I. General assessment of the proposal

The proposal for a regulation on an EU Biotech Act (hereinafter: the Proposal), presented by the European Commission on 16.12.2025 aims to amend Regulation (EU) 536/2014 on Clinical Trials on Medicinal Products for Human Use (hereinafter: the Regulation) in order to improve the regulatory framework for clinical trials in the EU.

In this regard, the German Medical Association (GMA, *Bundesärztekammer*) in principle views the Proposal favourably. We especially welcome the strengthening of the role of ethics committees regarding Part I of the assessment report and minimal-intervention clinical trials. Furthermore, the GMA welcomes the fact that the revised protection standards in the World Medical Association's (WMA) Declaration of Helsinki regarding the inclusion of vulnerable groups in research projects have been implemented.

The simplification of the Investigational Medicinal Product Dossier (IMPD) and the promotion of biosimilar production are expressly welcomed.

Nevertheless, the GMA recognises the need for improvements, set out below.

It has to be stressed that the proposed improvement in procedural efficiency is conditional upon a smooth operation of the Clinical Trials Information System (CTIS). Previous experiences with CTIS indicate that particular attention must be paid to its functionality and that appropriate and necessary resources should be made available.

Moreover, facilitating the conduct of a clinical trial must not lead to a lower standard of evidence or weaken protection for participants. Robust evidence for new medicines is the foundation for rational and cost-effective medicinal product therapies. The proposal appears to be oriented towards industry needs and innovation, while aspects relevant for patients (e.g., quality of care, evidence-based clinical added value) are only addressed indirectly. It is remarkable that no reference is made to Health Technology Assessment at EU or national level. Considering the growing share of medicine costs in total healthcare expenditure, accelerated authorisation must not prejudice early benefit assessment and decisions on eligibility for reimbursement.

II. Position of the German Medical Association – Detailed assessment

1. Extension of the supplementary protection certificates

The Commission proposes that medicinal products which are developed using innovative biotechnological processes and present patients with a therapeutic advantage should be promoted through an extension of supplementary protection certificates as described in Article 27 (Chapter IV) of the Proposal.

Assessment of the German Medical Association:

- ***The proposed extension of supplementary protection certificates in accordance with Regulation (EU) Nr. 469/2009 would delay the potential market entry of a biosimilar by 12 months.***

- ***As biosimilars are generally less expensive than the reference biological medicinal products, the proposed extension of supplementary protection certificates would cause price increases for health insurance systems.***
- ***While the extension aims to promote innovation, it is not economically viable. Moreover, further delaying their market entry may discourage the development of biosimilars altogether, eventually compromising the security of supply. Therefore, Recital 57 and Article 27 (Chapter IV) of the EU Biotech Act should be deleted.***

2. Shortening authorisation timelines

The proposal provides for a shortening of the authorisation timelines for multinational clinical trials from 106 to 75 days (including the validation and ethical review). When there is no request for information to the sponsor, timelines for initial clinical trial authorisations are reduced from 75 days to 47 days. Considering the increasing scientific and regulatory expertise in the field of ATMPs, the additional 50 days for assessing these products are deleted. The assessment period for substantial modifications is reduced from 96 days to 47 days, with options for parallel substantial modifications. If there is no request for information by the sponsor, the timeline for the assessment of substantial modifications is reduced from 64 days to 33 days from submission until decision.

Assessment of the German Medical Association:

- ***The proposed shortening of authorisation timelines properly addresses a central problem of Europe as a research hub. However, shortening authorisation timelines carries the risk of overburdening ethics committees. If timelines are insufficient for substantive assessments there is a risk that assessments are carried out as a mere formality, to the detriment of quality. Patient protection however must not be compromised.***

- ***The significant shortening in the processing timelines necessitates streamlining procedures in ethics committees, especially in respect to scheduling and frequency of committee meetings. This requires the establishment of robust reserve capacity and a sustainable organisational support structure for ethics committees, which must be supported at national level.***

- ***For the implementation of shortened timelines, sufficient technical support through CTIS is crucial. This requires that CTIS calculate timelines correctly, ensure that the correct documents are provided for each process, operate reliably, and support the processing of multiple Requests for Information (RFIs) simultaneously.***

3. Validation of Part I of the application dossier

Shortened timelines are achieved by synchronising the validation and evaluation phases. In line with the planned strengthening of the role of the Reporting Member State (RMS), it is

envisaged that the validation of Part I of the application dossier will be carried out solely by the RMS. Accordingly, the involvement of the Member States Concerned (MSC) and, with it, the deadline for the MSCs to report validation deficiencies has been removed.

