



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 Europäische Akademie GmbH's management has decided to re-launch its website (www.ea-aw.de) in the course of a technical updating procedure. The concept of the new homepage displays both the academy's new corporate design as well as a new approach to navigation: It now concentrates on thematic fields rather than the organisational structure. Related topics, such as energy and traffic, appear alongside each other on one page, whether they relate to project groups, publications, conferences, or any of the academy's other activities.

The website is subdivided into three separate but overlapping overall thematic areas – technology, health, and environment – giving the reader a quick, but profound insight into the academy's range of topics and activities. On each level, users can freely decide on how much information they want to receive, and access different pages in various ways. The service system has also been improved, e.g. navigation is simple and user-friendly and contact information is easily accessible.

Most publications, such as the Newsletter and the Graue Reihe, can be downloaded as well as mail-ordered from the respective publishing companies via an external link. In keeping with its international outlook, the Europäische Akademie will also shortly re-launch its English-speaking website. Until then, the current English website will remain active.

KM/FW

FOCUS

Research on Minors

Felix Thiele

The therapeutic situation of minors is unsatisfactory. For example, a large part of pharmaceuticals which is given to them is used “off label” or “off licence”, resulting in disproportionately numerous adverse side effects. What seems even worse, for many paediatric conditions there is no validated therapy available leaving minors behind as “therapeutic orphans”. Amongst the reasons for this unsatisfying situation there are a not well-developed regulatory framework for performing morally acceptable clinical research on minors and evidence for market failure of the classical pharmaceutical business model.

■ Clinical research on minors is an increasingly urgent problem. For example, a large part of pharmaceuticals which is given to children and adolescents is used “off label” or “off licence”, i.e. either the pharmaceuticals have, due to lacking research data, no license for paediatric use or they have at least no license for the specific medical condition they are used for. In these cases paediatricians cannot base their treatment decisions on scientific data but have to fall back on subjective experience. This ongoing lack of specialised and targeted research in pharmaceuticals for paediatric use is partly due to the wrong but persistent belief that children can be seen as “small adults”, who can simply be administered smaller dosages of medicines adapted according to age and weight. Exposing minors to medication unsuitable and risky for them is, however, both morally and legally questionable. Adverse side effects are disproportionately numerous in minors. More and better medicines for children that have been researched according to sound scientific standards are therefore urgently needed. Even if “off label” and “off licence” use is an

established practice in paediatrics it remains an unfortunate one. Besides, it should be mentioned that the state of clinical research in other vulnerable populations such as the mentally ill is also far from satisfying. Here, too, pharmaceuticals are partly not licensed. In some cases effective pharmaceuticals have not been developed yet (e.g. dementia).

Recently, politicians have taken steps to remedy this deplorable state – e.g. by introducing the regulation (EC) No 1901/2006 on medicinal products for paediatric use. The realisation of this and other regulations alike, however, is causing a number of ethical, legal and economic problems: It is debated, to begin with, to what extent and on which ethical and legal foundation risky research on minors is acceptable at all. In addition, the realisation of clinical studies in smaller groups of patients (infants, minors, adolescents) is complex, time-consuming, and therefore very costly. Thus, the question arises whether the established ways of drug development are appropriate at all for fulfilling societal needs. Finally, the obvious globalisation of clinical research raises concerns often expressed in the fear that due

to a “research colonialism” benefits and risks of research might be unjustly distributed between the western and the developing world.

Moral acceptability of clinical research on minors

Clinical research on minors faces a moral dilemma: On the one hand side there is a justified interest if not a moral obligation to intensify research on minors aiming at the improvement of our diagnostic and therapeutic options for them. On the other hand the research poses risks on minors that are not necessarily compensated for by medical benefits.

