government is taking account of a trend which can be observed worldwide, [...] that, in view of the high risks, pharmaceutical companies are increasingly only willing to continue new lines of vaccine development if there are appropriate candidates with sufficient information from preclinical and early clinical development."[55]*

The research framework programme of the European Commission is of special importance; in the period from 2007 to 2013 6.1 billion Euros are earmarked for healthcare. This represents 11 per cent of the total expenditure for research, thus making healthcare the second strongest field of European research funding after communications technology.[50]

In recent years the collaboration of companies with academic institutions has been strongly funded. The most comprehensive funding programme up to now was sealed in 2007: the European *Innovative Medicines Initiative (IMI)*.[51] The budget of two billion Euros originates from the European Commission (7th Research Framework Programme) and the pharmaceutical industry in equal shares. Patent protection for research results is considered a matter of course.[52]

## The US trendsetter: Bayh-Dole Act 1980

Before 1980, publicly sponsored inventions in the United States were always owned by the State. In the course of President Reagan's privatisation policy even the universities were allowed to hold patents and to license them to companies. The intention of this provision, which is called the Bayh-Dole Act, was to support further development of public inventions by the industry. It is based on the assumption that without patents public developments would gather dust in libraries without finding their way to the market. Commercial utilisation was intended to provide universities with additional money by means of license profits.

Many hopes could not be fulfilled. This becomes obvious in an evaluation of the experience after 28 years of the Bayh-Dole Act.

*Technology transfer:* Until now, there is no empirical evidence that Bayh-Dole promoted technology transfer for the benefit of the US society.[56]

*Profits:* Income from public institutions by license fees is comparatively low. In 2006 they amounted to 1.85 billion USD, which corresponds not even to five per cent of the total governmental research budget.[57] Only a very few American universities make any appreciable profits at all, for most of them license income hardly carries weight. Besides, about half of the income must be put into administration and legal fees for patent disputes. The bottom line is that most patent agencies of US universities are working to break even.

In the last years, more and more countries have adopted legislation similar to the Bayh-Dole Act: Germany, Norway, France, but also aspiring threshold countries such as China, Brazil, India or South Africa. There is a patenting boom worldwide, at present the number of new patents is increasing by about two per cent annually. In 2005 56,000 patents were granted for the most important markets (USA, EU, Japan).[58] At the same time, public research expenses were reduced, often on the grounds that the academic institutions had to work on a profit-oriented basis and had to market their research in a better way.

Scientists who have examined this trend systematically have reservations: "The present trend of legislation in Bayh-Dole style is based on an over-valuation and miscalculation of the economic benefits in the USA."[59]

*Photo: © Christopher Howey, Fotolia.com*

## Germany: Utilization Initiative 2001

Following the US example, the German Federal Government started the *Utilization Initiative* in 2001.[60] "[It] is the target of the BMBF patent policy that a patent application is made for every economically usable research result in Germany and that as many good inventions as possible are used commercially."[61] *Patent marketing agencies* or *Technology Transfer Offices* have been founded for all universities. Scientists are obliged to inform the competent utilization agency about every invention.[62] Works of commercial interest are to be patented and conveyed to interested industrial enterprises. The agencies are in charge of patent applications and license negotiations, but also of the foundation of own companies by the scientists. Since 2008 the patent utilization initiative is no longer financed by the Federal Ministry for Education and Research, but as a SIGNO programme by the Federal Ministry for Economy.[63] This programme is supposed to provide "efficient technology transfer between universities and companies".[64] As many years pass between basic research and approval to market drugs, the first drugs arising from the Utilization Initiative will take even longer.

*"[It] is the target of the BMBF patent policy that a patent application is made for every economically usable research result in Germany and that as many good inventions as possible are used commercially."*[73]

*German Federal Ministry for Education and Research*

Comprehensive governmental funding of company foundations began as early as 1997 with the BioRegio programme. With further programmes such as BioFuture, BioPharma or GoBio, the BMBF funds business foundations by academics. For this purpose, 370 million Euros have flown into the field of biotechnology up to 2008.[65] Despite the existence of over 500 biotech companies, only a few new drugs have been marketed to date. Icatibant by the Berlin manufacturer Jerini, who has recently been acquired by the British Shire group for 350 million Euros, is a known drug.[66] This example reflects a typical course of events: Innovation is created – publicly sponsored – in public institutions and is then further developed in small outsourced institutions. Big companies pick and choose.

This poses the question: Does the Utilization Initiative work in Germany? An initial evaluation on behalf of the BMBF comes to the conclusion that the patent utilisation agencies "managed to strengthen patent awareness at universities significantly and to increase the number of invention reports."[67] Concerning the number of company foundations, however, research institutions such as Fraunhofer, Helmholtz or Max-Planck Institutes are leading. They started commercialisation partially even before the Utilization Initiative. Max-Planck-Innovation cites 38 foundations of biotech companies since 1990.[68] Ascenion sites 14 spin-offs.[69]

A detailed analysis of the performance of the Utilization Initiative is still outstanding. But it seems that commercial success of patent utilisation is modest up to now. Despite a high number of patent applications – there are no less than 625 German patents of medical faculties for the period of 2003/2004 alone[70] – no clear data on successfully concluded contracts is available. Usually, the signing of a license agreement with a company includes non-disclosure provisions. It remains unknown, therefore, with which companies and on which terms public institutions made contracts. It is more of an exception that the pharmaceutical manufacturer Bayer publicly announced a "preferred partnership"[71] with the Cologne university hospital for drug development. Silence is maintained on the range of payments by Bayer and on the expected service in return.[72]


*"Knowledge creates wealth – the innovation policy of the Federal Government"*

## How does patent protection work?

A patent is a time-restricted protection of an invention. The holder has the exclusive right to decide on production and marketing. The legal rights of use may be extended or assigned to others by granting licenses. Usually, the patent holder requests license fees and/or profit sharing for this (also known as royalties). The purpose is to ensure financial compensation for the outlays which had been necessary in the forefront of the invention. The exclusive competition position allows for a later amortization of the investments through the price. In this way an incentive is created for inventions.

