



EUROPÄISCHE AKADEMIE

zur Erforschung von Folgen wissenschaftlich-technischer Entwicklungen
Bad Neuenahr-Ahrweiler GmbH

Direktor: Professor Dr. Dr.h.c. Carl Friedrich Gethmann

NEWSLETTER

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EDITORIAL

■ The press and public relations work of the Europäische Akademie covers a wide range of activities. So far, in the year 2006, for example, the corporate design and the logo have been redesigned and introduced into all operational fields of the academy.

Reports on numerous events of the academy were published in the various media (print media, TV, radio). Up to the month of June, three studies were presented in Berlin and Cologne. The following books: *Nanotechnology. Assessment and Perspectives*, *Organmangel – Ist der Tod auf der Warteliste unvermeidbar?* and *Leben mit Lärm?* were published in the Springer series “Scientific Ethics and Technology Assessment”.

In June, the congress “The future of space travel. Its benefits and its value” was held. In September, the academy celebrated its 10th anniversary. In addition to numerous guests, the Minister for the Department of Science of Rhineland Palatinate, Professor Dr. Jürgen Zöllner, who also took part in a round of discussions on the founding of the academy, was among the congratulants. In October, the Europäische Akademie, in cooperation with the Kreissparkasse savings bank of Ahrweiler, is running a lecture evening, at which Professor Bernd Raffelhüschen will speak on the subject of the sustainability of social security. The annual “Ahrtaggespräch” (Ahr Valley Talks) and a discussion with the press will take place in November.

In spring 2007, the next volume of the book series will be published: *Intervening in the Brain – Changing Psyche and Society*, which will be presented in Berlin.

In conclusion, attention shall be drawn to the enclosed “Forschungsprogramm” (Research Programme), which provides information on the current status of the projects of the Europäische Akademie. The English version of the current programme will be published in the near future.

KM/FW

FOCUS

Pharming – the next step in the debate on gene technology?

Margret Engelhard

Pharming is a new branch of biotechnology that employs transgenic plants or animals as living “factories” to produce human or animal pharmaceuticals. Goats, for example, have been transformed with the human gene for antithrombin (an anti-clotting factor). These genetically modified animals express this human protein in their milk, which is after a processing step ready for its pharmaceutical assignment. The term “pharming” is a merge of the words “pharmaceuticals” and “farming”, and thus characterises the mingling of two highly different industries. The stakes on pharming are high, in terms of lives that may be saved and economic profits that may be gained. If pharming is made a success, it can bring drug producers and biotechnology firms billions of dollars in sales over the coming decades. However, this new application of biotechnology also raises a number of questions regarding risks and ethical implications, e.g.: how can animal health and welfare be ensured, is such inference with and instrumentalisation of plants or animals acceptable and do plant-made pharmaceuticals pose risks to humans and the environment (particularly if they are produced in plants that also serve as food or feed crops)?

Recombinant pharmaceutical proteins – the advent of biotechnology

■ Only twelve years after the discovery of the genetic code, which describes the connection between genes and the formation of proteins, and four years after the first artificial introduction of a gene into an organism that thereby became “transgenic” or “recombinant”, in 1977 the first human gene was cloned into a microorganism in order to produce recombinant human proteins. This experiment is often referred to as the advent of biotechnology. Five years later, “humulin”, the first recombinant pharmaceutical, received marketing authorisation in the USA. Humulin is human insulin that is produced by transgene *Escherichia coli* bacteria. Before its development, bovine and porcine insulin was used to treat diabetes mellitus patients.

These early commercial products were extracted directly from pancreatic tissue of slaughterhouse cows and pigs.

