

# Biomedical Research in Germany: The Role of Ethics Committee and State Medical Association

Jürgen Hoffart, MD, Arndt Teichmann, JD, and Ignaz Wessler, MD

**B**iomedical research with human volunteers, human tissue, or identifiable human data must follow ethical, legal, and regulatory standards. In Germany, biomedical research is regulated by federal and state laws as well as by the Code of Deontology (the professional code, *vide infra*). Ethics committees (institutional review boards) have been established in Germany since 1973 to safeguard the well-being and rights of human subjects involved in biomedical research. According to the Code of Deontology, investigators are obliged to seek the advice/vote of their local ethics committee before starting biomedical research. The Code of Deontology does not state that approval by the ethics committee is required, but in practice it is interpreted as requiring a positive vote before the study can begin. Under German federal law, clinical trials with drugs or medical devices must have a favorable opinion (i.e., approval) of the ethics committee before the trial starts. Thus, German physicians engaged in research must adhere both to the Code of Deontology, which governs their activities as physician investigators, and federal and state laws that govern the conduct of clinical trials with drugs or medical devices in Germany.

Germany consists of 16 federal states (Bundesländer). By law every state has a state medical association (Landesärztekammer), acting as an organization under public law; the largest state has 2 such associations. The Federal Medical Association (Bundesärztekammer) is the umbrella institution of all 17 state medical associations but does not act as an organization under public law. Among other responsibilities, the Federal Medical Association works to provide consistency among the 17 state medical associations. For example, basic principles describing how to act as a physician are outlined in the Code of Deontology. The Bundesärztekammer has harmonized the Code of Deontology among the different state medical associations and released a general example (Table 1, Ref. 1). Every state medical association has enacted this code with minor

modifications. It is only when the Code of Deontology is enacted by the state medical association that it becomes binding law (Table 1, Ref. 2).

Every physician is required to be a member of the respective state medical association in which he or she is working. All physicians are obliged to follow the Code of Deontology (Table 1, Ref. 2), which starts with the vow, "When I become a member of the medical profession I vow that I will act in favor of humanity. I will act as a physician with respect to conscientiousness and dignity."

Article 15 of the Code of Deontology outlines some ethical principles of medical research. Section 1 states that physicians must submit a research proposal for all studies involving human subjects or human tissues to their respective ethics committee and seek their advice/votes before starting the project. Section 3 states that institutional affiliations and interactions between the physician/investigator and the sponsor should be declared when the results are published. Section 4 states that the physicians should abide by the ethical principles for medical research involving human subjects as outlined in the Declaration of Helsinki established by the World Medical Association (Table 1, Ref. 3).

In addition to the Code of Deontology there exist several Federal Laws and Regulations that address research with drugs (Table 1, Ref. 4), medical devices (Table 1, Ref. 5), and radiation exposure in medical research (Table 1, Ref. 6). Through these laws the Federal government defines the role of the ethics committee for the latter clinical trials. For example, the Ordinance for Good Clinical Practice (Table 1, Ref. 7) defines the complete material submitted by the sponsor to the ethics committee as well as the procedure for the committee performing the ethics review.

The federal medicinal and medical device laws mandate that

1. Only ethics committees established by the state law are authorized to review and approve such trials. Unlike the situation in the United States, there are no private ethics committees in Germany authorized to approve such trials.
2. Favorable opinion (corresponding to "IRB approval") of the clinical trial by the responsible ethics committee is required in addition to the approval of the appropriate national authority: human studies with drugs and devices must be approved by the Federal Institute for Drugs and Medical Devices, called the *Bundesinstitut für Arzneimittel und Medizinprodukte*

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From the Landesärztekammer Rheinland-Pfalz, Mainz, Germany.

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Address correspondence to Ignaz Wessler, MD, Landesärztekammer Rheinland-Pfalz, Deuschhausplatz 3, D-55116, Mainz, Germany. Address e-mail to Wessler@laek-rlp.de.

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**Table 1. Web Sites**

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(Table 1, Ref. 8); human studies on vaccines, antibodies, allergens, and tissue preparations must be approved by the Paul Ehrlich Institute (Table 1, Ref. 9).

