

Model contract clauses for clinical trials with drugs, conducted under the responsibility of a pharmaceutical company (industrial sponsor)

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- *Preamble*

Germany is currently a well-positioned, internationally competitive location for conducting clinical trials. This is reflected in its position as number 2 in Europe for the number of clinical trials held in the country, and number 3 worldwide, after the USA and UK. Maintaining and further improving this strong position is in the shared interest of all stakeholders in the field of clinical research, patients, trial sites and sponsors of clinical trials.

The conduct of clinical trials is often subject to time pressure, with the factor of time playing an important role in international competition, particularly in the period leading up to the start of a clinical trial. In order to be able to begin a clinical trial as early as possible, it should be possible to conclude the underlying contracts between the parties involved quickly and easily, with comprehensive content. As such, it would be useful if guidelines, in the form of model contract clauses providing examples of specific contractual provisions that regularly recur in contracts governing the conduct of clinical trials, were available to potential contractual partners during their respective negotiations; this would result in simplified negotiations in these areas.

To pursue these common goals, representatives from the Medizinischer Fakultätentag (MFT, German Association of Medical Faculties), the Verband der Universitätsklinika Deutschlands (VUD, German Association of University Clinics), the Koordinierungszentren für Klinische Studien (KKS network, Coordinating Centres for Clinical Trials) and the Verband forschender Arzneimittelhersteller (vfa, Association of Research-based Pharmaceutical Companies) have drafted these model contract clauses below, which are intended to take into account the various interests of all involved. The consideration of the respective interests here may also offer indications for similar contractual relationships in the field of health research.

- *Instructions for use*

The model contract clauses presented below cannot be binding but are intended to provide guidance to members of the drafting organisations and other third parties for the negotiation of clinical trial agreements for Phase I-IV clinical trials. They should be regarded as suggested wording for the regulation of individual matters that regularly form part of such negotiations. This is not a complete contract template.

The following should be considered with respect to the use of these model contract clauses:

- In practice, clinical trial agreements are typically concluded either between the client (the sponsor or one of the affiliates of the sponsor) and the trial site (institution/contractor) (**two-party contract**)¹ or between the trial site, investigator and client (**three-party contract**) as contracting parties. These model contract clauses are based on the two-party contract model. In order to ensure that the interests of all parties involved are sufficiently taken into account, it is necessary for the investigator and other physicians of the investigating team to accept certain obligations in the form of a declaration. A corresponding model text is attached as annex to these model contract clauses. In the case of a three-party contract, the obligations of the investigator may also form part of the clinical trial agreement between the trial site, the investigator and the client. In this case, it should be ensured that the investigator is explicitly named as a party to the contract and that the individual text of the contract is supplemented with elements from the attached model annex.
- There are periods/terms indicated in the model contract clauses which shall serve as an orientation. However, it is, of course, left to the contracting parties to contractually determine a concrete term for each individual case.
- The conduct of clinical trials may be supported through the involvement of Clinical Research Organisations (CRO) on the client's side and/or on the trial site's side. If the model contract clauses provided below are used for clinical trial agreements involving one or more CROs, it is advisable to clearly delineate the respective areas of responsibility and services between the parties involved in the clinical trial agreements or to recommend the use of these model contract clauses in cases where a CRO acts as a contractual partner instead of the industrial sponsor/client. In cases where a CRO is appointed by an institution/contractor, it is recommended that a three-party contract (trial site, CRO and client) be concluded.
- These model contract clauses are not intended for use in contracts governing the conduct of non-interventional studies/observational studies.
- Furthermore, these model contract clauses do not cover financial considerations nor services eligible for remuneration as part of a clinical trial – see the *“Joint recommendations for the preparation of a total services calculation for remuneration related to the conduct of a clinical trial in a trial site”* by the MFT, the VUD, the KKS network and the vfa.