Some companies, however, use their patents to seal off the market. They protect their core technology by a ring of patents. This creates "patent clusters" of up to 1300 patents for a single drug.[74]

*"The role granted to formal intellectual property rights in the management of a peculiar class of inventions is therefore less a question of economic rationality than a social and political issue shaped by complex arrangements of actors, with their peculiar set of power, resources, interests, and ideologies."*[78]

*Jean-Paul Gaudillière, Scientific Historian*

Validity: Patents do not automatically apply worldwide. In fact, it is necessary to apply for patents in every country. International agreements provide some simplifications. For example, a patent may be granted for several European countries at the European Patent Office by means of a test procedure. The most important non-European patents for drugs are applied in the USA, Japan and Canada. Patent protection only applies in the country where it has been applied for and granted. For every country there are costs for the application, patent lawyers and translations, as well as annual fees for maintaining the patent. Nowadays, patents on drug agents are usually valid for at least 20 years.

## Patents are not a natural law

Whether and how drugs should be patented has been the subject of debate since chemical-pharmaceutical production exists.[75] However, the frontlines have not always stayed the same. In 1877, the German Chemical Society demanded in a petition to the Reichstag that patent protection for drugs should be restricted to manufacturing processes. The industry felt that free research was threatened by product patents. This is why the active agent remained excluded from the patent. Doctors and pharmacists also resisted patents. They argued on the basis of their professional ethics: it was not their task to make profits, but to heal people. Patents would lead to high prices and thus close down access to the drugs for many people. For over almost 100 years, doctors and pharmacists argued against treating drugs as normal commercial goods. This was why drugs were excluded from patenting in most European countries.[76] The turnaround came in the 1950s and 1960s – slowly having been prepared by structural changes in the pharmaceutical industry. The production of drugs had switched from the pharmacist to large companies, which also marketed their products on an international level (cosmopolitan drugs)[77]. Research had also changed: Companies built their own

*European Patent Office, Munich, Photo: © Richard Huber*

large research and development departments. In 1968 patent protection for drugs was implemented in Germany. The situation in other developed countries was similar.

Due to the TRIPS agreement of the World Trade Organization there is strict patent protection for drugs in almost all countries of the world. The agreement obliges the signing states to grant patent protection on drugs for at least 20 years.

**Making social responsibility the ruling principle of universities: The Philadelphia Consensus Statement: [83]**

*We believe that universities have an opportunity and a responsibility to take part in those solutions. University scientists are major contributors in the drug development pipeline. At the same time, universities are dedicated to the creation and dissemination of knowledge in the public interest. Global public health is a vital component of the public interest. [...] To this end we [...] urge universities to adopt the following recommendations:*

- *Promote equal access to university research*
- *Promote research and development for neglected diseases*
- *Measure research success according to impact on human welfare*

*First signatories included several Nobel laureates, publishers of renowned journals and university rectors.*

*Photo: Christopher Black, WHO*

## Social responsibility of science

Every year governments invest billions in scientific research. Science is paid for by society. It is in interaction with society and thus has social responsibility.[79]

Worldwide there are a growing number of initiatives demanding social responsibility of academic research. Starting from the discussion about academic patents on Aids drugs, students in the USA have initiated a network at various universities. As *Universities Allied for Essential Medicines* they are already active at over 30 universities in the USA and Canada. Researchers are also involved, including numerous Nobel laureates.[80] US university commissioners for patent utilisation founded a work group *Technology Managers for Global Health*. Renowned scientists have requested their universities to follow socially compatible research and license policies (see box *Philadelphia Consensus Statement*), leading university managers for technology transfer are reinforcing their efforts for fair licenses (see box *Stanford White Paper*).

While scientific success is measured by the number of publications, the impact factor and, today, also the patents, the social relevance of research still plays only a modest role. In future, the social relevance is also to be made measurable.[81] Successful technology transfer could be assessed in terms of an *access-to-knowledge-matrix*.[82]

*Photo: Marko Kokic, WHO*

## Equitable License: Elements of a fair license

License agreements between public institutions and private companies offer the possibility of re-emphasizing the social responsibility of science. What would a license look like, which is not only aimed at maximum license income, but also takes into account that as many people as possible have access to the products and technologies?

The prototype of an Equitable Access License[86] was developed at the Yale University in reaction to the dispute about the HIV drug d4t (see page 8). The patent owner (an academic institution) holds the right of disposal for developing countries and can grant other manufacturers further licenses at any time to ensure the supply of poor countries. For various reasons, the industry did not accept this model as general standard for later contracts, but it did trigger the development of new types of contract.

Every license is negotiated individually. At this point, we would like to list the essential framework conditions which can be considered in the license agreement. On the following pages we will present recent pioneering projects and case studies.