To allow for a balanced assessment of research on human beings it is a long established moral standard to allow such research only if there is an informed consent that can be revoked at any time, and if there is an adequate risk-benefit ratio. Though there is a broad consensus on the basic moral principles guiding research on human beings in general, several concepts of crucial importance for the moral evaluation of clinical research on minors are unclear: the conceptual clarification and practical implementation of, amongst others, ‘proxy consent’, ‘*minimal risk*’, ‘*acceptable risk-benefit ratio*’, and ‘*therapeutic versus non-therapeutic research*’ are contested issues. Moreover, there are still no instruments available that would allow, for example, an easy standardised case-to-case evaluation of the capacity to consent on minors. In effect there remains a large gap between the theoretic understanding of the fundamental moral principles guiding research on minors, and the practical implementation of these principles in everyday clinical practice. Irrespective of the indicated shortcomings of the moral framework, however, clinical research on minors is a morally recommendable and legally acceptable scientific endeavour if performed after careful assessment and under very strict safety regulations.

Economic feasibility of research on minors

The technical realisation of clinical research on minors is a complex matter. To begin with, talking of “minors”, from a physiological point of view, we face an inadequate simplification of a heterogeneous collective to be differentiated into at least five developmental stages: premature infants, newborns, infants, children, and adolescents – each group showing specific characteristics influencing the way a pharmaceutical compound is being effective and metabolised. In addition to the challenges of designing a medically sound research scheme, the administrative requirements are high: for example, an adequate risk-benefit ratio of the planned research

must be demonstrated to the authorities prior to actual experiment. Also the implementation of adequate consent procedures – i.e. in minors the proxy consent of their parents plus, if possible, the minor’s assent – must be ensured. Finally, anyone embarking on a research project on minors must be aware of the generally sceptic public attitudes towards this branch of medicine and hence the potentially devastating public response to adverse incidents possibly occurring in the course of a research project.

In the last decades clinical research, especially the development of new pharmaceuticals, has been almost exclusively in the hands of private for-profit companies. Despite the now common criticism of “big pharma” we should not forget that this model has been beneficial for both companies and society for a long time. There are indications, however, that the structure of the pharmaceutical industry is changing. One reason for that may be that the classical business model of the pharmaceutical industry based on the development of so-called blockbusters, i.e. drugs for large patient collectives, has limitations in view of the needs of smaller patient groups such as children and adolescents – not to speak of all the age-, gender-, and ethnicity-specific variations in therapeutic needs increasingly discovered.

Unfortunately, recent European policy action aiming to improve clinical research for minors – such as the already mentioned regulation (EC) No 1901/2006 on medicinal products for paediatric use – mainly focuses on stimulating the for-profit pharmaceutical industry to invest more capacities into research for minors. Though the incentives offered, e.g. patent extensions, may be fruitful, further efforts should be made to augment privately funded for-profit clinical research with alternative non-profit research schemes – efforts that have already been undertaken in the United States of America for some years.

Clinical research on minors outside the western world

A main concern of researchers both from universities and industry remains to find sufficient numbers of minors as test persons. Often parents simply do not like the idea that their offspring takes part in clinical research and are not susceptible even to good arguments, for example the claim that children are nowhere better monitored than in a state-of-the-art clinical trial. This reservation cannot be simply overcome by more extensive consent procedures but also needs a personal and trustful relationship between parents and researchers. However, in countries providing

universal health care parents will be less prone to give consent because of external motivations such as access to treatment. The common tendency of parents in the western world not to expose their beloved ones to a perceived risk is natural, though not necessarily noble, and clinical researchers have to adjust to it.

On these grounds it does not come to a surprise that there is a tendency to perform the clinical research, which is needed for licensing of new products in the West, outside the western world. It is well-known that many studies on minors are conducted in countries such as Romania, Ukraine, and India. The worry, thus, is that the trial requirements for market authorisation of pharmaceuticals imposed by the regulators will give rise to “research colonialism”.

