

## Review Article

# Agreements in clinical studies at German university clinics

Raees Ahmed\*, Thomas Voigt, Matthias Siegert, Christoph Gerst

Legal Department of Universitaetsmedizin Goettingen, Germany

**Received:** 05 March 2020

**Accepted:** 21 March 2020

### \*Correspondence:

Dr. Raees Ahmed,

E-mail: [raees.ahmed@med.uni-goettingen.de](mailto:raees.ahmed@med.uni-goettingen.de)

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### ABSTRACT

The article aims to give an overview of the contractual situation in Germany, which arise in clinical studies. The goal of the authors is to show any potential sponsor of a clinical study, who is interested in cooperation with German partners such as universities or other study sites, what kind of agreements may be expected and to give a brief overview about necessary themes included within the contractual negotiations. The different contractual settings are considered from the perspective each different type of agreement. The authors have chosen amongst all possible types the ones which are the most common in a clinical study, such as CDA, MTA, grant agreement, clinical study agreement, CRO-service agreement etc. The authors show the complexity of the contractual setting of a clinical study and emphasize to pay close attention to the contractual settings. Even though the content of the agreement is mostly universal in nature, in some cases, Germany has some very special rules (e.g. regarding employees' inventions), which any potential sponsor should keep in mind.

**Keywords:** Clinical trials, Clinical studies, Agreement, CDA, MTA, Grant agreement, Clinical study agreement, Services agreement

### INTRODUCTION

In health care system clinical research plays a leading role in the research and development of innovative drugs, medical products, advanced therapy and therapy optimizations and includes all studies that are conducted on the human subjects in order to obtain scientific knowledge. Clinical research (in the field of medicinal product, medical devices and treatment methods) can be divided into two areas: interventional and non-interventional studies, while in the case of non-interventional studies (NIS), only observation is carried out as part of conventional medical treatment ("usual practice") and are referred to as clinical studies. Epidemiological studies are also referred to as clinical studies. Clinical research with medicinal product that are not yet approved or have not yet been approved for the specific indications, and medical devices that are not yet on the market, occupy a special place in clinical research and are conducted as interventional studies.

Interventional studies with medicinal product and/or medical devices are commonly referred to as "clinical trials" in relevant laws and regulations. Clinical studies and clinical trials will hereinafter be referred to as "clinical studies".

The rules for conducting clinical studies of medicinal product and medical devices on humans are within legal and ethical tensions: on the one hand, this includes the freedom of research of sponsors and investigators, and then the constitutional obligation of the state to protect the life and physical integrity of consumers of medicinal product and medical devices that require conducting clinical studies of new medicinal product or medical devices, and on the other hand, the obligation of the state to protect the life and physical safety of subjects.<sup>1</sup>

The federal republic of Germany ranks first as the location for conducting clinical studies in European union and the third place after the USA and UK.<sup>2</sup>

Currently, 60 to 70 clinical studies are usually required before a medicinal product can be classified as effective and harmless in accordance with the regulatory authority.<sup>3</sup> Before starting a clinical study with a set of study participants, it is necessary to obtain not only the appropriate regulatory approval of the authorities and the ethics committee (and how in Germany to inform local health authorities), there are also agreements between various contract partners, for example, such as a sponsor (pharmaceutical companies/non-commercial researches), consultants, contract research organizations, clinical monitor, clinics/medical practices (study site), researcher (investigator), logistics, laboratories, biobanks, pharmacies, contract manufacturers. In accordance with local special rules, the agreements includes at least the features of conducting a clinical study, responsibilities for completing tasks, sharing costs and compensations, providing investigational product, rights for intellectual property and inventions, publishing, privacy and data protection, anti-corruption provisions, term, termination conditions, liability, applicable law and place of jurisdiction, as well as the language of agreements for multilingualism agreements.<sup>4-6</sup> This basic structure can be transferred to other research agreements.

As drug development is currently underway in parallel and around the world, the development of these agreements is becoming increasingly complex. At the same time, those involved must take into account the extraordinary graduated regulation in the framework of public law, civil law, criminal law and professional law, which in the case of multicenter studies often varies from country to country.

This article provides an overview of agreements that are considered for conducting a clinical study at the university in Germany and is based on authors' experiences.