Disclaimer: The model contract clauses below have been prepared by the representatives of the organisations involved to the best of their knowledge and on the basis of collective professional discussion and the respective practical experience gained by each. The legality and comparability of these clauses with German or European law may be assessed differently by any courts consulted. Furthermore, parties using the model contract clauses are not exempt from the requirement to document the specific facts and the intentions of the respective parties in each individual case, and on this basis to determine which

¹*Location-specific details of the trial sites can be taken into consideration on a case-by-case basis. This can be useful to facilitate differentiated consideration of the various employment bodies of the employees on a case-by-case basis, in order to represent the contractual obligations of the involved members of the investigating team.*

individual model contract clauses to use. The authors are hereby exempted from all liability.

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1. Publications.

The client shall be entitled to publish the results of the clinical trial at any time. In this respect, it must also be noted that the client needs to comply with statutory transparency obligations or any requirements arising from self-commitments, particularly regarding data concerning the investigator and the investigator's deputy, or the trial site.

The client acknowledges and accepts the basic right of the trial site to publish those results of the clinical trial generated at the trial site – whether these are favourable or unfavourable – for non-commercial scientific purposes. Publications include oral or written publications pertaining to the clinical trial, its results, or the investigational medicinal products used (hereinafter referred to as "Publication").

In order to protect the legitimate interests of the client, the trial site hereby undertakes to comply with the following procedure in respect of Publications.

1.1 Initial Publication.

The client shall be entitled to make the first Publication, regardless of the type of Publication.

If the clinical trial is part of a multi-centre clinical trial, the trial site hereby agrees that the initial Publication shall be a Publication of the overall results for all trial sites, and that all subsequent Publications by the trial site must make reference to this initial Publication. The Publication of the overall results of the clinical trial shall be coordinated by the client. A Publication of data from individual trial sites without the context of the overall results may not be able to make valid scientific statements. However, subject to the conditions specified in [Paragraph 1.2], the results generated at the trial site may be published before publishing of the overall results without the prior written consent of the client, provided that the overall results are not published within [generally between 12 and 24 months] after completion of the clinical trial.

1.2 Review before Publication.

The trial site and its staff shall only be entitled to make a Publication if the client has been given the opportunity to review the planned Publication before it is submitted or disclosed in any other manner, in accordance with the following provisions.

The trial site shall provide any manuscript intended for Publication at least [generally between 30 and 60 calendar days] before submission for Publication, in order to allow the client to identify Confidential Information and intellectual property. Following receipt of the manuscript/draft, the client shall check whether its interests will be impaired. The client shall inform the trial site promptly in writing of any Confidential Information and/or any request to delay the Publication in order to allow the client to secure or file patent rights.

The trial site shall delete the specified Confidential Information before submission for Publication.

The client may also comment on the content and/or suggest changes. The trial site shall consider such comments/suggested changes and implement them unless they affect the scientific accuracy or neutrality of the Publication.

Upon client's request, the term for Publication shall be extended by no more than [generally 90 calendar days] to allow the client to secure or file patent rights. If the client does not

notify the trial site within the periods specified above, the trial site shall be free to submit the provided manuscripts for Publication and to publish them.

1.3 Standards.

For all Publications, the trial site shall adhere to current academic standards, e.g. the authorship guidelines set forth in the *Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals* (<http://www.icmje.org/icmje-recommendations.pdf>) defined by the International Committee of Medical Journal Editors.

1.4 Disclosure of support.

In the case of Publications, lectures or other public statements made in connection with the object of the contract, the trial site shall make reference to its activities on behalf of the client and shall disclose the sponsor of the clinical trial in every Publication.

