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The Co-Sponsor in the conduct of a Clinical Trial in Germany

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Abstract

The sponsor is highly relevant in the conduct of clinical trials, both from a financial point of view and in terms of responsibility for study management. Until now, only one sponsor was designated as the primary contact for the conduct of clinical trials. The new regulation (EU) No 536/2014 allows the use of multiple sponsors, so-called co-sponsors. But this also raises new problems and questions for existing contracts and new contracts between sponsors, especially regarding the liability of one or more co-sponsors in the external as well as the internal relationship. This article highlights the issues arising from this amendment and clarifies the differences between a sponsor and a co-sponsor.

Keywords: Sponsor, Co-Sponsor, Clinical Trial, (EU) No 536/2014

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1. Introduction

Conducting clinical trials without a sponsor is inconceivable. A clinical trial is any examination carried out on humans intended to research or determine the clinical or pharmacological effects of medication or to detect adverse reactions [...] with the aim to ascertain the safety or efficacy of the medicinal products (section 4, paragraph 23 of the German Medicinal Products Act and regulation (EU) No 536/2014). Contrary to the lay perception, the sponsor does not only serve for the provision of financial means; he also has many other duties such as the responsibility for funding the clinical trials, but not necessarily the funding itself.(1, 2) These obligations are essential for clinical trials.

However, the new regulation (EU) No 536/2014 allows a new sponsor model in clinical trials, the so-called co-sponsor. This newly established existence of sponsor majorities represents a disintegration of the previous legal situation, which involved only one sponsor. The sponsor embodied a single entity, that is now split among several sponsors due to the new Regulation. This not only changes the areas of responsibility, but also the liability of the individual co-sponsor. The question remains whether a contract between the co-sponsors is necessary and how it affects each of them.

In the following, this article will state the implications of the EU regulation regarding the co-sponsor and how this affects the previous legal situation – the single sponsor as an entity.

2. Materials & methods

For this research article, the authors used a specific data base for law www.beck-online.de and digital journal archives (https://ezb.ur.de;www.digizeitschriften.de) at Universitätsmedizin Göttingen. Additionally, all assumptions are based on the authors own day-to-day experience as a lawyer or legal advisor at legal department of Universitätsmedizin Göttingen.

A. Sponsor

I. Term

The sponsor is legally defined in section 4, paragraph 24 of the German Medicinal Products Act and regulation (EU) No 536/2014 Art. 2 paragraph 2, no 14): "Sponsor means an individual, company, institution or organisation which takes responsibility for the initiation, for the management and for setting up the financing of the clinical trial."

As a result, the sponsor takes on many different areas of responsibility. Furthermore, the sponsor assumes special commitments such as the obligation to notify and report as well as to document and archive (Art. 36ff., Art. 40ff., Art. 52f., Art. 56ff. (EU) No 536/2014). This defines the sponsor as a complete unit according to the principle of the uniformity of the sponsor.(3, 4) The sponsor is not necessarily only financial support. In this context, he must be distinguished from the supporter, who typically assumes the role of financial support.(3, 4)

The sponsor may also be the investigator of the clinical trial within the meaning of section 4 paragraph 25, clause 1 of the German Medicinal Products Act (Art. 71 (EU) No 536/2014). In doing so, he not only bears the inherent responsibilities of a sponsor but is also the leader and main investigator of the clinical trial. This means that he is the principal investigator of the medical conduct of the clinical trial.(2, 5) Lastly, he is accountable for all hazards and risks associated with the clinical trial.(2)

II. Liability

The sponsor bears the overall responsibility for the correct conduct of clinical trials. Consequently all damages are attributed to him, including those caused by third parties in the process.(4, 6)

He may delegate his task to third parties, but this does not result in a transfer of the sponsor's responsibility, Article 71, subparagraph 2 of the regulation (EU) No 536/2014.(7) Therefore, the sponsor can only relinquish his responsibility if the law explicitly provides for it.(8) Additionally, the sponsor can transform his duties to act into supervisory duties by handing over his sponsorship tasks to third parties. This results in an obligation for the sponsor to ensure that the delegated tasks are carried out properly. In this matter, the sponsor is granted a right to information and intervention.

Incidentally, the civil and criminal liability norms are not displaced, because according to Article 75 of the regulation (EU) No 536/2014, "the civil and criminal liability of the sponsor, investigator, or persons to whom the sponsor has delegated tasks [...] shall not be affected".

B. Co-Sponsor

I. Term

According to the new EU regulation, it should also be possible for a clinical trial to have several sponsors, Article 71 et seq. of the regulation (EU) No 536/2014. This is called co-sponsoring, Article 72 of the regulation (EU) No 536/2014. The areas of responsibility of a single sponsor should be distributed among several sponsors by means of a written contract, so that the corresponding obligations and responsibilities also apply to them. If no contract is concluded, it is to be assumed that the obligations arising from the regulation are incumbent on all sponsors.