## **INFRASTRUCTURE OF UNIVERSITY CLINIC IN GERMANY**

In Germany there are currently 34 university clinics where clinical studies are carried out. As a rule, a university clinic is a hospital with so-called maximum care, i.e. they treat all clinical pictures. In addition, most university hospitals are affiliated with academic teaching hospitals. In addition, university clinics have a very good infrastructure and are highly suitable for carrying out clinical studies thanks to the high level of scientific expertise of their staff. Since most key opinion leaders teach and research at a university clinic, commercial sponsors can hardly avoid the involvement of university clinics as study sites for clinical studies.

The clinical studies can also be roughly distinguished by the type of sponsorship. Sponsor is either a commercial company, mostly a pharmaceutical company or medical device manufacturer, or the university clinics themselves take on the sponsorship if their scientists want to carry

out a clinical study themselves. The latter is often understood as an investigator-initiated-trial/study (IIT/IIS).<sup>7</sup> This is mainly because the actual IIT, i.e. those in which the physician/scientist actually takes on the role of sponsor, is become extremely rare.

If a clinical study is initiated, managed and financed by an industrial company, this industrial company takes on the role of the sponsor. The university clinic will then only be involved in this clinical study as a study site. The university clinic treats study participants according to the sponsor's specifications in accordance with a study protocol specified by the sponsor and thereby generates study data for the sponsor. This type of research is a service of the university clinic and is called contract research. If, on the other hand, the university clinic carries out a clinical study, which results from the ideas of the scientists themselves, and the university clinic takes on the role of the sponsor, it carries out the study on its own responsibility.

## **LEGAL BASIS**

With regard to the initiation and implementation of clinical studies in Germany, the laws, guidelines and recommendations applicable in Germany must be complied with. However, as Germany is organized as a federal state, the relevant regulations of the individual federal states in which the clinical trial is to be carried out are also important. In addition, due to the supranational nature of the European union, EU legal regulations must also be observed. This results in a potpourri of regulations, the main legal sources being the following: the German law on medicinal products, GCP-V (ordinance on the application of good clinical practice when conducting clinical trials with medical products for human use), the medical devices act, ordinance on clinical trials of medical devices, the model professional ordinance for doctors in their respective country-specific versions, the declaration from Helsinki, directive 2001/20/EC (in future replaced by regulation (EU) 536/2014), clinical trials regulation, ordinance (EU) 2017/745, currently directives 90/385/EEC, 93/42/EEC 98/79/EG (in the future replaced by: medical device regulation - MDR, regulation (EU) 2017/746, in-vitro diagnostic regulation - IVDR, EU-guidances), the ICH good clinical practices guideline, ordinance (EU) 2016/679 general data protection regulation (GDPR) and the federal data protection act, the notices of the responsible ethics committee and the federal authorities such as the Paul Ehrlich institute (PEI) or the federal institute for drugs and medical devices with regard to the data from clinical trials and the fact that all results from the clinical trials must be published in accordance with section 42b of the German law on medicinal products. other legal sources are: transfusion act, transplantation act, genetic engineering act, embryo protection act, radiation protection ordinance.

## **TYPES OF AGREEMENTS IN CLINICAL STUDIES**

In Germany, agreements are divided into main types according to the relevant civil code (BGB), for which specific regulations then apply. Agreements in clinical studies are mostly mixed forms of service and work agreements, but there are also contents of loan, transport or certain partnership agreements. It depends primarily on the performance owed in the individual case. As an example, a success of the service is owed by the creator in the case of a work agreement, whereas in the services agreements only the provision of a service is agreed, but a certain result is not guaranteed. A services agreement would be the obligation to prepare a final report, whereas the treatment of patients can only be a services agreement obligation, since one does not owe a certain outcome of the treatment. Against this background, the corresponding other provisions of the agreement are to be interpreted, such as how and whether it can be terminated, whether there are reduction rights for bad work and how liability is structured.

### **NON-DISCLOSURE AGREEMENT**

After contacting the sponsor and the study site, but before exchanging study-specific information or starting the feasibility process, it is advisable to first negotiate and sign a so-called non-disclosure agreement (NDA) or confidential disclosure agreement (CDA). The purpose of the CDA is on the one hand to protect business secrets, such as the protocols contractually, and on the other hand to sensitize the people involved to the sensitive nature of the information to be exchanged, because confidential information is exchanged already in the preliminary phase of the study planning, which is not to third should get.