Drugs like insulin that are too complex to be produced by conventional chemical synthesis and therefore have to be isolated from biological material or produced in transgenic living cells or organisms, are called “biopharmaceuticals” or “biologics”. They are therapeutic proteins, with hormones and monoclonal antibodies, as the most important examples, or nucleic acid-based drugs. Currently, fermenter grown recombinant *Escherichia coli*, bakes yeasts (*Saccharomyces cerevisiae*) or Chinese hamster ovary cell cultures are used as transgenic living expression systems for biopharmaceuticals. However, these methods are costly and of limited efficiency. With a rapidly increasing demand for biopharmaceuticals, first

cases of patient waiting lists are now caused by a shortage in production capacity. The rising demand for biopharmaceuticals is caused by two developments. First, there is an increasing number of people suffering from illnesses that can be treated with biopharmaceuticals. According to estimates by the WHO, for example, the number of people developing diabetes is likely to double by 2030. Secondly, an increasing number of newly developed pharmaceuticals are biopharmaceuticals.

It is hoped that the use of higher organisms as production platforms for biopharmaceuticals could overcome this logjam. In pharming, the enlargement of production capacities (e.g. growing more transgenic crops or breeding more transgenic animals) may be quicker, cheaper, and more flexible compared to current production processes that are dependent on industrial facilities. In addition, pharming is expected to be far cheaper than the use of traditional transgenic cell cultures, e.g. on the level of the estimated prize per gram raw protein or on the level of equipment maintenance costs as compared to the costs of keeping the transgenic animals. By overcoming technical or financial limitations, pharming may also enable the development of entirely new therapeutic compounds.

Plants and animals as production platforms for recombinant pharmaceutical proteins

Pharming technology has been applied to several animal species, e.g. goats, cows, pigs, sheep, rabbits and chickens. For example, transgenic chickens, cows and goats are used for the production of monoclonal antibodies. Also, sheep and cows have been transformed for the expression of human factor VIII and factor IX needed for the treatment of haemophilia, and for fibrinogen that is used in wound healing. Most often, the recombinant protein is expressed in the milk of transgenic mammals, but it can also be directed to the blood, urine or eggs (i.e. in birds). In the case of phytopharming, recombinant proteins – for example erythropoietin (EPO) – are usually expressed in the seeds or leaves of the recombinant plants (corn, rice, soybean and tobacco are the most prominent examples). Currently, an increasing number of field and clinical trials are running, and just recently the first protein produced by pharming gained market approval: in August 2006, the European Commission granted market authorisation to ATryn®. The US-based biotechnology company

GTC Biotherapeutics produces ATryn® in the milk of female goats that have a transgene for human antithrombin. Antithrombin is an important anticoagulant in human serum and is applied for the prophylaxis of venous thromboembolism in surgery of patients with congenital antithrombin deficiency. The antithrombin products that have hitherto been available are derived from human plasma. Recombinant human antithrombin can only be produced in higher organisms as expression platforms, because its complex structure precludes efficient production in traditional cell culture bioreactors.

The bioethical challenge

Beside the great hopes that pharming evokes, it raises a number of ethical, legal and social problems that should be discussed parallel to its scientific and industrial development. Moral arguments in support of pharming are based on its economical potential or on the expected benefits to patients. Moral arguments against pharming may arise from concerns regarding the use of plants and animals: to what degree may we instrumentalise, interfere with and alter higher organisms? Are there health and welfare problems specific for pharming animals? Moral arguments against pharming may also be based on human safety and ecological concerns: to what degree does pharming pose a risk to humans and the environment? Biopharmaceuticals are usually highly bioreactive compounds and thus in most cases toxic. Biological risks can therefore be identified in the areas of pharmaceutical safety, ecology and food safety.

Because pharming makes use of conventional domestic plants and animals it will be crucial how – and to what extent – pharming crops and animals can be kept separate from all stages in the food- and feed-production chains. The plausibility of a scenario of food-chain contamination was demonstrated by the first documented pharming-accident in 2002 in the USA, where 13,000 tons of vaccine-contaminated soy beans were discovered. Also, recent cases in Europe of contamination of rice with a genetically modified rice strain (LL RICE 601) that has never been approved for commercial use demonstrate impressively that neither confinement strategies for field trials nor import regulations have been efficient so far. In addition, it remains to be investigated whether confinement strategies are suitable for restricting consequences of pharming for nearby flora, fauna and soil microbiology. In this

context, we need to take into account the problem of risk assessment with a large degree of uncertainty: biotechnology in general and pharming in particular are relatively young developments, and there are, in many cases, no scientific findings on potential implications available (nor expected in the near future).