In clinical drug trials all stakeholders (sponsor, investigator, ethics committee, the appropriate national authority) are expected to be knowledgeable of the applicable regulations and follow the required procedures (e.g., German medicinal law [Table 1, Ref. 4], Ordinance for Good Clinical Practice [Table 1, Ref. 7]). Investigators acting as sponsor (i.e., “investigator-initiated trials”) must seek approval from both the appropriate national authority (either the Federal Institute for Drugs and Medical Devices or the Paul Ehrlich Institute) and the responsible ethics committee before starting the clinical trial. In multicenter clinical drug trials a single opinion for Germany is provided by the ethics committee responsible for the coordinating investigator, with guidance from the local ethics committees responsible for the individual trial sites. The ethics committee reviews the protocol, the patient written information sheet (corresponding to the written informed consent), the suitability of the investigator and the supporting staff, and the competence and experience of the trial site. The conduct of a drug trial is subject to audit by the appropriate national authority and the state government via inspection of the trial sites. In addition the sponsor files an annual safety report with the appropriate national authority and the ethics committee, and is required to report any serious unexpected adverse reactions within 7 or 15 days. Also in the case of basic research projects not regulated by federal laws, investigators are obliged to inform the ethics committee of serious adverse events immediately, as is outlined in the vote itself. Ethics committees do not control the research activities of physicians directly, do not police the

conduct of research, and do not have the authority to inspect trial sites or perform an investigation, unless authorized by the executive administration of the respective hospital.

Germany has 54 ethics committees, consisting of 17 ethics committees affiliated with state medical associations, 34 with universities or university hospitals, and 3 with their respective state governments. These ethics committees are authorized by state law. Most are organized in the “Permanent Working Group of Medical Research Ethics Committees,” which was established in 1983 (Table 1, Ref. 10). In most states, ethics committees are affiliated with universities or university hospitals (responsible for the physicians working at that university hospital) and, in addition, with the state medical associations or state governments (see above). The state of Rheinland-Pfalz (as with 2 other states, Hamburg and Saarland) has only 1 ethics committee, which is responsible for all physicians working in Rheinland-Pfalz, regardless of whether they are working at a university, at a local hospital, in industry, in public organizations, or as part of a physician practice.

In 1980 the State Medical Association of Rheinland-Pfalz (Landesärztekammer Rheinland-Pfalz, mercifully abbreviated as LÄK-RLP for the balance of this report) established its ethics committee as a multidisciplinary committee affiliated with LÄK-RLP. In recent years the ethics committee of LÄK-RLP has reviewed roughly 500 research applications each year. About 70% of the applications are for clinical trials on drugs and medical devices. The remaining 30% of applications are for basic biomedical research with volunteers (for example, to evaluate new pathophysiological hypotheses, test procedures, or new normative values) or human tissue (ex vivo) or for studies using identifiable human data (e.g., epidemiological projects). Physicians involved in basic science studies must follow the Code of Deontology as explained in the first paragraph in addition to the Data Protection Act.

Several academic hospitals are located in Rheinland-Pfalz, for example, Klinikum Ludwigshafen, a hospital in the city of Ludwigshafen. Every physician working at this hospital (and elsewhere in Rheinland-Pfalz) is obliged to seek advice/votes of the Ethics Committee of LÄK-RLP for all research projects. The hospital in Ludwigshafen is a tertiary care facility, similar to many university hospitals. It is an academic teaching hospital of the Medical Center of the Johannes Gutenberg—University Mainz. Most hospitals affiliated with universities have active research programs because of their high-quality clinical facilities and large numbers of patients with complex diseases. Additionally, most of the senior consultants in such hospitals have formal academic training, qualifying as “professor,” and combine clinical research with teaching medical students. These affiliated academic hospitals contribute significantly to biomedical research in Germany.

When an allegation of research misconduct is made, the first determination is whether the allegation is premature, unjustified, or frivolous. If the allegation appears meritorious, and is brought to the attention of a public ombudsman or institution, then a formal inquiry commences. However,

committees to investigate misconduct in biomedical research become active only after the level of suspicion reaches a critical threshold.