2. Confidential Information.

2.1 Definition/usage.

The trial site shall keep all information provided to it by the client or any affiliate of the client with regard to the clinical trial, the investigational medicinal products (*or trial medication*) or the present agreement, as well as all results arising from the trial (hereinafter referred to as "Confidential Information") strictly confidential. The trial site shall only use the Confidential Information for the purposes of the present agreement and shall not disclose this Confidential Information to any third party without the prior written consent of the client. This requirement for approval does not apply to the inclusion of companies affiliated with the trial site within the meaning of sections 15 et seqq. of the German Stock Corporation Act. The trial site may only make the Confidential Information accessible to persons who need to know the Confidential Information for the performance of services under the present agreement and who are obliged towards the trial site to maintain confidentiality on the basis of a written confidentiality agreement with terms at least as stringent as the terms concerning confidentiality set forth in the present agreement.

The requirement to maintain confidentiality shall not apply where the trial site is entitled to publish the confidential information in accordance with *[reference to corresponding provision in the clinical trial agreement]*.

2.2 Exceptions.

The above provisions concerning confidentiality shall not apply to information that the trial site can prove

- was already in possession of the trial site at the time of its disclosure by the client or an affiliate of the client; or
- was publicly known other than by breach of contract or an act or omission on the part of the trial site; or
- was legally acquired by the trial site from a third party not bound by any confidentiality obligation towards the client or any of its affiliates; or
- was generated by the trial site independently of the receipt of and without the use of any Confidential Information.

2.3 Disclosure.

The trial site may disclose Confidential Information to the extent necessary to comply with applicable law or an enforceable official or judicial order. In such cases the trial site shall, if permissible, inform the client in good time before the disclosure of the confidential information and cooperate with the client in respect of obtaining provisional remedy or other appropriate legal protection. The trial site hereby undertakes to make every reasonable effort to ensure that the Confidential Information to be disclosed is treated as confidential.

2.4 Continuing obligations.

The provisions in the present agreement concerning confidentiality and restrictions on use shall continue to apply for a period of 10 years, even after the early termination or expiry of the agreement.

2.5 Erasure/destruction.

Upon the client's request, the trial site shall destroy/erase all Confidential Information in its possession, where technically possible, or return it to the client. Even after the return or destruction of the confidential information, the trial site shall continue to be bound by the confidentiality provisions and restrictions on use specified in the present agreement.

3. Trademark clauses/use of name

The contracting parties mutually acknowledge one another's name and trademark rights. None of the contracting parties shall use the name or trademark of the others without that party's prior written consent, regardless of the form or medium used. This shall not include the use of trademarks or names for the conduct of the clinical trial that forms the object of the present agreement and/or their use for regulatory purposes and/or with respect to authorities and/or in registers for clinical trials (e.g. www.clinicaltrials.gov) and/or within the scope of the usual naming of authors in scientific journals. The provisions on confidentiality and publication shall not be affected by the above provisions.

4. Liability*

The contracting parties shall each be liable for intent and negligence. In the case of slight negligence, the liability of the contracting parties for damages not arising from damage to life, limb or health shall be limited to

(a) damages typical for this agreement that were foreseeable at the time of conclusion of the agreement, if the damages arise from the violation of a material contractual obligation, and

(b) to *[x times]*** the contract value if the damages arise from the violation of any other contractual obligation.

Material contractual obligations are those obligations whose fulfilment enables the proper execution of the agreement, and/or compliance with which the other contracting party regularly relies on and is permitted to rely on.

The above provisions on liability shall also apply to representatives and agents of the contracting parties.

** This is a comprehensive clause, meaning that further regulations concerning loss of turnover, loss of profit, infringement of third-party industrial property rights, etc. are not necessary.*

*** To be determined on a case-by-case basis by the respective contracting parties depending on the actual amount of the order value, the trial phase and the scope of the trial . As a rule, it can be assumed that this will be one to two times the order value unless the restriction seems inappropriate in the individual case.*

5. Audits/inspections

The obligations set forth in this section shall remain in full force and effect for at least 15 years after the termination of the present agreement or for the duration of the statutory data retention period, whichever is longer.