Assessment of the German Medical Association:

- ***A stringent validation of Part I of the application dossier through the RMS is supported. The validation process includes an assessment to determine whether the clinical trial falls within the scope of the Regulation or whether it constitutes a low- or minimal-intervention clinical trial. Such an assessment requires clinical and pharmacological expertise and is one of the core responsibilities of the relevant ethics committee. Against this background it should also be ensured that the competent ethics committee of the RMS is already involved in its validation, in line with the mandatory involvement of this ethics committee in the assessment of Part I. This requires sufficient timelines.***

Amendment 1	
Art. 5b Reg (EU) 536/2014	
Text Proposed by the Commission	**GMA Proposed Amendment**
1. Within seven days from the submission date, the reporting Member State shall validate Part I of application dossier referred to in Article 6 and notify the sponsor, through the EU portal, of the following: *(a) whether the clinical trial applied for falls within the scope of this Regulation;* *(b) whether the application dossier is complete in accordance with Part I of Annex I;* *(c) whether it confirms that the clinical trial is a minimal-intervention or a low-intervention clinical trial, respectively, if such a claim was made by the sponsor.* *2. Where the reporting Member State has not notified the sponsor within the period referred to in paragraph 1, the clinical trial applied for shall be deemed to fall within the scope of this Regulation and the application dossier shall be considered complete and, if applicable, the clinical trial shall be considered a minimal-intervention or low-intervention clinical trial.*	*1. Within seven days from the submission date, the reporting Member State shall validate Part I of application dossier referred to in Article 6 and notify the sponsor, through the EU portal, of the following:* *(a) whether the clinical trial applied for falls within the scope of this Regulation;* *(b) whether the application dossier is complete in accordance with Part I of Annex I;* *(c) whether it confirms that the clinical trial is a minimal-intervention or a low-intervention clinical trial, respectively, if such a claim was made by the sponsor.* ***2. The reporting Member State shall involve its ethics committee in the assessment of (1) (c).*** ***3.*** *Where the reporting Member State has not notified the sponsor within the period referred to in paragraph 1, the clinical trial applied for shall be deemed to fall within the scope of this Regulation and the application dossier shall be considered complete and, if applicable, the clinical trial shall be considered a minimal-intervention or low-intervention clinical trial.*

4. **Strengthening the role of the Reporting Member State/obligatory ethical evaluation of Part I of the application dossier**

In order to streamline the approval processes in multinational clinical trials it is necessary to give a stronger leading role to the RMS. For this reason, assessment by the RMS, including of the ethical aspects of the trial, as set out in Part I of the application dossier pursuant to Article 6 of the Regulation, should serve as a reference for the other MSCs.

To strengthen the mutual trust between Member States and foster high ethical standards, the ethics committees are to be involved in the assessment of ethical aspects of Part I of the application dossier, which must be included in the assessment report of the RMS. The MSC should complement the assessment by the RMS only when necessary, and be entitled to raise considerations from ethical, relevant national law or national standard of care perspectives.

Assessment of the German Medical Association*:*

- ***Strengthening the coordinating role of the RMS is supported, as this will reduce the duplication of effort, enabling Member States and sponsors to use resources more effectively while maintaining a high level of protection for participants, as well as the reliability of data.***

- ***The compulsory involvement of the competent ethics committee of the RMS in the evaluation of Part I of the application dossier is fully supported. This also corresponds to the legal situation in Germany.***

Amendment 2	
Article 6 (2) Sentence 2 Reg (EU) 536/2014	
Text Proposed by the Commission	**GMA Proposed Amendment**
The ethics committee of the reporting Member State shall review, from the ethical perspective, aspects covered by Part I of the assessment report. That ethical review shall complement the scientific and regulatory assessment and shall cover Part I of the application dossier in order to evaluate whether the subjects' rights, safety and well-being are being ensured in the clinical trial.	*The ethics committee of the reporting Member State shall review~~, from the ethical perspective,~~ aspects covered by Part I of the assessment report. That ~~ethical review shall complement the scientific and regulatory assessment and~~ shall cover Part I of the application dossier in order to evaluate whether the subjects' rights, safety and well-being are being ensured in the clinical trial* ***referred to Article 6 (1) a) and d) of this Regulation****.*

- ***The strengthened role of the RMS limits the aspects of the application dossier on which the MSC may submit considerations. While currently any considerations may be submitted, this will be limited to considerations that may result in a negative assessment by the competent ethics committee. This change is generally supported, as the restriction aims to reduce the total number of considerations and thereby the workload of the sponsors.***

5. Part II of the application dossier

The Member States Concerned should be able to rely on the assessment of the common aspects and elements of Part II of the application dossier to streamline the initial authorisation and make additional efficiency gains. To achieve this, MSCs may decide within 28 days of the submission date, whether to rely on the RMS's ethical review concerning the common elements of Part II of the application dossier and inform the applicant accordingly (Article 7 (2), third sentence).