**Elements for license agreements, which place a highest possible public benefit at the centre:** [87]

**Assignment of rights:**

*Preferably no transfer of ownership of the patent right to industrial partners.*

- *Preferably no agreements about exclusive licenses.*
- *The public research institution reserves the right to terminate the license if the patent is not used in the publci interest as defined.*

**Influence on utilisation:**

- *In case of public third party financing by politically accountable government bodies (Ministry of Research and Education BMBF, Ministry of Health BMG, Ministry of Econony & Trade BMWi) the state reserves the right of use.*
- *A concept about use, future exploitation and access will be agreed.*
- *The current status of use will be discussed at regular meetings. Non-appearance at scheduled meetings will be considered a reason for termination.*

**Ensuring availability in developing countries:**

- *The end products must be made available at an reasonable price. The concept includes access for developing countries as a target, and defines the steps as to how to reach this goal (access commitments).*
- *The products must be cheaper in developing countries than in developed countries (differential pricing); they should be offered to poor countries at production costs with minimum profit.*
- *Obligation to enable competition in poorer countries, e.g., by open licenses for the production in these or for these countries. This corresponds to the global market structure: exclusive license for developed countries, non-exclusive license for developing countries.*

*"We recommend that academic institutions make Socially Responsible Licensing a formal, stated institutional policy. Several benefits will follow from this. First and foremost, it is the right thing to do and it is important for academic institutions to be seen by their stakeholders to be out in front on such a major issue of public policy. Second, it will strengthen the licensing officers' hands in negotiations if they can point to an institutional requirement to include socially responsible licensing terms in the agreement. Finally, it can be a positive in philanthropic activities, helping form the basis for public health initiatives in developing countries."*[85]

*Ashley Stevens, Executive Director Technology Transfer, Boston University*

*Photo: © Maxtulipes, Fotolia.com*

## What can be done? A view around the world

The development of drugs and vaccines requires the collaboration of many actors: academic institutions, industry, non-profit-organisations. In the last years, a new variety of models has developed showing how different the development of a product can be until it is ready for the market. No case is like the other: with or without patent, exclusive or with various licensees. Public actors such as the WHO, individual governments or the US *National Institutes of Health (NIH)* often play an important role as initiator, agent and also as sponsor. *The IP Handbook – IP Management in Health and Agricultural Innovation* is a comprehensive project, in which case studies have been collected and experiences have been evaluated.[88] We have selected some pioneering examples which reflect the range of possibilities.

### Case study: Rotavirus vaccination

*Rotaviruses are one of the main causes for diarrheal illnesses worldwide. In the United States a rotavirus vaccine was developed at the National Institutes of Allergy and Infectious Disease (NIAID) and optimised in cooperation with the pharmaceutical company Wyeth.[89] The US Public Health Service concluded license agreements with various partners: the US Company Aridis Pharma is developing a vaccine especially for the virus stems in developed countries,90 a state institution in Brazil is developing exclusively for Latin America, and two Chinese companies will supply the national vaccination programme in China. Four companies in India have been granted the rights for India and other developing countries. The licenses comprise the required biological material and technologies. The licensees will be trained in laboratories of the NIAID. Marketing of the new vaccines is expected to start in a few years.*

### Case study: Cholera vaccination

*Infections with cholera bacteria cause severe diarrhoea and can even be fatal. Protection is available as oral vaccination. The vaccine Dukoral® was developed at the Swedish university of Goteborg. The Dutch company Crucell has the exclusive production and sales rights for developed countries.91 For Vietnam the university granted a license to the local manufacturer VaBiotech. The technology transfer was supported by the WHO and the UN vaccination programme IVI.92 A vaccination for the local population was developed with the National Institute of Hygiene and Epidemiology Hanoi which is manufactured by VaBiotech and meets international quality standards.93 The production of a vaccination dose in Vietnam amounts to 15 cents, in Germany a vaccination with Dukoral® costs approx. 25 Euros.*

**Case study: Malaria drug Lapdap®**

*Lapdap® is a drug for malaria treatment. It contains a combination of Chlorproguanil and Dapson – both long-known active substances.[94] The combination preparation is the result of a research project sponsored by the British Wellcome Trust. The product development was mainly carried out by scientists of academic institutions: the University of Liverpool, the London School of Hygiene and Tropical Medicine, African experts and the Wellcome Trust. The pharmaceutical company GlaxoSmithKline (GSK) was involved as industrial partner. GSK, the World Health Organization and the state British Department for International Development (DFID) took over the development costs in equal shares. Initial patent applications by GSK were refused when it turned out that the basic data on the product had already been published. This obviated the base for patenting and Lapdap® is completely patent-free. The drug is currently available on the private market in South Africa, Nigeria, Kenya and the Ivory Coast.*

**Case study: Production of Artemisinin**

*Artemisinin is a herbal substance against malaria.[95] It forms the basis for combination preparations recommended by the World Health Organization for malaria therapy to avoid the development of resistances. Limited availability and natural fluctuations in the production volume of the plant are crucial price factors. In order to produce the raw material at a lower price, a project on biotechnological synthesis has been started in 2004. The University of California Berkeley is responsible for the basic research in suitable microorganisms, the biotech company Amyris develops the manufacturing process, and the Institute for OneWorldHealth (iOWH) is in charge of the approval and the application in developing countries. The project is financed with 42.6 million USD by the Bill and Melinda Gates Foundation. The patents are held by the UC Berkeley, which has granted the two different licenses:*

- *The iOWH was granted a free license for the production of Artemisinin to be used in malaria medication for developing countries. The required licenses for the development of the production procedures were granted to Amyris, also without license fee.*
- *Amyris was granted the exclusive marketing rights for developed countries. This is the commercial incentive for the company.*

*Another commercial incentive is that the production processes are also used for other substances which have a chemical relation to Artemisinin (so-called terpenes). Amyris holds the worldwide exclusive right on utilisation of the production technology for these, and the university receives license fees. In the meantime a contract on large scale production was concluded with Sanofi-Aventis, marketing was announced for 2010.[96]*

**Technology transfer with social responsibility: the Stanford White Paper [84]**

*The Text (strongly reduced in the following) was adopted by several US patent utilisation managers in 2007.*

*"It is our aim in releasing this paper to encourage our colleagues in the academic technology transfer profession to analyze each licensing opportunity individually in a manner that reflects the business needs and values of their institution, but at the same time, to the extent appropriate, also to bear in mind the concepts articulated herein when crafting agreements with industry.*

- *Universities should reserve the right to practice licensed inventions and to allow other non-profit and governmental organizations to do so.*
- *Exclusive licenses should be structured in a manner that encourages technology development and use."*