### **LETTER OF INTENT**

It is advisable to conclude a letter of intent prior to planning the clinical study, if a type of cooperation or appropriate research funding is to take place between the participants. A letter of intent expresses the desire of both sides to work together in a corresponding research project and in the future to conclude an agreement on the conditions stated in the letter. Declarations of intent are also referred to as letter of intent (LoI) or memorandum of understanding (MoU). Depending on the design, these are sometimes more, sometimes less binding. The range extends from a legally non-binding declaration of wanting to research together to hard agreements that already regulate certain points for the cooperation or research support agreement to be concluded later.

The content of such a document depends mostly on the individual case. A letter of intent - as is typically the case - signed at an early stage of the process usually (in addition to procedural questions) only regulates the essential cornerstones of the planned business

relationship, i.e. exchange of information, investment in human and financial resources with regard to the planned business. It also happens that a letter of intent is only signed in the final phase of the negotiations. In such cases, the negotiation result is often recorded by adding the current status of the draft agreement or e.g. Preparatory activities separated from the main agreement and bindingly regulated in the preliminary agreement in order to create legal and planning security for everyone for this phase.

### **MATERIAL TRANSFER AGREEMENT**

Material transfer agreements (MTA) are intended for the purposes of research and development to regulate the exchange of test material in the form of biological or chemical compounds (e.g. test mice, plasmids, tissue samples) between two parties. One party makes the investigation material available to the other party either for its own purposes or for scientific cooperation. MTAs can be concluded separately or can also be included in a comprehensive research agreement such as a clinical study agreement or in a cooperation agreement. If only a separate MTA is used without a comprehensive research agreement, it is advisable to conclude an NDA in advance. In clinical studies, the study participants can take samples that are examined by a central laboratory. These samples can also be stored in a biobank for further or other research. For this purpose, an MTA is agreed between the parties.

### **RESEARCH AND DEVELOPMENT AGREEMENT**

Research and development agreements tend to be client-friendly. The contractor undertakes to carry out certain research and development work for the client and to transfer the resulting (intellectual) property, in particular study data and patentable inventions, exclusively to the client. The financial resources are borne exclusively by the client. The contractor sometimes owes the achievement of certain development goals in terms of success, on the other hand only the performance of certain research services in terms of efforts. In this way, the client secures the work results, especially the rights to inventions for commercial utilization. This type of collaboration is called contract research and opens the way to the development and further development of pharmaceuticals and medical devices or serves to improve therapies.

### **COOPERATION AGREEMENT**

A cooperation agreement primarily deals with the joint implementation of the study project between equal partners. The work involved is divided among the partners according to their particular specialty. They perform their services not for a specific client, but for the cause. At the same time, they use their own know how and their own intellectual properties-rights and usually give the partner appropriate usage rights for the purpose

of project implementation with the help of mutual licenses. Community rights to the emerging intellectual property are established thereby. In this context, regulations regarding the utilization during and after the expiry of the agreement term are also included in the agreement at reasonable and customary market conditions.

Public funding is very often granted to the individual partners, which leads to special features of the agreement. In Germany, funding is often provided through state funding programs from individual federal states, the federal government or the EU. The cooperation partners then have a double duty. On the one hand, they are obliged to the cooperation partners according to the cooperation agreement, on the other hand they are subject to the provisions of the donation notices issued to them as administrative acts, the instructions and, above all, ancillary provisions regarding the receipt of the grant, which must be observed. But also, in the case of private funding agencies (foundations, associations, pharmaceutical companies) who do not grant funding through an act of sovereignty (a decision), but on the basis of a corresponding grant agreement, this hybrid status exists. The regulations of the cooperation partners among themselves must therefore always reflect the corresponding requirements of the sponsor. The requirements usually include specific requirements for the use of the results, publications and reports. Many sponsors even oblige the particular beneficiary to conclude a corresponding cooperation agreement.

The main focus of the cooperation agreement is the definition of the subject of the cooperation and the individual contributions of the partners. These contributions are regularly summarized in annexes that should at least contain the project description. It should be noted that due to the cooperation for a specific purpose (namely the implementation of the project) the cooperation by law is to be regarded as a company under company law (more precisely: a company under civil law, a kind of German "Ltd."). Even without a corresponding written agreement, this company is created purely by implicit action, i.e. by starting the joint activity. This legal consequence cannot be completely prevented by the parties to an agreement, we say that the legal valuation is not available. However, the corresponding consequences, such as shared responsibility, the need for joint decision-making, liability of each partner not only for themselves, but for the actions of others, can be reduced by appropriate regulations. Against this background, regulations on the structure of the company are particularly important, as well as the assignment of the industrial property rights and copyrights that arise during the execution of the agreement and, along with this, a clear definition to delimit the study and development work to be provided in each case.