5.1 Monitoring and audits.

The client or its representatives are obliged to monitor the conduct of the clinical trial. The trial site shall grant employees of the client and/or its representatives, after arrangement concerning time, access to its buildings, facilities, all documents relevant to the clinical trial, and the members of the trial group as required for monitoring the conduct of the clinical trial. The client shall inform the trial site promptly of any monitoring findings affecting the safety of the trial subjects or the conduct of the clinical trial. The trial site or the investigator shall also make the trial subjects aware of these findings.

5.2 Inspections.

The trial site acknowledges that the clinical trial is subject to inspection by supervisory authorities from countries worldwide, including the US FDA, and that such inspections may occur during and after completion of the clinical trial and may also include the inspection of documents relevant to the clinical trial.

- a. Notification. The trial site shall notify the client or its representatives immediately if the trial site is being or is set to be inspected by a supervisory authority in connection with the clinical trial. The trial site shall also notify the client or its representatives if during inspection of another clinical trial for a different client, a critical or major* finding is identified which constitute with respect to the contractual clinical trial a hazard for patient safety and/or data integrity at the trial site.

**It is left to the contracting parties to contractually specify the threshold beyond which notification is required in relation to the respective clinical trial.*

- b. Presence during inspections. Where an inspection or measure implemented by a supervisory authority affects the trial that is the object of the present agreement, the client and/or its representatives shall be entitled to be present during this inspection with respect to the contractual clinical trial.
- c. Inspection findings and statements. The trial site shall promptly provide the client or its representatives with copies of all inspection findings that it receives from a supervisory authority in connection with the clinical trial. Before the trial site responds to any findings arising from an inspection by a supervisory authority, it shall – where legally permissible – discuss and align the response with the client.

5.3 Cooperation.

The trial site shall cooperate with representatives of the supervisory authority or the client or their agents during the performance of inspections, monitoring and audits, and shall

ensure that the trial documentation is managed in such a way that it is accessible without restriction to those performing the aforementioned activities. The trial site has a general obligation to take all measures necessary to correct a deficiency identified during an audit/monitoring or an inspection.

5.4 Clarification of discrepancies.

The trial site shall promptly clarify all discrepancies identified between the study data and the medical files of the trial subjects.

6. Archiving

In accordance with ICH requirements and local statutory requirements, the trial site shall retain all documentation and electronic documents relating to the trial, including source documents and investigator site files (hereinafter referred to as "Trial Documentation"), for a period of

- 1) 15 years after the end of the trial or
- 2) for any longer retention period required under the applicable statutory law*.

The Trial Documentation must be stored securely in a appropriate location and manner. The trial site must maintain records of the location at which the Trial Documentation is stored, in order to ensure that it is readily available to monitors, ethics committees, auditors and authorities upon request.

The trial site may destroy the Trial Documentation after the retention period has expired unless the client requests (i) a longer retention period or (ii) where legally permissible, the transfer of the Trial Documentation to the client or a third party specified by the client at least 3 months** before the expiry of the retention period. In case of (i), the parties shall conclude an agreement with respect to the further retention.

Note: The parties must agree on a case-by-case basis whether the trial site must ask the client concerning the destruction/extended retention of the documentation or whether the latter should contact or inform the institution/contractor accordingly on its own initiative. It was not possible to agree on a final, common model wording for this aspect. In principle, key documents pertaining to the clinical trial, including case report forms, should be stored for at least 15 years after the end of the trial. If a clinical trial is also subject to radiation protection regulations, the minimum retention period shall be 30 years. It is possible to deviate from this by means of a contractual regulation.