Assessment of the German Medical Association:

- ***The 28-days timeline in Art. 7 (2) places the MSC in a situation where it has to decide on whether to rely on the RMS's ethical assessment of the common elements of the application dossier before having knowledge of the RMS's full assessment, which will only become available 42 days from the submission date (Art. 6 (4)). This uncertainty is increased by the fact that the common elements of Part II of the application dossier (pursuant to Part II of Annex I) have yet to be defined.***

- ***"Common elements" may include aspects and elements in which European legislation is relevant. These may include, for example, data protection and the handling of biological samples. In contrast, the qualification of investigators, the suitability of trial sites, and in particular the process of obtaining informed consent fall within the competence of the affected member states (MSC). An ethical assessment of these aspects by the RMS alone is not conceivable from a professional perspective.***

6. Role and tasks of the Clinical Trials Coordination and Advisory Group (CTAG)

The Commission envisages a closer cooperation between Member States' competent authorities and ethics committees to further align practices subject to national competence. This includes an extension of the role and tasks of the Clinical Trials Coordination and Advisory Group (CTAG). The CTAG would in particular be empowered to issue or endorse guidance documents related to clinical trials conduct and supervision.

The proposal provides that each Member State appoints one member and one alternate member to the CTAG for a term of three years, which may be renewed once. Both representatives should possess expertise in the field of clinical trials. The members of the CTAG are to be selected on the basis of their competence and experience in the field of clinical trials and are to represent the competent national authorities and the ethics committees of the Member States.

Assessment of the German Medical Association:

- ***Promoting the harmonisation of assessment aspects which fall within national competence is, in principle, supported. The proposed change in the composition of the CTAG, pursuant to Article 85(2) of the Regulation is also welcomed.***

- ***However, the significant expansion of the responsibilities of CTAG is viewed critically, particularly in the absence of a corresponding underpinning of its legitimacy. Considering the tasks assigned to the CTAG, including issuing or endorsing guidelines for the conduct and supervision of clinical trials, it is necessary to establish appropriate structures and procedures at both national and European level, in order to ensure that its work is reviewed for compliance with European law.***

Amendment 3	
Article 85 (3) Reg (EU) 536/2014	
Text Proposed by the Commission	**GMA Proposed Amendment**
For the purpose of the fulfilment of their tasks, CTAG members shall be able to rely on the contribution of experts from national competent authorities and ethics committees. These experts shall participate in CTAG meetings where relevant.	*For the purpose of the fulfilment of their tasks, CTAG members shall* ***~~be able to rely on the contribution of experts~~*** ***consult with representatives*** *from national competent authorities and ethics committees. These* ***~~experts~~*** ***representatives*** *shall participate in CTAG meetings where relevant.*

7. Combined Studies

Innovative and personalised therapies often combine medicinal products with medical devices, including in vitro diagnostic medical devices. When developing such therapies, clinical trials of one or more medicinal products may need to be combined with clinical investigation of one or more medical devices or performance studies of one or more in vitro diagnostic medical devices. The authorisation and conduct of such combined studies are complex due to the application of requirements of two or three pieces of Union health legislation and the fact that these are typically conducted across several Member States. To streamline these processes, the proposal introduces a dedicated pathway for the authorisation and conduct of such combined studies, involving coordinated assessment across Member States.

Assessment of the German Medical Association:

- ***A dedicated procedure for the assessment of applications for combined clinical trials as proposed in the new Article 14c of the Regulation is welcomed, but requires appropriate technical support through the integration of the relevant databases (CTIS and EUDAMED). This could be implemented in CTIS through the integration of additional modules.***

8. Risk-adapted approach for low- and minimal-intervention clinical trials

Based on the experience gained from the application of the Regulation, the Proposal seeks to further tailor the requirements for the authorisation and oversight of clinical trials according to the risks they pose to the participants. In this context, the risk categorisation scheme is

further refined by differentiating between *minimal-intervention clinical trials* which implies clinical trials with authorised products, and *low-intervention clinical trials* which use authorised medicinal products outside their initial marketing authorisation. Clinical trials that meet the criteria for minimal-intervention clinical trials should only require a prior ethical review.