Special features arise when the cooperation wants to conduct clinical studies with medicinal products or

medical devices. The applicable regulations provide (currently) the individual responsibility of sponsor, which is to be understood as responsibility in criminal, civil, and regular terms. This concept therefore stands in the way of a collaborative research approach. The agreement must therefore be cautious proceeded.

## **GRANT AGREEMENT OF A NON-COMMERCIAL CLINICAL STUDY**

A grant agreement is usually understood as supporting a research project with financial or material resources. Such agreements have the following background: In general, it is assumed that clinical studies are mainly initiated, financed and carried out primarily by pharmaceutical companies with the aim of the data obtained for commercial use, i.e. for drug approval or conformity assessment of the medical device for market approval. Nonetheless, non-commercial research is also becoming increasingly important: university clinics and research institutes, as well as professional societies, not only generate scientific ideas for the clinical studies of medicinal products and medical devices, but also increasingly create structural prerequisites for proper implementation these tasks. Typically, these projects cannot be financed solely by the initiating clinics and research institutions. The missing amounts or even the using investigational medicinal products, investigational substances, investigational medical device products or diagnostic tools must be raised by so-called third-party funds from the institution. The funding in the form of financial or material support, such as the provision of material resources or investigational medical products/medical devices come not only from the pharmaceutical industry, but increasingly also from public institutions or foundations. Such support is particularly important for pharmaceutical companies. In the event of a positive result, the data obtained from the study can be used for market approval/expansion, since the repeated conduction of the clinical study for market approval is not allowed for ethical reasons. The Grant Agreement then regulates, among other things, the amount of funding, the responsibilities of the parties and property rights to the (raw) data generated, as well as the exchange of services. Care should be taken to ensure that the ownership rights to the data remain with the clinic/research institution and that the sponsor is only granted a simple right to use the final report, which is unlimited in terms of time and location.

## **CLINICAL TRIAL AGREEMENT/CLINICAL STUDY AGREEMENT**

In most cases, a sponsor alone, even if he is a university clinic, will not be able to generate the number of cases to get statistically reliable statements on the research question. In this situation, the sponsor has to look for other investigators or institutions that support him in the recruitment of suitable patients and treat patients according to their specifications and generate study data.

In other words, he needs additional investigators and study sites, who then work for the sponsor through contract research. Research projects and clinical studies are often supervised by medical scientists as members of the university clinics. In most university clinics it is now common practice for the university clinic and the sponsor to sign the agreement as contracting parties, with the investigator as an employee of the university clinic, also signs the agreement without becoming a contracting party. The clinical trial agreement (CTA) provides the basis for the allowance of activities in the context of carrying out clinical studies. These are created by the sponsor and signed by the clinical management. The responsible investigator signed for notice. CTAs are for all types of studies, e.g. for non-interventional studies (NIS), for studies with medicinal products and medical product and for studies on human subjects with clinical relevance, due to the slightly different research approach and the closer reference to the usual practice of physicians ("Real-Life-Setting"), NIS increasingly uses registered practice-based physicians and private hospitals.

When drafting agreements for pharmaceutical companies with investigators, members of the specialist circles and public officials, the information and recommendations in the "common position on the criminal assessment of cooperation between industry, medical facilities and their employees" must be observed. This applies regardless of the extent to which the concerned investigators are civil servants, public sector employees or employed doctors in hospitals under public or private sponsorship. With regard to the development of the agreement between investigator and sponsor, especially at university hospitals, a precise description of the subject of the agreement must be made, whereby the purpose of the clinical study should be defined in advance in a preamble to the agreement. The CTA must also be related to the attached study protocol.

The CTA should also include agreements on the number of patients in the clinical study and the provided timeframe. Ideally, a systematic process for the approval of the contractual agreements must be installed in the phase of initiating projects in cooperation with university clinic, which takes due account of the proportionality between rights, obligations and remuneration. In practice, there are often draft agreements from sponsors that are very one-sidedly advantageous in their favour.