The trial site must inform the client about any possible changes to the type of archiving used for the Trial Documentation (e.g. introduction or discontinuation of an electronic data recording system). In the case of electronic archiving, the trial site shall ensure that the data is available throughout the entire retention period, can be rendered readable within an appropriate timeframe, and corresponds to the original data. The trial site shall inform the client if, due to unforeseen circumstances, its clinic, institution or practice is no longer in a position to store the aforementioned Trial Documentation accordingly.***

*The currently valid statutory data retention period will be extended to **25 years** under EU Regulation No.536/2014, which will soon become directly applicable – see wording “at least 25 years” in Article 58 of EU Regulation 536/2014. The period of 15 years specified in the present model contract clauses must therefore be amended to 25 years, no later than on the date when EU Regulation No. 536/2014 becomes directly applicable. The contracting parties should bear in mind that various study projects may take place over longer periods and, if necessary, EU Regulation No. 536/2014 may also apply to clinical trials

that commenced before the Regulation actually becomes directly applicable. It should also be taken into account that a minimum data retention period of **30 years** applies to those clinical trials subject to the radiation protection regulations, in accordance with the provisions set forth in those regulations.

******The determination of a specific period is for the contracting parties in the individual case.

*******In accordance with the provisions set forth in Article 58 of the future EU Regulation No. 536/2014, the client and the trial site shall be jointly responsible for the comprehensive archiving of the master files pertaining to the clinical trial for a period of at least 25 years.

7. Equipment or materials provided

[Note: This clause should only be included in a agreement if required. Further provisions may be necessary if the equipment/materials are provided by a third party.]

Where the client provides for equipment or materials for use by the trial site for the purposes of conducting the contractual clinical trial, or arranges for provision by a third party, these must be listed in a separate Annex *[e.g. Annex B: Equipment and Materials]*. Such materials may include, inter alia, computer software, methods, assessment scales and other aids that are the property of the client or a third party, or are licensed for use (referred to collectively as "Equipment").

Provision of the Equipment shall be limited to the duration of the clinical trial and the Equipment must be returned promptly to the client or the third party following the end of the clinical trial; the client or the third party appointed shall ensure that the Equipment is taken back. Alternatively, and provided that the parties agree, the Equipment may be purchased by the trial site for the fair market price*. The client and the trial site hereby agree that the provision of the Equipment does not constitute remuneration or partial remuneration and that it shall be used exclusively for the conduct of the contractual clinical trial. The trial site shall ensure and guarantee that the equipment provided shall be used exclusively to perform the services due to the client in connection with the clinical trial. The trial site shall handle the equipment with due care and shall store it in a secure environment in such a way that it is protected against unauthorised use, theft or damage.

*If desired, cost regulation for the transfer of use shall be agreed individually between the contracting parties. If necessary, the provision of Equipment shall also be regulated in a separate contract.

8. Termination/cancellation

8.1 Reasons for termination/cancellation.

This contract shall end as soon as one of the following events occurs:

- a. Rejection by the ethics committee. This agreement shall end if the clinical trial cannot be initiated due to a negative decision by the ethics committee.
- b. Refusal by the competent higher federal authority. This agreement shall end if the clinical trial cannot be initiated due to a refusal by the competent higher federal authority.
- c. Completion of trial. This agreement shall end as soon as the clinical trial is completed, i.e. as soon as the activities prescribed in the clinical trial protocol – including, e.g. completion of all examinations listed in the clinical trial protocol, handover of all fully completed case report forms (CRF) and closure of the trial site, including data cleaning and completion of the trial database and handover of the final clinical trial report – have been completed for all trial subjects.

d. Early termination of the clinical trial. This agreement shall come to an end if the clinical trial is terminated as follows:

(1) Termination of the clinical trial within the agreed notice period. The client may terminate the clinical trial agreement in writing by giving 14 days' notice.