Photo: © Albo, Fotolia.com

**Case study: Drug against Chagas**

*Chagas is an infectious disease caused by unicellular organisms (Trypanosoma cruzi) which is widespread in South America. There are only limited therapeutic possibilities and these are associated with severe side effects. A research association has set the target of developing a more gentle treatment. This is based on active substances which were developed at the University of Washington in the course of cancer research but which also affect unicellular organisms. In collaboration with chemists and physicians, Yale University is examining their application against Chagas. A low-cost license for further preclinical tests has been developed with the Institute for OneWorldHealth (iOWH).*[97]

**Case study: Patent-free malaria medication**

*The combination preparation Artesunate/Amodiaquin has been marketed as a patent-free malaria drug since 2007.*[98] *Initiator was the Drugs for Neglected Diseases Initiative (DNDi), a consortium of public research institutes in Asia, Africa and Latin America involving Doctors Without borders. The drug was developed in cooperation with several universities and the pharmaceutical manufacturer Sanofi-Aventis. The production of test medication and conception of the industrial production were carried out as commissioned work by German Rottendorf Pharma. The clinical studies required for marketing approval were performed by the African project partners. The drug has been approved in 23 African countries and is produced by Sanofi-Aventis in Morocco. Sales at production costs allow for therapy costs of 50 cents. As no patents are involved, the production of generic medication is also possible. Negotiations with further manufacturers are in progress.*

*The costs of development amounted to 6.4 million Euros from 2002 to 2009 (40 per cent clinical studies, 45 per cent pharmaceutical development and approval). The financing is almost completely covered by public funds. It is a novelty that drug development costs have completely been disclosed.*[99]

*In 2008 the malaria preparation Artesunate/Mefloquin was marketed in Asia and Latin America using the same concept.*

**Case study HIV vaccine[100]**

*The International Aids Vaccine Initiative (IAVI) is one of various networks working on the development of an HIV vaccine. The aim is to effectively link as many research methods as possible. IAVI intends to combine the needs of public health with the demands of researchers and companies. Contracts have been structured in such a way that they allow for the optimum supply of poor countries with vaccines. The following principles apply:[101]*

- *Patents on research results are recognized in principle.*
- *All parties involved submit material and information to a research group. They are therefore all partners of the resulting developments.*
- *IAVI reserves the right to grant licenses for further development and marketing. This is to ensure that the innovations are also accessible to poorer countries.*
- *Marketing agreements have different structures. There is an agreement on exclusive worldwide marketing, market shares (exclusive right for developed countries, IAVI continues to hold the rights for developing countries) and also that all rights remain with IAVI.*
- *Agreements with the industry always include provisions on product access (access commitments): The vaccines must be offered in developing countries at a reasonable price, but may be more expensive in developed countries (differential pricing).*
- *If the supply of poorer countries by an industrial partner does not work, IAVI can dispose of the required data, technologies and licenses as necessary to guarantee the supply.*

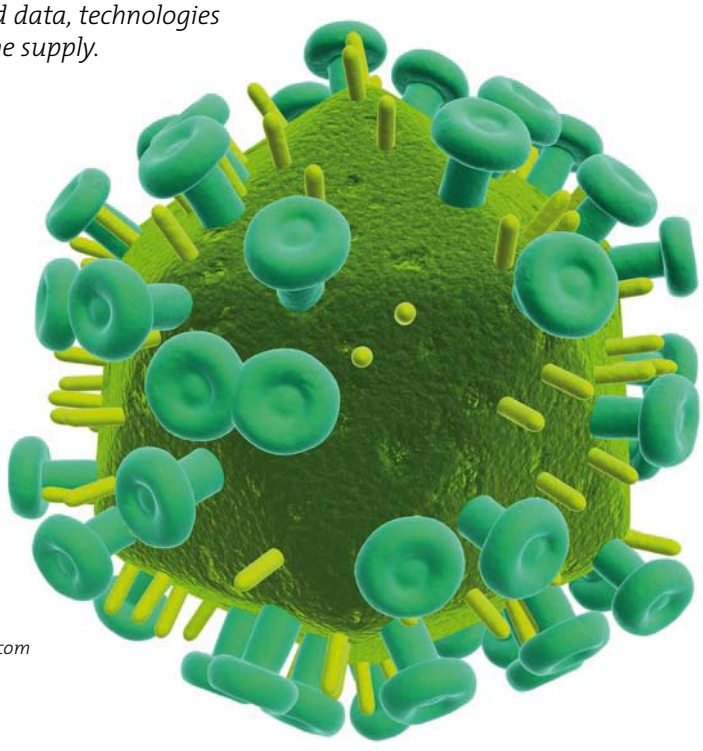


*Illustration:© Sebastian Kaulitzki, Fotolia.com*

**National Institutes of Health: Guidelines for Patenting[109]**

- *Non-exclusive or co-exclusive licenses shall be granted wherever possible to develop competitive products.*
- *If public health requires, holders of exclusive licenses are obliged to grant sub-licenses. This is aimed at extending the development possibilities for new products.*
- *The NIH extend the public benefit of their technologies by supporting the development of competitive products for the same application.*
- *If technology is not appropriately made available to society, the NIH may turn an exclusive license into a non-exclusive license. This allows the granting of additional licenses to other companies for the further development or sales.*
- *The goal is to exemplify and promote the highest level of social responsibility in the conduct of science.*[110, 111]

## Government license policy in the USA:

### National Institutes of Health

With a research budget of 30 billion USD annually, the National Institutes of Health (NIH) are one of the most important research funding bodies. 90 per cent of the funds are allocated to research projects in universities, 10 per cent flow into research in their own institutions.