In the case of a non-commercial study, the clinic management should expressly agree to the clinical studies being carried out by the investigator in accordance with the submitted CTA. Likewise, for example, the investigator and sponsor obligations, the remuneration issues and employment law aspects of third-party Grant Agreements with university clinics as well as the task delegation to study centers must be documented.

## **OUTSOURCING CLINICAL STUDIES TO EXTERNAL SERVICE PROVIDERS**

In the meantime, the proper conduct of the clinical study in compliance with national and international regulations has become difficult and complex process. Both pharmaceutical companies and university hospitals often do not have any special know-how or their own human or material resources and capacities to carry out clinical studies. Therefore, in the role of sponsor, they commission an external service provider. Depending on the scope and type of the provided service, these can be a contract research organization (CRO), coordination center for clinical studies (KKS), a freelancer, consultant or contract manufacturer/pharmacy. For financial and strategic reasons as well as to ensure appropriate flexibility, the implementation of a clinical study or individual aspects thereof is outsourced to external service providers. This trend is called Outsourcing and has been gaining increasing attention in the pharmaceutical industry for years. In 2008, external clinical study services had an annual volume of \$8 billion.<sup>8</sup>

### **CRO - CLINICAL SERVICES AGREEMENT**

CROs have special know-how and are sometimes specialized in certain therapeutic areas. There are currently around 1000 different CROs worldwide, including around 100 in Germany. In Germany, some CROs have joined together to form the federal association of medical contracting institutions (BVMA).<sup>9</sup> A CRO can assume the sponsor's duties and obligations in the planning, implementation, monitoring and evaluation of a clinical study. The CROs provide either individual or different services such as regulatory affairs, project management and monitoring, biometrics and data management, pharmacovigilance, laboratory tests or logistical tasks. The CRO also often acts as a "legal representative" (a regulatory requirement for conducting clinical studies within the EU) for a sponsor based outside the EU or the EEA.

An alternative to CROs are the KKS, which are part of a university hospital as a CRO service center and which perform similar tasks at a national level in Germany as the CROs. Most KKS are united in the so-called KKS network.<sup>10</sup> Another option at the international level is the European clinical research infrastructures network (ECRIN), which enables carrying out of the multinational studies.<sup>11</sup>

The extent of the tasks undertaken by a CRO in consultation with the sponsor must be contractually specified in detail. In order to avoid ambiguities and a possible later internal regress, it has proven itself in practice that the delimitation of responsibility is formed as a task list with a checkbox. Either the cross is placed with the sponsor or with the CRO. Despite the transfer of responsibility to a CRO, the sponsor always bears the

overall responsibility for the clinical study and thus also for the quality and credibility of the generated data. The CRO - services agreement represents a permanent obligation between the sponsor and the CRO, i.e. the parties strive to collaborate on several projects or individual orders over a longer period of time and are not interested in changing the contracting partner.

Therefore, the CRO should be carefully selected and the conditions for trusting cooperation should be set out in a framework contract. As the sponsor is also responsible for compliance with the corresponding quality criteria in the clinical study, he must in particular audit the CRO, and above all he must ensure that this audit right is contractually recognized by all of his subcontracting partners/service providers. For new individual orders or modifications to individual orders, the specific dates of the parties' performance obligations are defined in an order (Work Order), whereby the provisions of the framework contract continue to apply. In some countries outside Germany, both the sponsor and the CRO have to become contracting parties to the CTAs.

### **FREELANCER AGREEMENT**

For years it has been observed that within the frames of carrying out the clinical studies, sponsor-specific study tasks, e.g. monitoring measures for quality control and auditing measures for quality assurance are transferred to qualified freelancers. One of the main reasons for this is the financial aspect, as the cost of hiring a freelancer is lower than hiring a CRO. In addition, the total costs for the sponsor's internal employees compared to a freelancer are also significantly higher. The freelancers mainly work from their own offices or from home. Moreover, they are also more connected to the sponsor than the CROs. A temporary services agreement is concluded for the cooperation, according to which the freelancer performs his service as a monitor or auditor as an independent entrepreneur. When drafting the agreement, employees should have typical specifications from the sponsor, such as commitment to instructions or involvement in the sponsor's operational organization should be avoided in order not to slide from the employment relationship into a de facto employment relationship with all its legal consequences.