In addition, the future development and regulation of pharming is likely to be influenced by public perceptions of and attitudes towards it. Expectations, beliefs, fears and moral attitudes need to be evaluated and taken into account. Societal dimensions of phytopharming and zoopharming probably differ: it could be the case, for instance, that zoopharming is preferable to phytopharming from an economical point of view, but not socially acceptable, and that zoopharming products therefore may not capture the market.

The legal regulation of production, release, processing, and marketing of pharming-products is diverse and lies within the responsibility of a number of institutions, which might cause uncertainties. Phytopharming, for example, represents a novel merge of green and red biotechnology, with the consequence that different authorities are responsible. The deliberate release of genetically modified organisms is regulated by the EU directive 2001/18/EG and by national gene technology law, whereas the European Medicines Agency (EMA) is responsible for the evaluation and supervision of medicines for human and veterinary use. There may also be a need for preventive regulation by the European Food Safety Authority (EFSA) due to the risk of contaminations in the food and feed chain discussed above.

Discussion is needed concerning the measures which industry and government regulators can adopt to optimise the prevention of risks connected with pharming, and whether these actions are sufficient. The Europäische Akademie has recently started a new project on pharming with the title: “Pharming. Genetically modified plants and animals as future production sites of pharmaceuticals?” It analyses the potentials and risks of pharming and aims at determining the need for and means of legal regulation and policy action for its responsible further development.

Final remarks

Since the rise of biotechnology, the political discussions on gene technology have always been highly polarised, and often characterised by simple black-and-white arguments. This polarisation has often harmed

both sides more than it has helped. However, in the case of pharming, the debate might develop in a new direction. People that fundamentally oppose gene technology might rethink their position in cases where pharming offers the only possibility to produce life-saving drugs. The risk of unwanted vaccine consumption along the early morning cereals on the other hand might prompt gene technology advocates to reconsider their arguments. Thus an extensive discussion on pharming might also bring along a more constructive and fruitful debate on the use of gene technology in general.

Dr. phil. Margret Engelhard, Dipl.-Biologin, is member of the scientific staff of the Europäische Akademie Bad Neuenahr-Ahrweiler GmbH. She has recently finished her project on organ donation and is now coordinating the project group "Pharming".

WORKING GROUPS

Eröffnungsveranstaltung weiterbildender Masterstudiengang „Medizinethik“

■ Deutschlandweit einmalig bietet die FernUniversität in Hagen in Kooperation mit der Europäischen Akademie GmbH und der Johannes-Gutenberg Universität Mainz einen weiterbildenden Masterstudiengang zur Medizinethik als Studium neben dem Beruf, aber auch als Fortbildungsmaßnahme für Ärzte an. Zur Eröffnungsveranstaltung des im Sommer 2006 akkreditierten Fernstudiengangs lädt die FernUniversität alle Interessierten ein. Zeit: 30.10.2006, 11:00 – ca. 13:00 Uhr, Ort: Technologiezentrum (TGZ), Universitätsstr. 1, Erdgeschoss, Ellipse. Anmeldung unter Medizinethik@fernuni-hagen.de erbeten.

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Expert meeting "Pharming"

■ The project group "Pharming. Genetically modified plants and animals as future production sites of pharmaceuticals?" met at the Berlin-Brandenburgische Akademie der Wissenschaften on September 14th and 15th, 2006. Five invited experts contributed perspectives concerning plant molecular pharming, bioethics, legislation, business ethics and regulation, which will soon be published in the "Graue Reihe".