The NIH have been coordinating large-scale state research programmes for several decades now. A malaria programme started in 1941 in which 14,000 compounds were tested for efficacy. Then, in 1943, a programme started on penicillin production. This was followed by several large-scale programmes on the identification of potential active substances managed by the National Cancer Institute the NIH.[102]

NIH-supported research results were patented and licensed by the Office for Technology Transfer (OTT). The license income amounts to 80 million USD annually, thus the NIH is one of the frontrunners.[103]

### Public responsibility

It is the target of the NIH patent policy to turn research results into available products as soon as possible. This is justified by a responsibility towards the tax payers.[104] The availability of drugs was first taken into consideration in license agreements in 1995 with the so-called *White Knight clauses*. They are named after the company with which such an agreement was made for the very first time. Priority has been given to the benefit for the US population:

- The licensee must train the user in the correct use of the invention (e.g. training programmes for healthcare personnel).
- State social programmes for indigenous persons without insurance must receive the product free of charge.

### Developing countries: Competition instead of price control

In 1990 price guidelines for the HIV drug AZT were introduced for the first time (reasonable pricing clause). Thereupon pharmaceutical companies boycotted further license agreements with the NIH, and the price control was abolished in the mid-1990s.[105]

In place of this, the NIH favoured the principle of *Competition instead of price control*. Several non-exclusive licenses are preferably granted to stimulate the competition between

researchers and manufacturers (for example rotavirus vaccine, see page 21). The NIH take active care of technology transfer and are very experienced by now due to many license agreements with developing and emerging nations.[106]

There are many specific licenses in the field of infectious diseases aimed at improving access for developing countries: for example, the licensee has to present an access plan for poor countries. There are many different ways of accomplishing this, either by reasonable prices or by sub-licensees in developing countries. The Aids drug ddI was originally licensed exclusively to BristolMyersSquibb, then, after ten years, non-exclusively to various competitors (for example in Mexico). The NIH also grant licenses to non-profit research projects.[107]

Such agreements are also made for defined development phases or milestones:

- Performance of certain clinical studies in developing countries
- Implementation of research institutions in developing countries
- Training of personnel in developing countries

These guidelines often refer to research on natural substance originating mostly from poor countries with large biological diversity. The countries of origin are to be involved in the financial and scientific success.[108]

*"The main task of the NIH is healthcare, not making money. "*

*Steve Ferguson, NIH Office of Technology Transfer*

## Drug production in threshold countries

An approach for new license models is to differentiate license conditions depending on the countries. An exclusive license for rich countries may provide commercial incentives for product development; however, a non-exclusive license for poorer countries may provide price-lowering competition.

A meaningful dividing line of the license agreements could be drawn in accordance with the World Bank's classification of countries:112 on the one hand, the countries with high per capita income, on the other hand, the countries with medium and low per capita income. There are some good reasons to grant various non-exclusive licenses for threshold countries such as India, Brazil or China. This is where you can find strong pharmaceutical production. The involvement of local manufacturers of generic medicine creates regional competition and thus supports a low-cost drug production.[113]

*Photo: Evelyn Hockstein, WHO*

The situation of worldwide vaccine production illustrates the importance of local production in threshold countries. UNICEF takes care of the most vaccination programmes in developing countries and for this purpose purchases approximately 40 per cent of the worldwide vaccine production.[114] To avoid supply shortages, they buy from various manufacturers. The tendering procedures for the vaccine supply particularly take regional production into consideration. 21 manufacturers from 18 countries, including Brazil, Cuba, India, Indonesia and Senegal, are UNICEF suppliers. This was how it was possible to purchase the vaccines at significantly lower prices in the last years.

## Frequent concerns

### Risk from re-imports?

There are concerns that the protected market, in which the exclusive license applies, might be attacked by re-imports of low-priced generic medicine, for example from India. Experience from previous projects shows that this is not the case. Even globally operating pharmaceutical companies serve different markets with the same product, but under different conditions. If an HIV drug is offered for a fraction of the world price in Africa, they simply use a different package or change the colour of the tablets. As the European drug market is well controlled and sealed off from outside, it is hardly possible to illegally re-import these products from Africa.

**Bad Quality?**

How can you provide a guarantee that generic medicine produced in threshold countries also meets high quality standards? For this purpose the World Health Organization developed a programme for quality assurance. The so-called WHO prequalification ensures a high standard. Many international healthcare programmes only accept generic medicine which is produced according to these standards – an important contribution to patient safety.

*Photo:© Anyka, Fotolia.com*

**Research at our expense?**

Frequent criticism refers to the so-called Free Rider problem:[115] Why should Indian companies be allowed to produce cheap copies of drugs which were developed in our country with high investments? Several points have to be considered here:

- As a growing number of clinical studies are carried out in developing countries, they also contribute to global research.[116]
- Threshold countries have extended research and development enormously in the last years. The number of publications and patents from these countries is continuously increasing.
- In a way, the pharmaceutical industry of some threshold countries is passing a phase of catching up on industrialisation. By initial copying (of generic medicine) their own know-how and product capacities are growing, which eventually leads to the development of their own innovation potential.[117] About 100 years ago, the development of the European pharmaceutical industry also proceeded by Copying and Improving.
- Usually licensees of non-exclusive licenses also pay royalties to patent holders.

# VI Conclusions

*Photo: Chris de Bode, WHO*

Research has a social responsibility. The best new drugs are of no use if therapy cannot be afforded. This applies both for new drugs in developing countries and innovations in our part of the world. All of the actors in medical drug research have to make their contribution to the search for solutions to the problem of insufficient supply.

Public research has particular responsibility. It is always sponsored by society and is thus under an obligation to society. This is why new models need to be found to transfer basic research into product development which put academic research into the service of providing a global benefit. Equitable licensing is a possible path.

Equitable licensing models do not have to be restricted to medical products. They can also be helpful in herbal research for food supply, in providing low-priced communication technology for poor countries, or for technologies for independent energy supply.