### **CONSULTING AGREEMENT**

The consulting agreement is a special form of the services agreement, which is worth considering separately here. Such an agreement is usually concluded between a pharmaceutical company and a medical facility or an employee of a medical facility or a physician and has the aim of realizing a defined task or providing a service. In return, the consultant receives appropriate remuneration based on the amount of time, recommendations, specialist training, qualifications, general reputation and level of difficulty. The typical consultant can draw on a high level of specialist

knowledge and broad experience in his field. The consultant either offers his services only on the phone or performs the service personally on site. For example, a doctor can be used as a consultant when planning clinical study for a particular therapy.

Depending on the setting, consultant committees such as data monitoring committees (DMCs), data safety monitoring board (DSMB), endpoint, and adjudication committees are established by the sponsor as part of clinical studies in accordance with the "guideline on data monitoring committee". These committees consist of an independent interdisciplinary group of experts who may review open-label tolerability and efficacy data during the duration of the study and may recommend that the study can be stopped early for safety reasons. Additional committees can be set up, such as steering committees (SCs) and clinical advisory boards. All of these committees should operate according to pre-established rules of procedure.

If the above-mentioned bodies are established, written consulting agreements must be concluded with each consultant. This is the only way to avoid disputes about the type and scope of the advisory service.

### **PHARMACY CONTRACT OR CONTRACT MANUFACTURING AGREEMENT, SUPPLY AGREEMENT**

In clinical studies, investigational medicinal products/devices as well as placebos or comparative medicinal products/devices are often used. These include medicinal products that are not approved and approved medicinal products if they are used in a clinical study in a different pharmaceutical form or for an unauthorized application (Off-Label-Use) or to receive additional information about the authorized medicinal product.

When manufacturing an investigational product, which also includes labelling, complex regulatory requirements, such as good manufacturing practice (GMP) but also to comply with national and international specific regulations. In addition to the manufacturing process, there are also individual aspects such as filling, packaging, labelling and final approval. In particular, if the corresponding sponsor is not the marketing authorization holder or the manufacturer of the medical device that is to be used in the clinical study, contractual regulations for the manufacture, delivery and use are advisable, if not even prescribed by law in certain situations (e.g. §9 AMWHV).

For time, financial, resource or capacity reasons, the following questions often arise: Does the pharmaceutical company or the university clinic, in the function of the sponsor, have the investigational medicinal product used in the clinical study manufactured, delivered, labelled or, in the case of a split range of tasks, who does what; an external special contract manufacturer or "only" a

pharmacy based locally at the study site is activated; how an investigational product manufactured outside the EU can be imported into Germany or vice versa, how can you deliver an investigational product manufactured in Germany to a study site outside the EU.

For this work performance/delivery as a whole or as individual aspects thereof, the parties conclude a contract manufacturer agreement including supply agreement. Then it also regulates, among other things, whether the sponsor provides the contract manufacturer/pharmacy with the appropriate formulation or all raw materials for the processing activity; how high the fee is, but it must be ensured that all intellectual properties rights to the recipe and the product-specific manufacturing process remain with the sponsor. As clinical studies are usually carried out in a multicenter or multinational manner and investigational medicinal product have to be made available to the participating study sites, the sponsor also faces a logistical challenge. The contract manufacturer/pharmacy also coordinates the storage, distribution, provision, delivery, transport and destruction of the investigational medicinal products according to GMP guidelines and specific conditions.

#### **PATENT PURCHASE AGREEMENT/LICENSE AGREEMENT**

If patentable inventions arise during the conduct of clinical studies, the sponsor of the study is emphatically interested in securing these inventions for their own purposes or in marketing. This is particularly true of the pharmaceutical company as a sponsor, as he has to secure the inventions for market approval. Most of the time, therefore, the CTAs already contain corresponding clauses for transferring the intellectual properties (potentially) generated by the investigator in the clinical study. However, there is a worldwide peculiarity in Germany, namely the employee inventions act. It regulates what happens when a wage earner, or an employee, makes an invention. These inventions then do not automatically belong to the employer (the study site), but the employer only has the option to be the first to acquire this invention. In addition, there are further requirements for university clinics from the respective country-specific university laws. Against this background, the final transfer of employee inventions from an employee of the university clinics (the study site) to the sponsor will only be possible through sophisticated clauses or through a separate contract. To this end, the parties could conclude a Patent Purchase Agreement, which provides for the market remuneration for the transfer of the patent. Another option would be a license agreement. This would only allow the exploitation and use of the patent, while the patent owner remains the same. When entering into a license agreement, the patent holder transfers all rights of use to the licensee.