Assessment of the German Medical Association:

- ***This provision is welcomed. Sponsors, in particular non-commercial sponsors who conduct the majority of minimal- and low-intervention clinical trials in the Union, would benefit from reduced administrative burden through simplified and risk-proportionate regulatory requirements, without compromising the safety, well-being and rights of participants.***

9. Inclusion of members of vulnerable groups in clinical trials

To ensure that clinical trials accurately represent the target population in all its diversity, and to enhance the treatment options for vulnerable populations, medicinal products which are likely to offer significant clinical benefit should be fully and appropriately studied for their effects in these specific groups. This includes requirements related to their specific characteristics and the protection of the health and well-being of participants belonging to these groups. The protection of vulnerable populations such as, e.g., incapacitated participants, minors and pregnant or breastfeeding women, requires a proper consideration of the risks of exclusion against risks of inclusion in clinical trials. This is in accordance with the 2024 version of the WMA's Declaration of Helsinki.

Assessment of the German Medical Association:

- ***It is expressly welcomed that, pursuant to the newly added Article 10(6) of the Regulation, the risks both of including or excluding vulnerable groups from clinical trials should be considered, in line with the 2024 revision of the Declaration of Helsinki. This will enable the balanced integration of vulnerable groups into research without compromising protection.***
- ***We recommend replacing the term "research subjects" with "research participants", as in the 2024 revision of the Declaration of Helsinki. The term "participants" seems more appropriate as it emphasises their active role.***

10. CTIS – Clinical Trials Information System

The Proposal provides that the European Medicines Agency, in consultation with the Commission, draws up a development plan for CTIS. This is intended to ensure that all required system functionalities are available by a date yet to be specified. A summary of the development plan with the key milestones and timelines is to be published on the Agency's website.

Assessment of the German Medical Association:

- ***The functionality of CTIS to fully support all current and future provisions of the Regulation is of fundamental importance. Due to severe disruptions in the functioning of CTIS experienced since its mandatory launch in 2022, an independent evaluation of the functionality of CTIS should be carried out prior to the preparation of the development plan, taking into account the feedback of all user groups.***

Amendment 4	
Article 98a Sentence 2 Reg (EU) 536/2014	
Text Proposed by the Commission	**GMA Proposed Amendment**
This would include a submission, after consulting the Commission, of a revised development plan for EU Portal and database to the Agency's Management Board 1 month after entry into force of Regulation (EU)…/… of the European Parliament and of the Council [include reference to Biotech Act proposal]. The development plan shall ensure that all required system functionalities are available by the date of application as defined in Article [..] of Regulation (EU)…/…[Biotech Act proposal].*	*This would include a submission, **after an evaluation of the EU Portal functionality by all stakeholder groups and** after consulting the Commission, of a revised development plan for EU Portal and database to the Agency's Management Board 1 month after entry into force of Regulation (EU)…/… of the European Parliament and of the Council [include reference to Biotech Act proposal].* The development plan shall ensure that all required system functionalities are available by the date of application as defined in Article [..] of Regulation (EU)…/…[Biotech Act proposal].*

11. Regulatory Sandboxes

Disruptive and innovative approaches to clinical trials may require adaptations to the rules governing clinical trial approvals and conduct. To harness the benefits of innovations while providing necessary safeguards, it is may become necessary to create a safe space for testing new regulatory approaches and technologies. This may include the use of AI in trial design, data collection, analysis and participant interaction.

To this end, the Commission proposes to establish controlled experimental environments in the form of *regulatory sandboxes*, allowing regulators to test new methods for authorising and conducting clinical trials, for example, when some requirements of the dossier cannot be fully complied with, while ensuring strong safeguards for participant protection and data robustness. Insights gained from sandbox activities should inform future guidance and, where appropriate, legislative amendments.

Assessment of the German Medical Association:

- ***The establishment of a regulatory sandbox through an implementing act (Article 27d(7)) would enable the Commission to derogate from the provisions of the Regulation without any limits being specified. This includes derogating from***

provisions central to protecting the rights, safety, and well-being of the persons concerned. Patient protection and ethical standards must not be compromised, even in the context of regulatory sandboxes. Substantive decisions that impact on fundamental rights require debate and proper involvement of the European Parliament and the Council and thus must not be taken through implementing acts by the Commission. It is therefore proposed to examine whether the establishment of regulatory sandboxes should occur via delegated acts pursuant to Article 89(5), or otherwise to specify limits in Article 27d to the derogations which regulatory sandboxes may provide.

