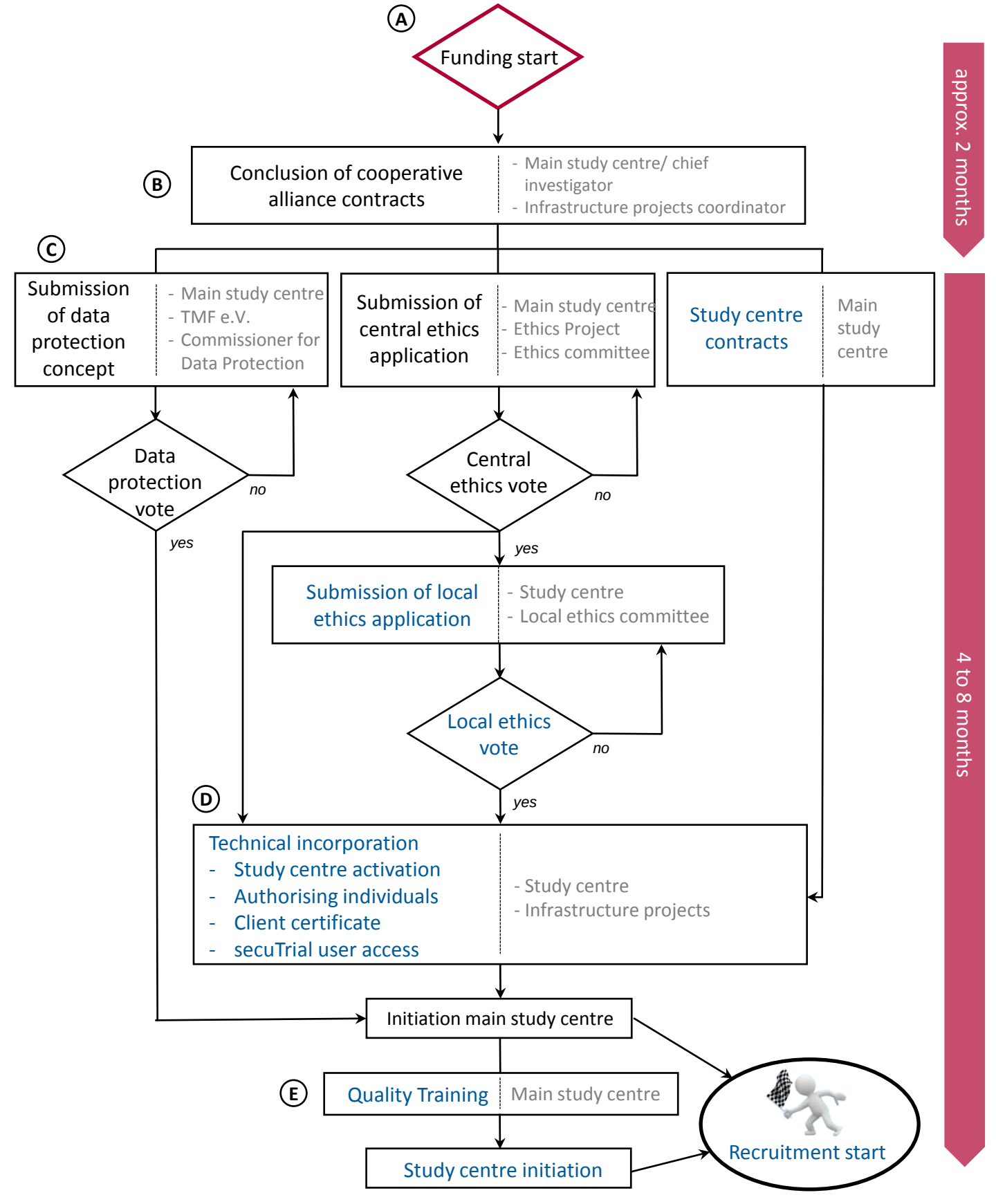
DZHK
DEUTSCHES ZENTRUM FÜR
HERZ-KREISLAUF-FORSCHUNG E.V.