In December 2009, Professor Joachim Boldt, at that time the Chair of the Clinic of Anaesthesiology and Intensive Care at Klinikum Ludwigshafen, published an article in *Anesthesia & Analgesia* describing the results of a clinical trial.<sup>1</sup> Dr. Shafer, Editor-in-Chief of *Anesthesia & Analgesia*, sent a letter of concern to LÄK-RLP in May 2010 after the results were questioned by readers. Dr. Shafer directed his inquiry to the president and therewith to the executive board of the LÄK-RLP. LÄK-RLP is authorized to investigate whether a physician has followed the Code of Deontology or respective laws. Such investigations are not done by the ethics committee, but by a separate group at LÄK-RLP. A violation of good scientific practice in a clinical trial represents a violation of the Code of Deontology, and it is under this authority that LÄK-RLP conducted its investigation of Professor Boldt. During the investigation it became clear that Professor Boldt, the responsible author, did not follow the Code of Deontology. The results of this investigation have been published in the retraction note.<sup>2</sup> Early in November 2010, the respective department of the state government of Rheinland-Pfalz was informed of the outcome of the investigation. The state government then referred the matter to the Office of the Public Prosecutor. On November 26, the administration of Klinikum Ludwigshafen and Professor Boldt agreed that his practice at the Klinikum Ludwigshafen be terminated.

Meanwhile, 2 investigation committees have been established, a local committee at the hospital and a committee of the LÄK-RLP. The committees will determine whether recent articles published by Professor Boldt and his coauthors have adhered to the regulations outlined in federal laws and in the Code of Deontology. They will also determine whether the studies followed regulations regarding Safeguarding Good Scientific Practice (Table 1, Ref. 11). These requirements include storage of original data for all published research for 10 years. This process will take a long time, but will hopefully answer the question of

whether original data are available to support the results published by Professor Boldt. The committees will also determine the role of the coauthors in any misconduct. As is noted by Dr. Shafer in this issue of *Anesthesia & Analgesia*, these events have cast a shadow of doubt over a large body of work. It will take considerable time and effort to address these concerns and provide academic transparency.<sup>3</sup>

In Germany the Code of Deontology is taken very seriously. A physician who is found by the State Medical Association to have broken the code may be fined up to 100,000€. The Office of the Public Prosecutor is involved if the physician is suspected of breaking federal laws. Violation of federal laws is a criminal offense, and penalties can include loss of license to practice medicine.

Every violation of the principles of ethical research is one case too many. Each violation lowers the confidence of patients looking for the best care, and damages trust in the scientific community. Within a hospital, physicians and the nursing staff should be aware of the possibility of research misconduct, and should be encouraged to contact the ombudsman or institution as soon as possible if they become suspicious; it can also be helpful to contact the State Medical Association concerned. In addition, medical journals should require a copy of the approval by the responsible ethics committee with every manuscript submission.

All countries have policies and procedures to ensure the ethical conduct of biomedical research. As is noted by Professor Förstermann in his editorial in this issue of *Anesthesia & Analgesia*,<sup>4</sup> there are lessons to be learned from this experience. Government, hospitals, clinicians, and journals should look to these lessons so that this type of misconduct cannot be repeated. ■■

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# Ein Tsunami der besonderen Art

## Gasteditorial von Prof. Dr. Eike Martin



Prof. Dr. Eike O. Martin ist Direktor der Klinik für Anästhesiologie des Universitätsklinikums Heidelberg. Er leitet die vom Klinikum Ludwigshafen eingesetzte Untersuchungskommission zu den Studien von Prof. Dr. Joachim Boldt.