(2) Termination of the clinical trial without notice by the client. The client may terminate the clinical trial agreement with immediate effect for good cause by notifying the trial site in writing. Good cause shall include the following: Failure to meet the trial performance objectives due to insufficient enrolment of trial subjects; unauthorised deviation from the clinical trial protocol or reporting obligations; circumstances endangering the health or well-being of trial subjects in the view of the client; measures by supervisory authorities in connection with the clinical trial or investigational medicinal products; cases where the clinical trial must be terminated for medical/ethical reasons; breach of the applicable laws, ICH GCP, obligations of confidentiality by the trial site, inadequate quality of documentation or a breach of provisions set forth in the section on anti-corruption [*e.g. reference to the corresponding section in the agreement*] of this agreement or any other sections of this agreement entitling the client to terminate the agreement without notice.

(3) Termination of the clinical trial without notice by the trial site. The trial site may terminate the clinical trial with immediate effect for good cause by notifying the client in writing. Good cause includes without limitation, that the trial site is required by the competent ethics committee or the competent supervisory authority to end the clinical trial or if it is necessary to terminate it in order to protect the health of trial subjects or if (i) the client is in arrears with payment to a not inconsiderable extent or has been in arrears with payment for a substantial period and (ii) the trial site has already warned the client about this issue.

8.2 Payment in the case of termination of the clinical trial.

In case of early termination, the following provisions shall apply with regard to the outstanding payments for trial-related costs:

a) Payments in case of early termination: Unless otherwise specified in this subsection, in case of early termination the client shall make payments, in accordance with the annex to the trial budget and the terms of payment, for all services completed properly prior to the receipt of the notice of termination; less any payments already made for such services. The client shall also bear all non-cancellable costs provided that these have been incurred properly, approved by the client in advance; to the extent as these cost cannot be sufficiently minimised. *Personnel recruited specifically for this clinical trial, with approval of the client, may continue to be financed by the client, but only in case of temporary employment and up to the earliest possible date on which the respective employment relationship can be terminated**. If the clinical trial cannot be initiated due to a negative decision from the ethics committee or refusal by the competent higher federal authority and without any fault on the part of the trial site, the client shall reimburse the trial site for any ethics committee fees, fees charged by the competent higher federal authority and all other expenses approved in advance in writing by the client.

b) Non-compliance with contractual provisions: If the client terminates the clinical trial agreement due to a breach of contract by the trial site, the client shall not make any further payments to the trial site on the basis of the present agreement, regardless of any measures undertaken by the trial site or any third-party agreements concluded by the trial site prior to the termination, unless the services were provided properly before the breach of contract occurred.

** This highlighted sentence is intended to cover a special case that does not often occur; therefore, the wording should only be used as needed/in individual cases.*

8.3 Return of Equipment and materials.

Unless otherwise agreed in writing between the parties, the trial site shall return all Equipment and materials provided by the client or a third party appointed by the client for the conduct of the clinical trial promptly upon termination of the present agreement; this shall include any unused investigational medicinal products, unused case report forms and all Equipment and materials provided by the client or by a third party appointed by the client. The client may also agree with the trial site that certain materials may be destroyed at the trial site. In this case, the trial site must destroy the materials in question in accordance with the client's specifications and shall provide proof/documentation of same. The client may also make other arrangements with the trial site in the individual case.

8.4 Continuing obligations.

- a) In the event of early termination of the agreement, regardless of the reason for termination, only the obligation of the trial site to continue conducting the clinical trial and of the client to pay the remuneration shall end.
- b) Obligations concerning financing, Confidential Information, Trial Documentation, inventions, Publications, insurance coverage provided by the client, suitability and anti-corruption shall persist after the termination of this agreement, regardless of the reason for the termination; this shall also apply to all other provisions set forth in this agreement that continue to apply after the expiry of this agreement by virtue of their nature and intent.

8.5 Continued treatment of patients already recruited in the event of termination.

In the event of termination, trial sites, where possible and reasonable, shall continue medical treatment of patients already included in the trial, at least in accordance with the recognised medical standards.

8.6 Consequences for recruitment.

Where the trial site has received notice of termination or where it has itself submitted notice of termination, the trial site shall not recruit or include any further subjects for or in the contractual clinical trial.