#### **LABORATORY AND BIOBANK AGREEMENT**

Depending on the design of a clinical study, samples are taken from the study participants in the form of body fluids and tissues for laboratory diagnostics and examined. The samples are examined in compliance with the good laboratory practice (GLP) requirements and other regulations in local laboratories or in a central laboratory. For this, it is recommended for the sponsor to record the collaboration and the laboratory services in a laboratory agreement, which also regulates who is responsible for the transport of the laboratory kits and the samples.

In addition, samples for further or other research are often collected and stored in a biobank with high demands on regulations and quality. This often happens with research consortia, which can then use the samples to conduct further research beyond the initial research purpose. Biobanks enable cooperation and information exchange as well as the use of existing resources and avoidance of redundant research. There are 4 types of biobanks for researches: biobanks from university clinics, from commercial providers, from study participants and company-internal biobanks. Here, it is advisable to conclude a corresponding biobank contract with the corresponding biobank.

#### **CONCLUSION**

The implementation of clinical studies is not only a very important task from the logistic, organizational and economic points of view, but also imposes certain non-trivial requirements on legal registration and security. As has become clear from the previous overview, there are a large number of legal relationships between the various participants within a clinical study. With all commonalities as a contractual relationship, each of these legal relationships has its own special content, which must be observed in individual cases. In our opinion, there is no "one-fits-all" solution here. Above all, the attempt to simply integrate corresponding draft agreements from other legal circles into German law only leads to more difficult negotiation phases and to more frustration among the contracting parties. The article therefore intends to familiarize practitioners who want to conduct clinical studies in Germany with the conditions there. This is particularly important because the contract structure must be structured in such a way that it can be used for the duration of the project so that the partners know what they have to do and when. On the other hand, there can always be difficulties in the provision of services, so that the agreements must have appropriate mechanisms for conflict resolutions. Finally, when drafting the agreement, it must be ensured that responsibility under civil law is clearly regulated, but also that the people involved are not responsible for criminal or professional law through their work in the study. Last but not least, from our point of view an important function of the agreement drafting is to use the points

there again like a kind of checklist that one has thought about the risks dealt with there. All of this means that, in our view, the contractual regulations for research projects must be given sufficient attention. Otherwise, in the event of a conflict, the person who did not let them work carefully looked it up.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

## REFERENCES

1. Dieners/Reese, Handbuch des Pharmarechts. 1st ed. Beck Muenchen; 2010.
2. Deutschland: Weltweite Nr. 3 bei klinischen Studien der Industrie.; Available at: <https://www.vfa.de/de/arzneimittelforschung/forschungsstandort-deutschland/klinische-studien-deutschland.html>. Accessed 26 February 2020.
3. Wille M, Kleinke S. Klinische Pruefungen von Arzneimitteln an einer deutschen Hochschule: Was ist bei der Gestaltung des Pruefarztvertrages zu beachten? *Pharm R*. 2004;8:300-8.
4. Stief/Bromm, Vertragshandbuch Pharma und Life Sciences. 1st ed. C. H. Beck; 2015.
5. Weitnauer/Mennenoeh, Life Sciences Agreements in Germany. 1st ed. C. H. Beck; 2014.
6. Jung/Schuebel, Vertraege für Klinische Studien nach AMG und MPG. 1st ed. C. F. Mueller Verlag; 2011.
7. Bulicz J, Fritsch D. Pruefer-Initiierte-Studien (Nichtkommerzielle klinische Pruefungen) in Deutschland – Juristische Verantwortlichkeiten und strafrechtsrelevante Haftungsaspekte des pharmazeutischen Unternehmers. *Pharm R*, 2011;10:401-8.
8. Festel G. Outsourcing chemical synthesis in the drug discovery process. *Drug Discov Today*. 2011;16(5-6):237-43.
9. Bundesverband Medizinischer Auftragsinstitute e.V.; Available at: <https://www.bvma.de/>. Accessed 26 February 2020.
10. Koordinierungszentren für Klinische Studien. Available at: <https://www.kks-netzwerk.de/>. Accessed 26 February 2020.
11. European Clinical Research Infrastructure Network. Available at: <https://www.ecri.org/>. Accessed 26 February 2020.

**Cite this article as:** Ahmed R, Voigt T, Siegert M, Gerst C. Agreements in clinical studies at German university clinics. *Int J Clin Trials* 2020;7(2):142-9.