Amendment 5	
Article 27d (7) Reg (EU) 536/2014	
Text Proposed by the Commission	**GMA Proposed Amendment**
7. The Commission may establish a regulatory sandbox by means of implementing acts, after taking into consideration opinions referred to in paragraph 6. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 88.	*7. The Commission may establish a regulatory sandbox by means of* ***~~implementing~~ delegated*** *acts, after taking into consideration opinions referred to in paragraph 6. Those* ***~~implementing~~ delegated*** *acts shall be adopted in accordance with* ***~~the examination procedure referred to in Article 88 and~~ Article 89 (5). Provisions of this regulation that are central to the protection of the rights, safety and well-being of the research participants remain unaffected.***
Article 89 (5) Reg (EU) 536/2014	
5. A delegated act adopted pursuant to Articles 27, 39, 45, 63(1) and 70 shall enter into force only if no objection has been expressed either by the European Parliament or the Council within a period of two months from notification of that act to the European Parliament and the Council or if, before the expiry of that period, the European Parliament and the Council have both informed the Commission that they will not object. That period shall be extended by two months at the initiative of the European Parliament or the Council.	*5. A delegated act adopted pursuant to Articles 27,* ***27d,*** *39, 45, 63(1) and 70 shall enter into force only if no objection has been expressed either by the European Parliament or the Council within a period of two months from notification of that act to the European Parliament and the Council or if, before the expiry of that period, the European Parliament and the Council have both informed the Commission that they will not object. That period shall be extended by two months at the initiative of the European Parliament or the Council.*

III. Additional Need for Amendment

1. Clinical Trials in Emergency Situations pursuant to Article 35 of Regulation

Regarding clinical trials in emergency situations, the Regulation follows the concept of presumed consent. Article 35(1)(b) ensures that the participation of individuals in emergency

situations incapable of giving consent is admissible if there is a scientifically justified expectation that the inclusion provides a direct individual benefit to the patient.

However, Article 35(1)(f) specifies that the clinical trial may only pose a minimal risk to, and impose a minimal burden on, the participant in comparison with the standard treatment of their condition. The GMA considers this additional requirement to be problematic. Being overly restrictive, it conflicts with the relevant provisions of the Declaration of Helsinki.

Article 28 of the Declaration of Helsinki requires that an intervention involving persons incapable of giving free and informed consent *either* personally benefits them *or* entails only minimal risk and minimal burden. Measures that are associated with only minimal risks and burdens in comparison to regular treatment, while still promising clinically relevant benefits are rare in the care of emergency patients. These patients are frequently seriously ill and require surgical care and/or intensive medical treatment. The restriction contained in point (f) significantly impedes inclusion in relevant clinical trials, given the already high protective requirements, and undermines efforts to obtain robust results in this sensitive area.

Amendment 6	
Article 35 (1) f) Reg (EU) 536/2014	
Current Regulation	**GMA Proposed Amendment**
(f) the clinical trial poses a minimal risk to, and imposes a minimal burden on, the subject in comparison with the standard treatment of the subject's condition.	~~**(f) the clinical trial poses a minimal risk to, and imposes a minimal burden on, the subject in comparison with the standard treatment of the subject's condition.**~~

2. Group-beneficial research pursuant to Article 31(1)(g)(ii) of the Regulation

Pursuant to the Regulation, incapacitated adult participants may be permitted to clinical trials which benefit the population (or group) which the incapacitated individual represents (Article 31(1)(g)(ii)), under defined conditions, provided that no stricter national rules have been enacted (Article 31(2)). This is the case in Germany where the German Medicinal Products Act (*Arzneimittelgesetz*) requires for clinical trials in accordance with Article 31(1)(g)(ii) express prior written consent of the individual concerned.

In such a declaration of consent (*Probandenverfügung*), a potential participant who is capable of giving informed consent may specify in writing, and following medical counselling, whether they consent to participation in certain future “group-beneficial clinical trials”, in the event of their future incapacity. In light of the current version of the Declaration of Helsinki, consideration should also be given to examining how experiences with the implementation of the national regulation have developed.

The Central Ethics Committee of the GMA has addressed this issue in its position paper "Group-beneficial Research with Incapacitated Persons" (in German).

The German version of this position paper is available on the website of the GMA.