It would be short-sighted to solely accuse the pharmaceutical industry of relocating precarious research projects in order to minimise risk to their own business-success. To begin with, a large proportion, though certainly not all, of research-tourism is done in accordance with the relevant legal regulations, and the clinical data generated outside the western world are regularly accepted for market authorisation in western countries. To accuse big pharma of neglecting their corporate-citizenship and their moral obligations does not take into account that much of what is criticised rightly from a moral perspective is done legally. The responsibility for a legal framework that does not prevent morally unwanted consequences does not belong, however, to companies acting under this framework but to those giving legitimacy to these rules – that means: to all of us.

Dr. med. Felix Thiele, M.Sc., is deputy director of the Europäische Akademie GmbH. He is head of the junior scientist group of the project group “Pharming. Genetically modified plants and animals as future production site of pharmaceuticals?” (duration 7/2006–12/2008). Currently he is establishing a working group on clinical research in vulnerable populations. See also the conference report “Clinical Research in Vulnerable Populations” on page 3 of this issue.

WORKING GROUPS

■ Project Group “Potentials and Risks of Psychopharmaceutical Enhancement”: 24–25/4/2008, Bad Neuenahr-Ahrweiler

CONFERENCES

“Clinical Research in Vulnerable Populations” – Conference of the Europäische Akademie Bad Neuenahr-Ahrweiler and the Berlin-Brandenburgische Akademie der Wissenschaften

■ Conducting research on vulnerable populations, especially on minors and the mentally ill, is becoming an increasing and urgent problem. For example, a large part of the pharmaceuticals used on minors and adolescents is not licensed for that particular age group; in some cases, effective pharmaceuticals do not even exist yet (e.g. for the treatment of dementia).

In order to address these issues, the Europäische Akademie and the Berlin-Brandenburgische Akademie der Wissenschaften have hosted a conference on “Clinical Research in Vulnerable Populations” in Berlin on 3rd and 4th April.

Experts from the fields of paediatrics, psychiatry, pharmacology, ethics, law, and the pharmaceutical industry were given a platform to raise such issues and discuss possible solutions. Although politicians have recently undertaken steps to remedy the deplorable state in this field, e.g. by introducing regulation (EC) No 1901/2006 on medicinal products for paediatric use, the implementation of such regulations is raising a number of ethical, legal, and economic problems: Overall, speakers showed great concern regarding the huge amount of data necessary in order to analyse the effectiveness of drugs for vulnerable segments of the population. The experts debated to what extent and on which ethical and legal basis risky research on such populations is acceptable at all. Furthermore, some additional realisations of clinical studies in smaller groups of patients (infants, minors, adolescents) are rather complex and time-consuming and therefore very costly. Thus, the question was raised whether the established ways of drug development are appropriate at all with respect to societal needs.

It also became apparent that a considerable number of pharmaceutical companies still regard children as miniature adults disregarding the need for age-specific medical treatments. Professor Seyberth (Universität Marburg) expressed his hope that the new

regulation be taken as a chance to provide the most relevant age groups (i.e. children and old age patients) with adequate pharmaceutical research; however, the majority of companies appear not to have adopted this view, nor translated it into organisational changes. In his talk on publicly versus industry funded research strategies in paediatric pharmacology, Benedetto Vitiello, M.D., (US National Institute of Mental Health, Bethesda) was able to show that the US experience with financial incentives of the past decade has been an overall success since they have helped to improve the quality of studies, with the market exclusivity programme being re-authorized and prolonged in 2007. Finally, Oxford child and adolescent psychiatrist and ethicist Jacinta Tan, M.D., Ph.D., spoke on the salient ethical issues of informed consent and competence (e. g. on group consent by parents and children).

Altogether, the participants agreed on the need of improving clinical research on vulnerable populations. The Europäische Akademie and the Berlin-Brandenburgische Akademie der Wissenschaften are now planning to establish an interdisciplinary project group on this topic.