The first contribution was made by Dr Schillberg (Fraunhofer-Institut für Moleku-

larbiologie und Angewandte Ökologie, Aachen), a member of the Pharma-Planta Consortium (an EU FP6-funded program involving 39 academic laboratories and industrial partners; see www.pharma-planta.org), which develops strategies for the safe and efficient production of biopharmaceuticals in genetically modified plants. Schillberg explained the advantages and challenges of phytopharming, and he provided an overview of current research, production and authorisation processes.

Professor Birnbacher (Universität Düsseldorf) spoke about bioethical perspectives on pharming, which he identified as a rather new topic in the bioethical scene. He distinguished between objections based on risks (i.e. to the environment, the production organisms or the consumers) vs objections against the method of genetic modification as such. Birnbacher's main thesis was that while risks and acceptance need to be taken into account in ethical evaluation, the impacts on potential beneficiaries of the new technology should also be considered.

Legal considerations from an animal welfare perspective were presented by Priv.-Doz. Dr Müller-Terpitz (Universität Bonn). He explained that animal pharming is principally compatible with international, European and national law, provided that it is justified by its usefulness to humans. However, jurisdiction and intensive legal debate are still missing, and certain aspects of animal pharming (e.g. cell nuclear transfer in the production process) are not yet unambiguously subjects of legislation.

Professor Eaton (Stanford University) presented and compared two case studies concerning the market introduction of food and drugs from transgenic sources: Monsanto's introduction of rBST (recombinant Bovine Somatotrophin, a production enhancer for cattle) in the USA in 1994, and GTC Biotherapeutics' recent release of ATryn® (a plasma protein with anticoagulant and anti-inflammatory properties) in Europe. Eaton concluded that companies ought to adopt business ethics that include transparency, interaction and education, and will benefit from taking consumers' concerns seriously.

Finally, Dr Joachim Schiemann (Biologische Bundesanstalt Braunschweig) spoke about the pharming-relevant work of the European Food Safety Authority (EFSA). Currently, the EFSA develops guidance for the assessment of genetically modified plants as production platforms for non-food/feed products. In the context of pharmaceuticals, EFSA's risk assessment responsibilities lead

to close collaboration with the European Agency for the Evaluation of Medicinal Products (EMA) – consultations regarding their interplay and division of responsibilities are planned for next spring.

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Spatial Planning and the Virtualisation of Life Worlds

■ Since July 2006 a one-year study is being prepared by the academy in cooperation with the Technische Universität Kaiserslautern (Lehrstuhl für Stadtplanung/urban planning). This study is part of the university's umbrella project on "Spatial Impacts of Virtualisation and its Technological and Societal Preconditions". The project is supported by the programme „Wissen schafft Zukunft“ of the Federal State Rheinland-Pfalz. The idea of the study is based upon the fact that modern information and communication technology (ICT) has become an inevitable factor of human life. Now, an upcoming challenge for the public arises from the emergence of ICT into communal life and the development of urban and rural regions. For example, the growing markets for e-shopping or e-working will change corresponding demands for mobility and housing significantly. This will have to be considered in the course of rational spatial planning together with other probably interfering mega-trends, like the consequences of demographic change in Europe. This interference might substantially influence the above mentioned demands for spatial planning. Moreover, spatial planning, IT and social politics will have to deal with the growing virtualisation of daily life. In this respect the ambiguity of citizens' expectations towards privacy and societal participation seems to be central. The critical reflecting of this ambiguity might offer normative knowledge which could enable decision makers and planners not to push possibly undesirable developments.

Recently, the project partners held an expert workshop on 16th October on the "Societal Framework for the Virtualisation of Urban Life". The next edition newsletter will report upon the results in more detail.