To make new license models a reality, there is further need of research: Which models and which license components can be realised best? What provides most benefit for developing countries? What can reduce our drug costs and ensure continued research at the same time?

An objective discussion requires transparency. Universities and other public institutions have to publish convincing information on license agreements. Of which kind are the licenses which are granted to companies? Are they exclusive or non-exclusive, are there any humanitarian conditions? What about the income and costs of patent utilisation? Patent utilisation agencies are there to serve society and therefore should have nothing to hide.

Often, the drug supply in poor countries is a catastrophe. Many drugs are unaffordable in Third World countries; there is almost no research of diseases of the poor. There will only be any changes if we search for solutions together. To patent or not to patent? Is there any “fair license“? The opinions are polarised. No matter which way we choose: The benefit for the people must be top priority. Publicly sponsored research may not only be measured by the height of license income achieved, but also has a social responsibility to provide affordable healthcare products.

# VII Endnotes


1 Report of the Commission on Intellectual Property Rights, Innovation and Public Health. World Health Organization, Geneva 2006.
2 Universal Declaration of Human Rights, section 25,1 World Health Organization, 1948. Section 12, International Covenant on Economic, Social and Cultural Rights, 1966.
3 Monitoring Financial Flows for Health Research. Global Forum for Health Research 2008. http://www.globalforumhealth.org/filesupld/MFF08/MonitoringFinancialFlows2008.pdf
4 http://www.signo-deutschland.de/hochschulen/ (Access 18.2.2009).
5 Sheldon Krimsky, Science in the Private Interest. Oxford 2003.
6 at the opening of the Institute for Science, Ethics and Innovation. http://www.manchester.ac.uk/research/institutes/isei/Quoted after IP-watch, 7. 7. 2008 http://www.ip-watch.org/weblog/index.php?p=1129.
7 Quoted after IP-watch 16. 1.2009.
8 http://www.unhchr.ch/html/menu3/b/a_cescr.htm.
9 Low and middle income countries according to the World Bank-definition.
10 Untangling the web of antiretroviral price reductions. Medicines sans Frontières 11th edition July 2008 (Geneva, 2008) http://www.msfaccess.org/fileadmin/user_upload/diseases/hiv-aids/Untangling_the_Web/Untanglingtheweb_July2008_English.pdf.
11 Chirac, Torreele: Lancet 367 (2006) 1560.
12 M. Moran et al, The new landscape of neglected disease drug development. Wellcome Trust (London 2005). http://www.wellcome.ac.uk/stellent/groups/corporatesite/@msh_publishing_group/documents/web_document/wtx026592.pdf.
13 World market according to manufacturer sales prices. IMS Health Global Pharmaceutical Sales by Region – 2007 www.imshealth.com (Retrieval 19.2.2009).
14 Calculated in Disability Adjusted Live Years DALYs. Report of the Commission on Intellectual Property Rights, Innovation and Public Health, World Health Organization (Geneva 2006), page 13 ff.
15 UNAIDS 2007 Aids epidemic update. (Geneva 2007). http://data.unaids.org/pub/EPISlides/2007/071118_epi_regional Prozent20factsheet_en.pdf.
16 Deutscher Bundestag Drucksache 16/8884 dated 23.4.2008, resolution dated 29.5.2008. http://dip21.bundestag.de/dip21/btd/16/088/1608884.pdf.
17 Global Burden of Disease 2004 Update: Selected figures and tables. World Health Organization 2004. http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/index.html
18 Report of the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (document A61/9 http://www.who.int/gb/ebwha/pdf_files/A61/A61_9-en.pdf ), based on the Report of the Commission on Intellectual Property Rights, Innovation and Public Health. World Health Organization (Geneva 2006). http://www.who.int/entity/intellectualproperty/documents/thereport/en/index.html.
19 The World Medicines Situation. World Health Organization, Geneva 2004, page 61.
20 Rote Liste, drugs list for Germany, version 2/2008. Trade price according to World Health Organization (2007). http://ftp.who.int/htm/AMDS/sourcespricesAPI.pdf (Retrieval 18.2.2009).
21 A. J. Stevens, A. E. Effort, Les Nouvelles XLIII June 2008, 85-101.
22 Triple combination therapy of d4T, 3TC and Nevirapine, annual costs per person. Untangling the web of antiretroviral price reductions. Medicines sans Frontières (July 2008) Untangling the web of antiretroviral price reductions. Medicines sans Frontières 11th edition July 2008 (Geneva, 2008) http://www.msfaccess.org/fileadmin/user_upload/diseases/hiv-aids/Untangling_the_Web/Untanglingtheweb_July2008_English.pdf.
23 C. Godt, Eigentum an Information, Mohr Siebeck (Tübingen 2007).
24 arznei-telegramm 2008, 9, 92-94.
25 Triple vaccination, prices Rote Liste 2/2008.
26 http://nobelprize.org/nobel_prizes/medicine/laureates/2008/
27 Advanced Cancer Therapeutics licenses technology to develop HPV vaccine. Business Journal 23.7.2008