Scientific coordinators of this conference were Professor Dr. med. Jörg Fegert (director of the Klinik für Kinder- und Jugendpsychiatrie/Psychotherapie, Universität Ulm); Professor Dr. med. Dr. h.c. Günter Stock (president of the Berlin-Brandenburgische Akademie der Wissenschaften, Berlin) and Dr. med. Felix Thiele (deputy director, Europäische Akademie GmbH, Bad Neuenahr-Ahrweiler). Speakers were Professor Dr. med. Hanfried Helmchen (former director of the Psychiatrische Klinik und Poliklinik, Freie Universität Berlin); Professor Dr. med. Hannsjörg W. Seyberth (former director of the department Kinderheilkunde I, Philipps-Universität Marburg); Benedetto Vitiello, M.D. (director of the child and adolescent treatment and preventive interventions research branch, US National Institute of Mental Health, Bethesda); Professor Dr. jur. Gerfried Fischer, LL.M. (chair Bürgerliches Recht, Internationales Privatrecht, Rechtsvergleichung und Arztrecht, Universität Halle); Dr. med. Birka Lehmann (professor and director Licencing 3, Bundesinstitut für Arzneimittel und Medizinprodukte, Bonn); Dr. med. André Hertkorn (Boehringer-Ingelheim, managing director of medicine, Biberach a. d. Riss); Philippe Auby, M.D. (director of the international clinical research department of paediatric neuro-psychiatry, Lundbeck, Paris) and Jacinta Tan, M.D., Ph.D. (senior clinical research fellow, Ethox Centre, Universität Oxford).

NEWS

Netzwerk für Technikfolgenabschätzung

■ Vom 28. bis 30. Mai wird die Tagung “Technology Governance – Der Beitrag der Technikfolgenabschätzung” als dritte Konferenz des deutschsprachigen “Netzwerks für Technikfolgenabschätzung” (NTA) in der Österreichischen Akademie der Wissenschaften in Wien stattfinden. Die Tagung widmet sich den konzeptionellen Fragen TA-geleiteter Governance und Innovationsgestaltung sowie ihrer Wirkung in ausgewählten Problemfeldern. Die Konferenz wird vom Wiener Institut für Technikfolgenabschätzung organisiert und durch Zuschüsse und wissenschaftliche Beiträge von der Europäischen Akademie sowie anderen Mitgliedsrichtungen des TA-Netzwerks unterstützt.

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“Organmangel. Ist der Tod auf der Warteliste unvermeidbar?”

■ The sponsors’ club of the Europäische Akademie GmbH has, within the framework of the working group on medical ethics, staged a lecture about insufficient transplant organs and whether death on the waiting list was inevitable. It was held on 6 March 2008. For the first time, one of the academy’s research projects dealing with medical ethics was presented within this framework. The speaker was Dr. phil. Margret Engelhard, Dipl.-Biol., project coordinator of this research project conducted by the Europäische Akademie (duration 7/03–6/06). The authors of a survey called “Organmangel. Ist der Tod auf der Warteliste unvermeidbar?” are calling for an increase in the willingness to donate organs. The speaker was stressing that, among others, due to problems within the registration systems of hospitals far too few potential organ donors are reported. She argued that additional funding to cover the hospitals’ costs may help to increase the number of transplants. Another measure recommended by the survey to increase this number is to switch from the consent to the dissent solution, generally permitting the removal of organs unless otherwise stated. The lecture was followed by a vivid discussion amongst the medical doctors present.

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“Ethics of Science and Technology Assessment”

■ In the book series of the Europäische Akademie two new publications will be released until summer 2008: “Die Regulierung elektrischer Netze. Offene Fragen und Lösungsansätze” (volume 32) by U. Steger, U. Büdenbender, E. Feess and D. Nelles (project group “Societal Implications of Electrical Power Grids”). G. de Haan, G. Kamp, A. Lerch, L. Martignon, G. Müller-Christ and H. Nutzinger will publish a book on the results of the project group “Verantwortung für zukünftige Generationen. Schulische Umsetzung von Nachhaltigkeit” (volume 33, title forthcoming).