Preparation (and Conduct) of Clinical DZHK Studies

3rd Phase: Start of funding until start of recruitment



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PREPARATION (AND CONDUCT) OF CLINICAL DZHK STUDIES
3rd Phase: START OF FUNDING UNTIL START OF RECRUITMENT

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This flowchart follows the flowchart “Application Procedure” and represents the “3rd Phase: Start of Funding Until Start of Recruitment”. It shows which work blocks need to be edited by the chief investigator and by each study centre. Furthermore, it provides important information and aids regarding the conduct of a study. The flowchart provides the temporal aspects and the order of the individual work steps.

Whereas the chief investigator needs to complete all work steps until inclusion of the first patient, the steps highlighted in **blue** font need to be completed by each study centre (including the main study centre) for technical incorporation into the scientific infrastructure of the DZHK.
This flowchart will be supplemented by the **Checkliste „Studienvorbereitung/-durchführung“ (Checklist “Study Preparation / Conduct”)** in which the individual work steps are sorted in detail by work block. These ensure that all necessary steps will have been completed by start of recruitment.

With the start of funding of a “DZHK study”, i.e., after conclusion of the allotment contract, the study will be added by the DZHK main office to the table (https://dzhk.de/research/clinical-research/clinical-studies/) of all current clinical DZHK studies. Furthermore, the study needs to be registered by the main study centre at https://clinicaltrials.gov/, mentioning the DZHK: Please use the name and acronym in brackets (“Deutsches Zentrum für Herz-Kreislauf-Forschung (DZHK)”), or the English variant “German Centre for Cardiovascular Research (DZHK),” to ensure success of several search strategies. A possible note during registration to omit the acronym can be ignored.

At the same time, the DZHK main office will organise a video conference “Study Kick-Off” for the chief investigator as a first meeting with the contact persons of the DZHK’s clinical-scientific infrastructure.

Simultaneously, the public relations section of the DZHK main office will consult with the study management on a press release regarding funding of the study, and the study logo and the study website will be agreed upon. DZHK studies will receive a DZHK study number.

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To consolidate the cooperative partnership, the study management and the infrastructure projects (TTP, DH, IKCL, ITLab and Ethics) must join contractually in an alliance project to conduct the study. On the one hand, they need to sign the existing ethics contract, which they will receive after initial contact with the Ethics Project. On the other hand, cooperative alliance contracts need to be concluded with all other infrastructure projects, using a master cooperation contract provided by the German Federal Ministry of Education and Research (Bundesministerium fuer Bildung und Forschung, BMBF). The cooperation contracts with the Ethics Project and infrastructure projects will be

concluded after or, optimally, at the time of conclusion of the allotment contracts (latest within a period of two months after conclusion of the allotment contracts). If this deadline cannot be met due to consultation-related delays, the chief investigator must apply for a deadline extension with the Funding Management Department (FMD).

Note: It must be ensured that the complete "Declarations of commitment of participating centres" as well as the "ICH-GCP Sponsorenerklärung" (ICH-GCP sponsor's statement) have been provided to the FMD and the DZHK main office.

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The study-specific data protection concept must be agreed upon by the chief investigator with the Technology and Methods Platform for the Connected Medical Research (TMF, data protection working group) and subsequently with the Commissioner for Data Protection of the main study centre's federal state. Reference shall be made to the data protection concept of the Central Data Management (CDM). The positive data protection vote of the DZHK is to be submitted to the FMD and to the DZHK main office.

Furthermore, the chief investigator needs to submit a central ethics application to his competent central ethics committee. Submission follows close consultation with the DZHK's Ethics Project. The positive ethics vote including the approved and final version of the patient informed consent form must be submitted to the TTP, the FMD, and the DZHK main office.

Study centre contracts must be concluded by the main study centre with each institution recruiting for this study.

In addition to the positive central ethics vote, each study centre needs to submit a local ethics application with the study centre's competent local ethics committee. The positive vote must be forwarded to the main study centre. The main study centre will provide the positive local votes to the Ethics Project and the TTP.