Es gibt Naturkatastrophen von ungeheurem Ausmaß: das Erdbeben in China, die Überschwemmungen im Pakistan und Australien, der Monsterzyklon in Australien und der Blizzard in den USA. Jetzt hat eine ganz andere Form der Katastrophe unser Fach in Deutschland massiv getroffen: Einen bis dato national und international ausgewiesenen Kollegen und eine anerkannte Autorität auf dem Gebiet der Volumentherapie. Er hat mehr als 300 Manuskripte, mehrere Bücher und viele Buchartikel über Volumentherapie publiziert – allein 41 Manuskripte in *Anesthesia & Analgesia* einschl. 7 Veröffentlichungen in den Jahren 2008 und 2009. Seit 1984 wurden auch in der *AINS* 27 Originalarbeiten von Prof. Dr. Joachim Boldt veröffentlicht.

Zunächst wurde durch den Herausgeber der Zeitschrift *Anesthesia & Analgesia* eine Publikation zurückgenommen (*Anesth Analg* 2009; 109: 1752–1762). Im Rahmen der sich sehr lange hinziehenden Recherchen, Kommunikationen und Diskussionen, nach Etablierung einer Untersuchungskommission der Landesärztekammer Rheinland-Pfalz, einer weiteren unabhängig eingesetzten Untersuchungskommission durch das Klinikum Ludwigshafen und einer Kommission der Gießener Universität, wurde das Ausmaß der zum überwiegenden Teil nicht eingehaltenen Regularien bei AMG-Studien (wie Ethikvotum, schriftliche Zustimmung der Patienten, Randomisierungspläne, Originaldaten und deren Zuordnung, Co-Autorenunterschriften etc.) eklatant.

Anfang Februar 2011 gab die Landesärztekammer Rheinland-Pfalz öffentlich bekannt, dass von 75 Studien nach dem AMG 68 Publikationen kein Votum der Ethikkommission hatten und von 30 Studien mit klinischer Fragestellung 22 Publikationen über kein Votum verfügten. 11 Herausgeber internationaler Publikationsorgane haben sich geeinigt, dass Publikationen ohne Ethikvotum zurückgenommen werden müssen (Editors-in-Chief Statement Regarding IRB Approval of Clinical Trials by Joachim Boldt. *Anesthesiol Intensivmed Notfallmed Schmerzther* 2011; 46: xxx-xxx). 90 Publikationen von Boldt sind vermutlich zum Zeitpunkt dieses Editorials zurückgezogen. Damit verbunden wird sich eine Reihe von Konsequenzen für Co-Autoren und Doktoranden ergeben – mit zum Teil erheblichen Folgen. Ganz zu

schweigen von dem schädigenden Ruf für unser Fach, dem Ansehen bei den uns anvertrauten Patienten und vor allem in der Science Community wird dieses Ausmaß von wissenschaftlichem Fehlverhalten schweren Schaden zufügen. Die Nichteinhaltung der formellen Vorschriften bei AMG-Studien und das inkorrekte Verhalten bei den klinischen Studien am Patienten ist die eine Seite – was schon schlimm genug ist. Die andere – aus meiner Sicht noch viel schlimmere Seite – ist die Frage nach den inhaltlichen Aussagen der betroffenen Publikationen. Es wird es noch lange dauern bis alle Unterlagen und Dokumente hinsichtlich Richtigkeit bzw. Manipulation überprüft sind, um festzustellen, ob die publizierten Zahlen, Abbildungen und v. a. Schlussfolgerungen korrekt bzw. falsch sind. Die bisherige Überprüfungen von 4 Publikationen, die sehr mühsam und zeitaufwendig war, lässt vermuten, dass die Ergebnisse nicht korrekt und vermutlich manipuliert sind.

Die Zurücknahme der Publikation in *Anesthesia & Analgesia* war zunächst eine kleine Welle – um im Bild des Tsunami zu bleiben – inzwischen wurde daraus jedoch eine riesige Welle, und wir wissen nicht, wie viele Kollegen noch davon mitgerissen werden. Inwieweit sie schuldig oder unschuldig sind, wird die Zukunft zeigen. Allerdings sind Co-Autoren auch mitverantwortlich für das, was publiziert wird. Bei einer Mitautorenschaft genügt es nicht, sich darüber zu freuen, erwähnt zu werden, ohne aktiv beteiligt gewesen zu sein. Als Folge dieses wissenschaftlichen Fehlverhaltens müssen wir in Zukunft noch mehr auf die Vorschriften achten.