PUBLICATIONS

Carl Friedrich Gethmann

■ Editor: *Ethische Aspekte des züchterischen Umgangs mit Pflanzen*, Berlin: Berlin-Brandenburgische Akademie der Wissenschaften 2008 (Materialien der Interdisziplinären Arbeitsgruppe “Zukunftsorientierte Nutzung ländlicher Räume”, No 16), together with S. Hiekel

■ “Kann Politik vernünftig sein?”, in: Helmut Schmidt, Peter Janich, Carl Friedrich Gethmann (eds.), *Die Verantwortung des Politikers*, Fink: München 2008, pp 27–43

LECTURES

Margret Engelhard

6/3/2008

■ “Organmangel. Ist der Tod auf der Warteliste unvermeidbar?”

Working group Medical Ethics, Europäische Akademie zur Erforschung von Folgen wissenschaftlich-technischer Entwicklungen GmbH, Bad Neuenahr-Ahrweiler

Thorsten Galert

26/4/2008

■ “Mit Pillen dem Geist auf die Sprünge helfen? Zur Ethik des ‘Neuro-Enhancements’”

Conference “Verkabelter Geist. Die neuen Techniken der Hirnforschung und ihre ethische Bewertung”, Evangelische Akademie Sachsen-Anhalt e.V., 25/4–27/4/2008, Lutherstadt Wittenberg

17/4/2008

■ “Neuroenhancement”

Radio interview, uniRadio 97.2 Berlin-Brandenburg, “Campus live!”, 7.30–7.40 pm

Carl Friedrich Gethmann

18/4/2008

■ “Globaler Wandel. Ethische und wissenschaftstheoretische Aspekte”

Workshop of the interdisciplinary working group “Globaler Wandel – Regionale Entwicklung”, Berlin-Brandenburgische Akademie der Wissenschaften, Berlin

18/3/2008

■ “Die ‘praktische’ Aufgabe der Wissenschaftsphilosophie”

Conference “Was ist Wissenschaft?“, Bonn

Kristin Hagen

10/4/2008

■ “Transgene Tiere – Anwendungen und ethische Aspekte”

Guest Lecture, Veterinärmedizinische Universität Wien, “Tierschutzethik und Mensch-Tier Beziehung”

PERSONALITIES



■ PROFESSOR DR.-ING. JOHANN-DIETRICH WÖRNER was born in Kassel in 1954. He is chairman of the executive board of the Deutsches Zentrum für Luft- und Raumfahrt e.V. (German Aerospace Center) since March 2007.

After studying civil engineering at the Technische Universität Berlin and the Technische Universität Darmstadt and his graduation in 1985, Wörner was employed at the engineering office of König und Heunisch until 1990. In 1982, he took a two year leave of absence to study earthquake safety in Japan. In 1990 he returned to the TU Darmstadt where he was made head of the testing and research institute. Before being elected president of the TU Darmstadt in 1995, he held the posts of technical director at the institute of glass construction, and dean of the civil engineering faculty.

Wörner was honoured with a series of prizes and awards such as the prize of the “Organisation of Friends” of the TU Darmstadt for “outstanding scientific performance”. He was also appointed member of the Berlin-Brandenburgische Akademie der Wissenschaften and is the official representative of the technical sciences section of the Deutsche Akademie der Naturforscher Leopoldina. Moreover, he has received honorary doctorates from several universities.

Wörner is also a member of various national and international supervisory boards, advisory councils, and committees. In June 2007, he was elected deputy chairman of the council of the European Space Agency.

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Professor Dr.-Ing. Johann-Dietrich Wörner, chairman of the executive board of the German Aerospace Center, is on the Managing Committee of the Europäische Akademie GmbH.

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