28 C. McNeil, Who Invented the VLP Cervical Cancer Vaccines?, Journal of the National Cancer Institute, Vol. 98, No. 7, April 5, 2006. http://jnci.oxfordjournals.org/cgi/reprint/98/7/433
29 Report of the Commission on Intellectual Property Rights, Innovation and Public Health CIPIH (WHO, Geneva 2006) page 71
30 CIPIH-Report (2006) page 74
31 Monitoring Financial Flows for Health Research. Global Forum for Health Research 2008 http://www.globalforumhealth.org/filesupld/MFF08/MonitoringFinancialFlows2008.pdf.
32 Neglected Disease Research & Development: How much are we really spending? The G-FINDER report. M. Moran et al, The George Institute for International Health (London 2008). http://www.thegeorgeinstitute.org/prpppubs.
33 B. Sampat, Am J Public Health 2009 99:9-17.
34 A. J. Stevens, A.E.Effort, Les Nouvelles XLIII 2008, 2, 85-101, there also footnote 7.
35 "The Role of Public Sector Research in the Discovery of New Drugs," J. Jensen et al., Poster at Annual Meeting, Association of University Technology Managers, San Francisco, CA, March 2007.
36 Süddeutsche Zeitung 3. März 2008 http://www.sueddeutsche.de/wirtschaft/85/434832/text/.
37 B. Sampat, Am J Public Health 2009 99:9-17.
38 on behalf of Michigan State University.
39 D. Chokshi, JAMA October 2007, 298, 1934-1936.
40 Erika Hickel, Die Arzneimittel in der Geschichte (Nordhausen 2008) S. 522-524.
41 J-P Gaudillière, History and Technology 2008, 24:2, 99 — 106.
42 D.G. Contopoulos-Ioannidis et al, Science 2008, 321, 1298.
43 What does pharmaceutical research really cost? BUKO Pharma-News 2005 page 6. J. Schaaber, Keine Medikamente für die Armen (Frankfurt 2005). page 78ff.
44 The Paul-Ehrlich Institute is responsible for vaccines, antibodies, blood products, etc.
45 Parliamentary State Secretary Thomas Rachel, Laborjournal 2008, 10, 69-70.
46 www.kks-netzwerk.de/.
47 http://www.dfg.de/forschungsfoerderung/einzelfoerderung/klinische_studien/index.html (Retrieval 3.2.2009).
48 http://www.bmbf.de/de/96.php (retrieved on 18.2.2009).
49 http://www.who.int/tdr/svc/about/funding/financial-contributors (Retrieval 3.3.2009).
50 www.forschungsrahmenprogramm.de/.
51 http://imi.europa.eu/index_en.html.
52 The Innovative Medicines Initiative (IMI) Strategic Research Agenda S. 119ff.
53 2 May 2005, letter to BUKO Pharma-Kampagne.
54 http://www.vakzine-manager.de/.
55 State Secretary Cornelia Quennet-Thielen (Bundestagdrucksache BT 16/11564 of 06.01.2009), http://dip21.bundestag.de/dip21/btd/16/115/1611564.pdf.
56 For detailed analysis and literature discussion refer to A. So et al, Is Bayh-Dole Good for Developing Countries? Lessons from the US Experience. PLoS Biology 2008, 10, 2078-2084.
57 Choshi and Rajkumar, JAMA 2007, 298, 1934-1936; Sobolski et al. JAMA 2005; 294, 3137-3140.
58 All patents, including non-medical fields. OECD Science, Technology and Industry Outlook 2008. Organisation for Economic Co-Operation and Development (Paris 2008).
59 A. So et al, PLoS Biology 2008, 10, 2078-2084.
60 C. Godt, Eigentum an Information, Mohr Siebeck (Tübingen 2007) page 166 ff.
61 Lage der Forschung in Deutschland. Deutscher Bundestag Drucksache 15/4793 of 31.1.2005. http://dip21.bundestag.de/dip21/btd/15/047/1504793.pdf.
62 § 42 Arbeitnehmererfindungsgesetz (ArbNErfG)
63 Förderrichtlinie zur Fortführung der Verwertungsoffensive – Verwertungsförderung 2. 11. 2007 (Bundesanzeiger 10. 11. 2007, 210, S. 7967-7968).
64 www.signo-deutschland.de (Retrieval 18.2.2009).
65 Compilation after Laborjournal 2008, 10, 64-70.
66 Jagd auf deutsche Biotechnologie-Firmen. Süddeutsche Zeitung 4.7.2008.
67 Kienbaum Management Consultants GmbH, Weiterentwicklung von Kriterien sowie Datenerhebung auf der Basis der Kriterien und Datenauswertung bezüglich der Kompetenz und Leistungsfähigkeit der Patent- und Verwertungsagenturen. Abschlussbericht 2006 (im Auftrag des Bundesministeriums für Bildung und Forschung).
68 http://www.max-planck-innovation.de/de/erfolgsgeschichten/ausgruendungen/index.php (As of January 2009).
69 http://www.ascenion.de/ausgruendungen.html (As of March 2009).
70 BMBF Landkarte Hochschulmedizin (State of evaluation: April 2008). http://www.landkarte-hochschulmedizin.de (Retrieval 18.2.2009).
71 Kooperation zwischen der Uniklinik Köln und Bayer. BAYNEWS Presseservice 26.3.2008.
72 Forschung an der Kölner Uniklinik: Im Auftrag der Pharmaindustrie. die tageszeitung 9.1.2009.
73 Lage der Forschung in Deutschland. Deutscher Bundestag Drucksache 15/4793 of 31.1.2005 http://dip21.bundestag.de/dip21/btd/15/047/1504793.pdf.
74 European Commission DG Competition, Pharmaceutical Sector Inquiry Preliminary Report 28. Nov. 2008 http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/preliminary_report.pdf.
75 C. Wagner, Die Geschichte des deutschen Arzneimittelpatentschutzes. Pharma-Brief Spezial 1/2003, 6-8.
76 J-P Gaudillière, How pharmaceuticals became patentable: the production and appropriation of drugs in the twentieth century. History and Technology 2008, 24:2, 99-106.
77 Erika Hickel, Die Arzneimittel in der Geschichte (Nordhausen 2008) S. 517 ff.
78 J-P Gaudillière History and Technology 2008, 24:2, 99-106.
79 Sheldon Krimsky, Science in the Private Interest (Oxford 2003).