Co-sponsorship was developed because clinical trials were often initiated by loose networks of scientists or scientific institutes in one or more member states, which made it difficult to identify one or the right participant as the sponsor.

This created legal and practical problems for these networks of scientists.(9) As a solution to this problem Co-sponsorship was allowed.

II. Contract design and liability

Initially, each co-sponsor is responsible for the entire clinical trial. However, because of the new regulation, it is now possible to split responsibilities between them as part of the concept of co-sponsorship.

According to Article 72, paragraph 2 of the regulation (EU) No 536/2014, the regulation sets a certain minimum content of the contract concerning responsibilities. Correspondingly, the sponsors must assign only one sponsor (10) for each of the following areas of responsibility: Approval procedure according to point (a) of paragraph 2 of the regulation (EU) No 536/14, contact person during the conduct according to point (b) of paragraph 2 of the regulation (EU) No 536/14 and the person responsible for corrective measures according to point (c) of paragraph 2 of the regulation (EU) No 546/14.

In addition, all co-sponsors shall jointly identify a responsible sponsor who can fulfil the measures required by a member state and provide information on the clinical trial as a whole.(9) All other unassigned obligations are automatically the responsibility of all sponsors, Article 72, paragraph 2, clause 3 of the regulation (EU) 536/2014.

In general, a distinction must be made between different accountabilities in the concept of co-sponsorship.

Article 72, paragraph 1, clause 1 of the regulation (EU) 536/2014 applies according to the administrative law. Consequently, each co-sponsor is administratively responsible for the obligation arising from the regulation. However, an exception to this principle is the written contract that the co-sponsors can conclude on the division of their responsibilities. This division needs to be understandable and comprehensible. If there is no definite division, all co-sponsors continue to be jointly responsible under administrative law.

Each co-sponsor is responsible to the authorities for the obligations agreed on in the written contract; because of that a non-responsible co-sponsor is not the addressee of an official measure. The legislator also provides for this by demanding a writing requirement exclusively for the division of responsibilities. This should allow to quickly find the specific contact person for an official measure.(11)

The civil liability of co-sponsors is not affected according to Article 75 of the regulation (EU) 536/2014 and can correspondingly be assessed under national civil law, for example, one co-sponsor could be liable for the conduct of another co-sponsor.

But a distinction must be made between a possible legal and contractual liability.

For a legal attribution, there would have to be a subordination relationship between the co-sponsors according to the legal attribution norms, which means that one co-sponsor would have to be superior to the other so that this sponsor can be liable for the legally subordinate co-sponsor. However, it can be assumed that the co-sponsors do not want to be subordinated, but to have an equal legal status among themselves.(11)

An attribution according to Article 72, paragraph 1 of the regulation (EU) 536/2014 fails because, on the one hand, this only refers to the administrative attribution and, on the other hand, Article 75 of the Regulation (EU) 536/2014 explicitly standardises the civil liability. As a conclusion, a legal attribution is not possible either within a subordination relationship or under the new regulation.

Furthermore, a contractual attribution could come into question.

For this, the co-sponsors would have to have concluded a contract among themselves. By agreeing to jointly conduct a clinical trial as co-sponsors, a contract may already be entered. But according to Article 72, paragraph 1 of the regulation (EU) 536/2014, a written contract is only necessary for the division of responsibilities; so, there is no need for a co-sponsorship contract as such. In this respect, the contract can also be implied. If there is a co-sponsorship agreement, it is questionable what the essentialia negotii of this agreement are, more specifically, what minimum content this agreement has or must have. The minimum content must be evident from the regulation. As a result, a co-sponsorship agreement requires several persons who agree to participate as sponsors in the conduct of a clinical trial and to abide by the resulting obligations.

This co-sponsorship agreement does not constitute as a creditors' agreement, a debtors' agreement, a guarantee agreement, a surety agreement or a contract for the benefit of third parties under German law. In all cases, it can be assumed that the co-sponsor does not want to conclude a contract with a third party and does not want to completely release another co-sponsor from its liability or stand in for it to a greater extent.(11)

For this reason, no special type of contractual obligation exists between the co-sponsors.

Instead, the co-sponsorship agreement could be regarded as a civil-law association under section 705 et sq. of the German Civil Code. For this, there would have to be a partnership agreement with the content that at least two partners pursue a common purpose in a certain way.(12)

First of all, a common purpose is required.