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NEWS

New publications in the series**“Wissenschaftsethik und Technikfolgenbeurteilung“**

■ Vol. 19: *Environment Across Cultures* (2003); Vol. 20: *Functional Foods* (2003); Vol. 21: *Embryo Research in Pluralistic Europe* (2003); Vol. 22: *Bridges between Science, Society and Policy. Technology Assessment – Methods and Impacts* (2004); Vol. 23: *Low Dose Effect in the Environment. Dose-Effect Relations and Risk-Evaluation* (2004); Vol. 24: *Bioethics in a Small World* (2004); Vol. 25: *On the Uniqueness of Human Kind* (2004); Vol. 26: *Enabling Social Europe* (2006); Vol. 27: *Nanotechnology – Assessment and Perspectives* (2006); Vol. 28: *Leben mit Lärm? Risikobeurteilung und Regulation des Umgebungslärms im Verkehrsbereich* (2006); Vol. 29: *Intervening in the Brain. Changing Psyche and Society* (2007).

Also the following studies were published by Springer: *Organmangel – Ist der Tod auf der Warteliste unvermeidbar?* (2006); Vol. 18 (Translation): *Sustainable Development and Innovation in the Energy Sector* (2005); Vol. 5 (Translation): *Environmental Standards. Combined Exposures and Their Effects on Human Beings and Their Environment* (2003).

Scientific Advisory Board

■ On 26th September the academy's Scientific Advisory Board held its 23rd meeting in Bad Neuenahr-Ahrweiler. Main topics were comments on the final draft of the project “Intervening in the Psyche”. The Board recommended some restructuring of the draft report and afterwards its resubmission for final approval. Furthermore, the academy's work of the last three-quarter-year was reviewed under new funding conditions and on the recently started project generation as well as on the academy's project horizon beyond.

LECTURES

Carl Friedrich Gethmann**23.9.06**

■ „Risikobeurteilung – Orientierung in der technischen Kultur“

17. Bundeskongress des Fachverbandes Philosophie Münster

28.9.06

■ „Über den Ursprung des Sollens“

Forum für Philosophie Marburg

29.9.06

■ „Zwingt der Naturalismus die Gesellschaft zum Umdenken bei Strafrecht und Erziehung?“

Forum für Philosophie Marburg, Podiumsdiskussion

12.10.06

■ „Die lebensweltliche Fundierung des Sollens“

DFG-Rundgespräch „Lebenswelt in Wissenschaft, Ethik und Politik“, Universität München

Thorsten Galert**2.10.06**

■ „What It Means to Ascribe Pain to Animals“

Tagung „Theology Meets Biology“, 2.–4. Oktober 2006, Katholische Akademie Schwerte

Felix Thiele**27.9.06**

■ „Wozu Umfragen? Zum Verhältnis von empirischer Sozialforschung, Wissenschaftsethik und Wissenschaftspolitik“

Tagung der Jungen Akademie zum Thema „Moralischer Relativismus“, 25.–27. September 2006, München

PERSONALITIES



Friederike Wütscher, born in 1971, studied German and English at the University of Cologne (1991 to 1997). During this time she had a six month scholarship which she spent at the University of North London. At Cologne University she worked as student assistant at the linguistic institute of the English department. In her University years she gained work experience in different journalistic fields, e.g. public relations agency, TV-station, and newspapers.

After her examination she worked for a publishing company which is specialised in scientific publications. Her main working focus was in editing, marketing and developing concepts for new publications.

In 1998 she began to work for the Deutsche Krankenhausgesellschaft (German hospital federation) as press officer. Here she was responsible for public relations and events and edited different publications.

In 2001 she started to work for the Europäische Akademie in editing scientific texts and public relations. She works in all fields of the academy which concern publications and events. By now she edited 21 volumes of the series „Wissenschaftsethik und Technikfolgenbeurteilung“ which is published by Springer-Verlag. She organises events to present the newly published volume and is also responsible for all public relations concerning journalists, the public and scientists. Furthermore, she is responsible for different publications like Research Programme, Research Report and the „Graue Reihe“. Recently she and other staff members organised the celebration of the tenth anniversary of the academy; together with her colleague Katharina Mader she presented two talks.

Friederike Wütscher is member of staff of the Europäische Akademie and responsible for public relations and scientific editing.

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