Was die Beschädigung unseres Faches im Ansehen in der nationalen und internationalen Wissenschaftslandschaft betrifft, ist schwer abzuschätzen; sie wird jedoch lange anhalten. Die entscheidende Frage, die sich viele Kollegen stellen: Warum handelt ein Kollege so, wie er gehandelt hat? Eine plausible Antwort darauf gibt es nicht.

In Abänderung eines bekannten Spruches muss das Motto unserer Forschungsaktivitäten lauten: „It's nice to be important – but it's more important to work scientifically correct.“

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### Organschaften

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Medline, Embase, Scopus  
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# Research Oversight in Germany: Safeguards and Shortcomings

Ulrich Förstermann, MD, PhD

The recent example of research fraud leading to the retraction of a publication in *Anesthesia & Analgesia* by Professor Boldt and colleagues from Klinikum Ludwigshafen, in Ludwigshafen, Germany,<sup>1</sup> has raised questions about the manner of research oversight in this country. There is wide agreement that biomedical research is important for the advancement of medical science, including disease prevention and improvement of life throughout the world. Additionally, successful and acclaimed research can also be a path toward increased recognition and income, and progress up the academic ladder. Some scientists contend that this intense competition among researchers is responsible for an inevitable incidence of research fraud.<sup>2</sup> As a consequence, regulations by research institutions, funding bodies, and eventually governments are needed to establish mechanisms of oversight that best guarantee the integrity of research results.

In the late 1990s, Germany was shattered by one of the worst cases of scientific fraud worldwide. The hematologists/oncologists Friedhelm Herrmann and Marion Brach, working together at the Albert Ludwigs University in Freiburg and later at the Max Delbrück Center for Molecular Medicine in Berlin, were discovered to have committed a series of forgeries and data falsifications, mainly in papers on leukemia and the role of cytokines.<sup>3,4</sup> In 1997, Germany's leading body for funding medical research, the German Research Foundation (Deutsche Forschungsgemeinschaft [DFG]), initiated an external task force. The 6-member committee incriminated at least 94 of 347 publications by Professor Herrmann, 29 of them showing clear evidence of forgery and/or data falsification. Professors Herrmann and Brach were dismissed from their university posts and forced to abandon their academic careers. In the wake of the case, the DFG established new binding guidelines for the prevention of fraud in research (i.e., "deliberate or grossly negligent falsification or fabrication of data").<sup>5</sup>

From the Office of the Vice President for Research, Johannes Gutenberg University; and Department of Pharmacology, Johannes Gutenberg University Medical Center, Mainz, Germany.

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Address correspondence to Ulrich Förstermann, MD, PhD, Department of Pharmacology, Johannes Gutenberg University Medical Center, 55101 Mainz, Germany. Address e-mail to ulrich.forstermann@uni-mainz.de.

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Also, the Federal Government and even the European Union tightened the rules governing the conduct of clinical studies. Today, Germany has very strict regulations for the conduct of clinical trials, which conform to international standards such as the Declaration of Helsinki of the World Medical Association on ethical principles for medical research involving human subjects (Table 1, Ref. 1) and the International Conference on Harmonization/Good Clinical Practice (Table 1, Ref. 2). Any physician performing a clinical trial with (novel or approved) drugs or medical devices is bound by the rules of the German Medicinal Products Act (Table 1, Ref. 3) and/or the German Medical Devices Act (Table 1, Ref. 4), the German Federal Data Protection Act (Table 1, Ref. 5), and the Professional Code of Conduct of the Bundesärztekammer (Federal Chamber of Physicians, the umbrella organization of the Landesärztekammern, State Chambers of Physicians) (Table 1, Ref. 6). The study by Boldt et al.<sup>1</sup> falls into this category.

All other clinical studies (e.g., new surgical procedures, nondrug therapies) are regulated by the German Federal Data Protection Act (Table 1, Ref. 5) and the Professional Code of Conduct of the Bundesärztekammer.