80 www.essentialmedicine.org.
81 Bubela, Strotmann: Designing Metrics to Assess the Impacts and Social Benefits of Publicly Funded Research in Health and Agricultural Biotechnology. International Expert Group On Biotechnology, Innovation and Intellectual Property 2008. http://www.theinnovationpartnership.org/data/ieg/documents/cases/TIP_Innovation_Metrics_Case_Study.pdf.
82 Sorensen, Chambers: Evaluating academic technology transfer performance by how well access to knowledge is facilitated – defining an access metric. J Technol Transfer 2008, 33, 534-547.
83 Philadelphia Consensus Statement: Toward Increasing Access to Medicines http://consensus.essentialmedicine.org/.
84 In the Public Interest: Nine Points to Consider in Licensing University Technology (6. March 2007). http://otl.stanford.edu/industry/resources/whitepaper-10.pdf.
85 in: Stevens, Les Nouvelles XLIII 2008, 2, 85-101.
86 http://www.essentialmedicine.org/EAL.pdf and http://www.essentialmedicine.org/article.pdf
87 Referring to So et al. PLoS Biology 2008,10 and Stevens, Les Nouvelles XLIII 2008, 2, 85-101.
88 www.iphandbook.org.
89 http://www.iphandbook.org/handbook/case_studies/cs13/.
90 http://www.aridispharma.com/rotavax.html.
91 Stevens, Les Nouvelles XLIII 2008, 2, 85-101.
92 International Vaccine Institute Annual Report 2006-2007 http://www.ivi.int/publication/annual_report/2007/annual_report1_2007_5MB.pdf.
93 D D Anh et al, Safety and immunogenicity of a reformulated Vietnamese bivalent killed, whole-cell, oral cholera vaccine in adults. Vaccine 2007, 25, 1149-1155 (doi:10.1016/j.vaccine.2006.09.049).
94 http://www.iphandbook.org/handbook/case_studies/cs16.
95 http://www.iphandbook.org/handbook/case_studies/cs20.
96 http://www.amyrisbiotech.com/index.php?option=com_antimalarial&Itemid=51.
97 http://www.iphandbook.org/handbook/case_studies/cs22/.
98 www.dndi.org.
99 C. Wagner, Erste Neuentwicklung eines Medikaments ohne Patentschutz. Pharma-Brief 3/2008 S.1-2.
100 see C. Wagner-Ahlfs, Zur aktuellen Situation der HIV-Impfstoff-Forschung (Tübingen 2008). http://www.aids-kampagne.de/fileadmin/Downloads/Impfstoffforschung/Impfstoff_update_2008_01.pdf.
101 Promoting Innovation and Access through Effective Management of Intellectual Property. International Aids Vaccine Initiative IAVI (without year) http://www.iavi.org/viewfile.cfm?fid=47181; conversation with Labeeb Abboud (IAVI) New York April 2008.
102 R. Gupta et al, Nature's Medicines: Traditional Knowledge and Intellectual Property Management. Current Drug Discovery Technologies, 2005, 2, 203-219.
103 Conversation with Steve Ferguson, NIH Office of Technology Transfer (Rockville, April 2008).
104 http://www.ott.nih.gov/policy/phslic_policy.html (Retrieval 18.2.2009).
105 Access to Essential Medicines and University Research: Building Best Practices. Workshop Report 25 Sep. 2002, The Center for Interdisciplinary Research on AIDS Yale University. http://www.yale.edu/aidsnetwork/Essential Prozent20meds, Prozent20final Prozent20report_Fall Prozent20conference.doc.
106 L. Salicrup et al, Partnerships in Technology Transfer. An Innovative Program to Move Biomedical and Health Technologies from the Laboratory to Worldwide Application. IP Strategy Today 12/2005. http://www.ott.nih.gov/pdfs/ISPT-12-2005-Salicrup-Harris-Rohrbaugh-NIH-Tech-Transfer.pdf.
107 E.g., for meningitis vaccine. See Vaccine Technology Developed by FDA Scientists Licensed by NIH OTT to PATH for Developing Country Use (15.3.2006) http://www.ott.nih.gov/current_issues/Issues-ended-04-20-2006.html.
108 Case studies see R. Gupta et al, Nature's Medicines: Traditional Knowledge and Intellectual Property Management. Current Drug Discovery Technologies 2005, 2, 203-219. For actual debate on the relation of patent protection and traditional knowledge refer to C. Godt, Eigentum an Information, Mohr Siebeck (Tübingen 2007).
109 http://www.ott.nih.gov/policy/phslic_policy.html (Retrieval 18.2.2009).
110 About NIH. National Institutes of Health 2009 www.nih.gov/about (Retrieval 18.2.2009).
111 L. Salicrup et al, Partnerships in Technology Transfer. An Innovative Program to Move Biomedical and Health Technologies from the Laboratory to Worldwide Application. IP Strategy Today 12/2005. http://www.ott.nih.gov/pdfs/ISPT-12-2005-Salicrup-Harris-Rohrbaugh-NIH-Tech-Transfer.pdf
112 http://www.worldbank.org/data/countryclass/classgroups.htm.
113 K. Outterson Market-Based Licensing For HPV Vaccines In Developing Countries. Drugs & Vaccines Jan/Feb 2008, 130-142.
114 Procurement and Pricing of New Vaccines for Developing Countries. IAVI Policy Brief #15, September 2008. https://www.iavi.org/viewfile.cfm?fid=49389.
115 See also K. Outterson, Free Trade Against Free Riders?. Pharma Pricing & Reimbursement 2004, 9, 254-255 http://ssrn.com/abstract=615144.
116 Refer to Health Action International, Clinical Trials on Trial, Berlin 21.Nov. 2008. Conference documentation: http://www.haiweb.org/01_about_europe_c.htm).
117 Andreas Kurz, Patentlösung gegen Produktpiraterie gesucht. Max Planck Forschung 3/2008 32-36.

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