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The DZHK will provide a clinical-scientific infrastructure for the Clinical Research section in order to allow for the high-quality collection, recording, and processing of consistent information across multiple studies and to enable study managements and applicants to perform high-quality analyses. All studies primarily and completely funded by the DZHK are obligated to use the infrastructure by complying with the Standard Operating Procedures (SOP) of the DZHK. Central parts are the Independent Trusted Third Party (TTP, Greifswald), Data Handling (DH, Goettingen), the IT & Biobanking Coordination (DZHK main office and the Institute for Clinical Chemistry and Laboratory Medicine (IKCL), Greifswald), and the Ethics Project (Helmholtz-Zentrum Muenchen).

The DH is running the web-based secuTrial input software. Using this software, phenotype data of study-specific electronic Case Report Forms (eCRFs) will be captured. Consultation between the chief investigator and the DH regarding study-specific eCRF adjustment should take place early on and will take 4 to 8 weeks, depending on the extent and complexity of the CRFs.

For legal data protection reasons, the personally identifiable information (IDATs) will be collected, stored, and pseudonymised at the DZHK's TTP. Furthermore, the TTP as central authority will manage subjects' informed consents (ICs). The web forms to record IDATs and ICs will be displayed in secuTrial.

Study centres cannot include any study participants in the study until the centre has been reported active by the study management ("chief investigator"), which confirms that the study centre has received an ethics vote, that the study centre contract has been concluded, and that the centre has been initiated by the study management.

In order to use the mentioned DZHK applications, "local study coordinators" at the enrolling study centre as well as further individuals involved in the study at the study centres need to be authorised by the chief investigator or an authorised person at the main study centre (deputy arrangement) (see Figure 1).

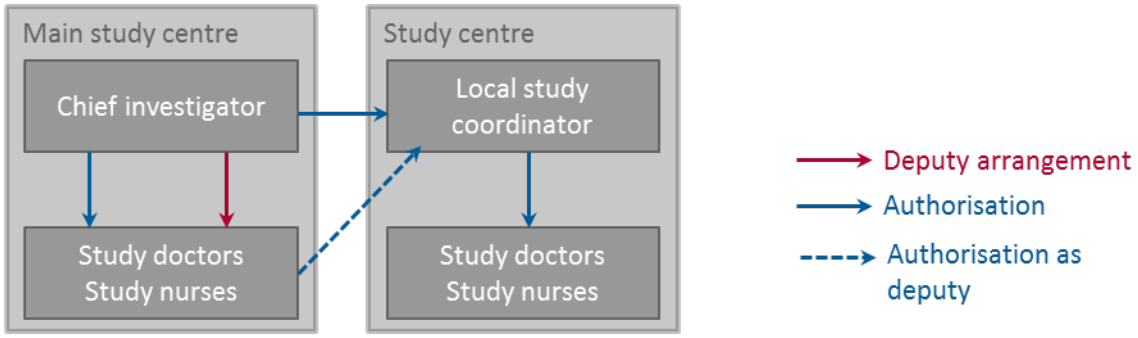

Figure 1: Delegation of authority processes

Users can neither request client certificates at the TTP nor user accesses to secuTrial until authorisation has been granted. The client certificate is a prerequisite for using secuTrial to allow for controlled communication between user and TTP. The general authorisation is also required for the authorisation of individuals at the study centre who are entitled to place biobanking orders. Only after this authorisation, basic and study sampling sets for biobanking may be requested at the IKCL. Early consultation with the IKCL regarding basic biobanking and study-specific biobanking is necessary.

The TTP and DH offer a webinar for the chief investigator where the processes for technical incorporation are explained and demonstrated as well as where questions are answered. When the DH and TTP have completed the implementation for the study, user and sampling tests will be executed and logged by the chief investigators. Subsequently, the new study is set to "productive" by DH and TTP and recruitment may commence.

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Finally, the main study centre or the study centre will be initiated and the first patient may be enrolled in the study. After initiation of several study centres, a “Quality Training” session for study staff will be held. Topics will include the management of specifics when recording data in the study. The DZHK main office will provide support for the organisation of the Quality Training, whereas the chief investigator and infrastructure projects will be responsible for the contents.

Note: Prior to the start of recruitment, a “(target) recruitment plan” must be provided to the DZHK main office once. After the start of recruitment, an updated “(actual) recruitment plan” and a “controlling report” must be submitted to the DZHK main office.