The 12th amendment of the German Medicinal Products Act in 2004 (Table 1, Ref. 3) implemented the European Union's Clinical Trials Directive 2001/20/EC<sup>6</sup> in national law in Germany. Chapter 6, sections 40 to 42a of the Medicinal Products Act, clearly regulates, among other points:

- The implementation of "good clinical practice (GCP) laid down in article 1, paragraph 3 of European Union's Clinical Trials Directive 2001/20/EC,"
- The mandatory "application for a favorable opinion from an ethics committee," and
- The obligation to file "an application for authorization of the study by the competent higher federal authority" (i.e., the Federal Institute for Drugs and Medical Devices) (Table 1, Ref. 7).

These rules apply equally to commercial drug trials and investigator-initiated drug trials.<sup>7</sup>

In the Professional Code of Conduct (Table 1, Ref. 6) of the Bundesärztekammer, the regulations applying to clinical research are listed in paragraph 15:

1. Physicians must seek advice on professional ethics and legal regulations from an ethics committee established by a faculty of medicine of a university or by a

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State Chamber of Physicians before conducting biomedical research on humans, except for purely epidemiological research. The same applies to research with vital human gametes and living embryonic tissue.

2. For the purposes of scientific research and teaching, facts and findings that are subject to medical confidentiality may only be disclosed to an extent that guarantees the anonymity of the patient, unless the patient expressly agrees to the disclosure of his/her data.
3. In publications of research results, any relationships of the physician to a contracting entity must be disclosed.
4. In research involving human subjects, physicians shall observe the ethical rules and regulations set out in the Declaration of Helsinki of the World Medical Association on ethical principles for medical research involving human subjects (Table 1, Ref. 1).

If violations of these regulations are brought to the attention of the Landesärztekammer, they have to investigate the case. However, research is not the main focus of the Landesärztekammern, and they do not have institutionalized procedures in place to look into allegations of fraud.

All German universities and university medical centers have established mechanisms to safeguard research integrity and promote good research practice and good clinical practice. All German universities and university medical

centers have institutional review boards (IRBs) or, alternatively, rely on ethical review boards (ERBs) established at their local Landesärztekammer.

No clinical drug trial or medical devices trial at a German university hospital can be started without the “favorable opinion” of an IRB/ERB. Investigators of industry-sponsored studies are subject to regular external audits and inspections of regulatory bodies that curb fraudulent activities. Drug trials require reporting of Suspected/Unexpected Serious Adverse Drug Reactions (SUSARs) within a defined time frame, and annual safety reports to the IRB/ERB and the Federal Institute for Drugs and Medicinal Products.

Many university medical centers have established professional clinical research infrastructures such as Coordinating Centers for Clinical Trials (KKS). The KKS Network was initiated by the Federal Ministry of Education and Research and provides comprehensive advice and support for planning, conducting, and evaluating clinical research projects, including quality assurance and internal audits.

All German universities have an independent ombudsman, who can be contacted confidentially by any researcher having a suspicion of, or evidence for, scientific misconduct. All German universities also have a committee for the investigation of scientific misconduct. After the Herrmann/Brach case (see above), the DFG makes any funding contingent upon the existence of those 2 bodies.

In addition, the DFG also has its own research ombudsman, which is a committee of 3 (Table 1, Ref. 8). This committee is open to *all scientists* (independent of any connection with the DFG) for advice of good scientific practice and reports of violation thereof. The committee offers help and protection for “whistleblowers,” reporting evidence of scientific misconduct. It guarantees strict confidentiality even after the conclusion of a specific case.

If allegations of scientific fraud pertaining to a DFG-funded project are brought to the attention of the DFG, their Committee of Inquiry on Allegations of Scientific Misconduct (Table 1, Ref. 9) reacts immediately and starts an investigation. These investigations are limited, however, to applicants, funding recipients, and others responsible for the use of DFG funds.