A common purpose exists if the partners as contracting parties reach an agreement on certain interests or goals to be pursued jointly and to achieve a certain success.(12) Even if the individual purpose of a clinical trial is different for each co-sponsor, the conduct of a clinical trial is a preliminary purpose which means that there is a common interest and thus also a common purpose.(11) Furthermore, they would have to be obliged to support this purpose and be able to claim the other for it.(13)

Corresponding to Article 72 of the regulation (EU) 536/2014, each co-sponsor must comply with the obligations arising from the regulation, which is why the clinical trial depends on each co-sponsor. Therefore, any co-sponsor can demand compliance from any other co-sponsor with sponsorship obligations. Consequently, the duty to promote the purpose is to be seen as a requirement of the civil law partnership in the perception of and compliance with these obligations.(11) In conclusion, the co-sponsorship agreement can be considered as a civil law partnership according to section 705 et sq. of the German Civil Code.

The liability of the individual shareholders – in this case, co-sponsors – is also based on this.

Internally, the co-sponsors can clarify their liability among themselves using a contract. If there is not yet a written agreement in this regard, the matter must be regulated in accordance with the known departmental responsibility under German law.(11) According to the departmental responsibility, the respective shareholder is fully responsible for the proper execution of the tasks in his assigned area of responsibility.(14)

Because the other partners are not responsible, they only have a supervisory duty, which means that they must check whether the task is being properly carried out by the respective partner.(15) This means that the responsibility of persons who are not competent for this area is limited.(15) The overall responsibility of those not in charge changes to a general duty of supervision and observation.(16) If necessary, the non-responsible co-sponsor has a right of recourse against the responsible co-sponsor under the contractual regulations and by the application of the principles of departmental responsibility for governing bodies.(11, 17)

In the external relationship, on the other hand, the co-sponsor is jointly and severally liable as a partner analogous to section 128, paragraph 1 of the German Commercial Code and according to section 421, paragraph 1 of the German Civil Code responsible to the full extent.(17) As a result, a contractual attribution of a civil law partnership comes into consideration.

Finally, as with the individual sponsor, criminal liability is not affected by the new regulation. By that, the individual co-sponsor can also be criminally prosecuted, whereby the other co-sponsors can be co-punished as accomplices or participants.(11)

III. Advantages and disadvantages

There are both advantages and disadvantages to the concept of co-sponsorship. First of all, the introduction of the co-sponsor reduces the workload of the clinical trials by distributing the responsibilities and tasks among several parties. Furthermore, due to the many co-sponsors, expertise, capacities and financial resources are used more effectively.(4) In addition to that, the multinational and multicentre conduct of clinical trials results in greater adaptability, for example in monitoring. In doing so, trial centres in different countries can be supervised and controlled better.(4, 18)

The newly approved sponsor majority also increases the possibility of forming into multiple research collaborations. Finally, because of this concept, there is another participation option in clinical trials besides the supporter and the sponsor: the co-sponsor.(4)

However, the co-sponsor also brings disadvantages. Due to the lack of experience with the concept of co-sponsorship, many legal uncertainties are created as well as yet undiscovered problems. Concerning the liability of sponsors in their external relations with third parties, there are still unresolved questions.(4, 17)

In addition, it must always be decided who should be the primary contact for health authorities and ethics committees. This not only increases the possibilities of contract constellations but also changes the content of the

contracts due to the legal systems. It is therefore imperative to permanently adapt to, for example, patent and liability law.(4) Furthermore, it is also more advantageous for the contracting party to only have one contact person and payee instead of several at the same time. This only complicates the contract design. In general, it can be assumed that co-sponsorship may give rise to numerous difficulties regarding the demarcation and responsibilities of other parties involved, which still need to be clarified.(4)

3. Discussion & Conclusion

The new regulation does not change much about the concept of sponsors. However, the newly allowed sponsor majority poses unresolved problems regarding liability and contract design. But it seems important to clarify all liability regulations between the co-sponsors in a written contract. If this is not clarified, it must be assumed that the co-sponsors are jointly and severally liable to the authority from an administrative law perspective; concerning criminal liability, on the other hand, one must proceed according to national law. Ultimately, the civil liability of the co-sponsors is not affected by the regulation; the co-sponsors are a civil law partnership. In the internal relationship, in the absence of a written contract within the scope of departmental responsibility in the case of governing bodies, a change of responsibility into a supervisory duty of a non-responsible co-sponsor is to be assumed. One the other hand, in the external relationship all co-sponsors are liable as joint and several debtors analogous to section 128, paragraph 1 of the German Commercial Code. As a result, third parties who may have been harmed are not affected by the existence of co-sponsorship, as they can address all co-sponsors in their external relations and are thus not subject to any aggravated conditions.

However, only time will tell how the co-sponsor concept will continue to play out and what other advantages and disadvantages will result from this new sponsor majority.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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