A different situation is found in teaching hospitals associated with German university medical schools. These institutions are usually community hospitals that are only loosely linked to their respective medical schools through contracts pertaining to clinical training of medical students in their last year. The Medical Center of the Johannes Gutenberg University (Mainz, Germany), for example, has 27 affiliated teaching hospitals in the state of Rhineland-Palatinate and other German states. Some of these hospitals are almost the size of a university medical center and the department heads often have adjunct university appointments. The appointment is not necessarily with the university signing the teaching contract with the hospital. Professor Boldt,<sup>1</sup> for example, has his adjunct appointment with the Justus Liebig University, Giessen, although Klinikum Ludwigshafen is a teaching hospital of the Johannes Gutenberg University, Mainz.

Clinical research is not the main focus of teaching hospitals. They tend to have limited research infrastructure

and no (or very limited) internal research budgets. DFG funding is also rare in these institutions; in fact, without an ombudsman and an institutional committee for the investigation of scientific misconduct, a hospital does not qualify for DFG support. Physicians performing clinical studies in these environments do so with little research oversight. This is the clinical environment of the recent Boldt case.<sup>1</sup> Most of these hospitals have no IRB within their organization (and the respective Landesärztekammer ERB can be “far away”). Finally, when there is evidence for scientific misconduct, the hospital itself usually has very little experience with conducting investigative procedures for handling the case. For outsiders, e.g., a journal editor, it can be difficult to find the right contact person and to determine which organization has the authority to look into the allegations.

That was the case at Klinikum Ludwigshafen, the institution at which Professor Boldt did his research. Initially, it was the Landesärztekammer Rhineland-Palatinate that started its investigation at the request of the Editor-in-chief of *Anesthesia & Analgesia*. When their committee obtained the first pieces of *evidence* for scientific misconduct, the Hospital Administration turned to the Research Ombudsman of the DFG (see above) and formed an ad hoc review committee, which recently presented its report.

It is important to repeat, however, that any physician performing clinical drug trials in a nonuniversity environment in Germany obviously has to abide by the rules of the Medicinal Products Act (Table 1, Ref. 3), the Federal Data Protection Act (Table 1, Ref. 5), and the Professional Code of Conduct of the Bundesärztekammer (Table 1, Ref. 6). Failure to do so is a criminal offense.

So what are lessons to be learned from the Boldt case? First, it is imperative that nonuniversity hospitals engaging in clinical research establish written standards of scientific conduct, truthfulness, objectivity, and integrity. This includes simple measures such as quality assurance and quality control instruments, e.g., standard operating procedures, independent monitoring, proof of patient existence, verification of source data, and the obligation to archive case record forms, not just secondary products of research such as tables or computer graphs. Second, the hospital administration must (and can easily) ensure that no clinical study is conducted without IRB/ERB approval. Third, the institution must create and guarantee an open atmosphere in which all potential authors of a paper, independent of their rank in the organization, can ask for and have access to original data. Fourth, the institution must make it clear that authorship on a paper to which one has not contributed in any manner is unethical. In this case, the retracted article<sup>1</sup> has 5 coauthors and their involvement in the study is largely unclear at this time. Finally, in cases of alleged fraud, the hospital itself must have (or be able to quickly set

up) an institutional committee for the investigation of scientific misconduct that has the authority to assess the validity of the allegations.

Institutions also need to increase their surveillance. That can include formal external auditing procedures, active mentorship for younger researchers, or the less formal approach of encouraging researchers to take seriously their responsibility to report misconduct. In this case, the installation of an ombudsman is very helpful. This must be a distinguished individual who is independent of all department heads and the central hospital administration.

Scientific journals can also help to reduce the incidence of fraud. Useful approaches that have been adopted by some journals are short declarations from each individual author that they have seen the original study data, and what their individual contribution to the paper was. In this respect, *Anesthesia & Analgesia* has made much progress in capturing the appropriate information from its authors (Table 1, Ref. 10). Additional helpful procedures are that all coauthors should be included in all e-mail correspondence between the lead author and the journal, should receive electronic distribution of all versions of a submitted manuscript, and should be urged to contact the editorial office if they disagree with anything in the manuscript. Finally, it may be useful for a journal to ask for a copy of the IRB/ERB approval for each clinical study. ■■

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