The Standing Committee of European Doctors (CPME) represents national medical associations across Europe. We are committed to contributing the medical profession's point of view to EU and European policy-making through pro-active cooperation on a wide range of health and healthcare related issues.

CPME voting recommendations on the European Parliament draft report on Biotech Act

- CPME[1] reaffirms that competitiveness and bioethics are not opposing goals. Therefore, medical ethics, scientific progress and patients' rights are not competing priorities, but inseparable. We call on the European Parliament to protect patients and help avoiding dangerous simplifications that could cause harm to them, and recommends the following:

  - To **support the European Commission proposal (Article 83)** which states that Member States shall ensure that competent authorities and ethics committees are adequately resourced and have the necessary experts and financial resources for the performance of their activities.
  - **To support amendment 991** which includes a reference to the World Medical Association's Declaration of Taipei regarding research involving health data, together with the Declaration of Helsinki.
  - **To support amendment 2528** that adds the part in bold to the definition of 'Informed consent' means a subject's free and voluntary expression of his or her willingness to participate in a particular clinical trial, after having been informed **in clear and understandable language which is tailored to his or her level of understanding** of all aspects of the clinical trial, that are relevant to the subject's decision to participate
  - **To reject amendment 370** which proposes the creation of a Clinical Trials Experts Committee chaired by the EMA, with one representative per Member State who would represent both the national competent authority and the national ethics committee, combining these two distinct and independent roles in a single representative.
  - **To reject amendment 271** which gives the Reporting Member State (RMS) a leading role in the assessment within the Clinical Trials Expert Committee.
  - **To reject amendment 288** that foresees that, within the Clinical Trials Expert Committee, the Reporting Member State should draw up a draft Part I of the Assessment Report and circulate it to the Clinical Trials Expert Committee.
  - **To reject amendment 291** which proposes that the Clinical Trials Expert Committee is to be responsible for evaluating and coordinating the feedback received from the Member States

[1] The CPME response to the European Commission questionnaire on the Biotech Act may be accessed here, the CPME statement on this matter may be accessed here, the CPME response to the European Commission Clinical Trials Study Survey may be accessed here, and the joint statement on the Biotech Act proposal together with the European Network of Research Ethics Committees (EUREC) and the Council for International Organizations of Medical Sciences (CIOMS) is available here.

on Part I of the Assessment Report. The RMS would play a leading role here, in that it is required to "take due account" of the feedback from the Member States Concerned (MSC) during the committee review phase.

- **To reject amendment 335** which introduces an accelerated and special procedure for the authorisation of multinational clinical trials. Under it, the Clinical Trials Advisory Group (CTAG) facilitates the procedure, maintains the list of participating Member States, provides a forum for best practice and advises the Commission. It also nominates two scientific representatives from technical experts in participating Member States for the Part I scientific assessment, including at least one ERN-designated expert for ERN-coordinated trials. EMA would then issue a single authorisation decision, including an integrated ethics opinion, within seven calendar days of validation.
- **To reject amendment 2879** which proposes the creation of an Ethical Assessment Committee within the Clinical Trials Advisory Group (CTAG), a body under the Clinical Trials Coordination and Advisory Group.

CPME position

- We see as a positive development in the Commission proposal the reinforced role of Research Ethics Committees in the governance of clinical trials, including their participation in coordination structures such as the Clinical Trials Coordination and Advisory Group (CTAG) (new Art. 85 para. 2 Clinical Trials Regulation), as it strengthens the integration of ethical oversight.
- In our view, strengthening research ethics committees networks across the EU, together with adequate and sustained funding, is essential to ensure timely and robust ethical review, also in emergency situations, and to implement accelerated (authorisation) procedures as envisaged under the Biotech Act (Art. 14b). Beyond the reinforced coordination between Competent Authorities and Ethics Committees as promoted by new Art. 83a CTR, we must stress the necessity to support and facilitate the networking of the Ethics Committees themselves. This is an essential condition for the harmonious implementation of the Biotech Act Proposal.
- Efforts to make European clinical research more efficient and attractive, including through better coordination, harmonised documentation, improved functioning of Clinical Trials Information System (CTIS) and proportionate regulatory requirements is fully supported. It is also believed that particular attention should be paid to investigator-initiated and non-commercial research, which may be disproportionately affected by increasingly short administrative deadlines.
- However, simplification should not come at the expense of independent ethical review or the ability of national ethics committees to take account of relevant local circumstances. Before introducing fundamentally new structures for ethical review, it would therefore seem valuable to engage closely with the national competent authorities and research ethics committees to understand how the current procedures function in practice, where the actual obstacles arise, and which improvements could be achieved without compromising existing safeguards.
- **In relation to the importance of independent national ethical review**

- The main concern with the proposal above is the difficulty of a single representative adequately representing both the national competent authority and the national research ethics committee. These bodies have different and distinct responsibilities and assess clinical trials from different perspectives. Their conclusions do not necessarily coincide.
- Also, an appropriate ethical assessment requires both medical and scientific expertise and the involvement of lay members who can contribute the perspective of research participants. These assessments must consider national circumstances, including the healthcare system, standards of care, patient populations and relevant cultural and societal considerations.
- If the national authorities and ethics committees would still need to conduct their respective assessments before a representative could participate meaningfully in a European committee, the proposed system might simply introduce an additional decision-making layer rather than reduce bureaucracy. Alternatively, ensuring adequate representation of all relevant perspectives at European level could require several representatives from each Member State, with considerable implications for resources, coordination and timelines.

- **In relation to the national decision-making authority and the Declaration of Helsinki**
  - The Declaration of Helsinki emphasises the importance of independent ethical review and sufficient familiarity with local circumstances and context. This is particularly important because standards of care, patient populations, legal frameworks and cultural circumstances may differ considerably between countries.
  - Therefore, we are concerned with the possibility of a Member State being required to accept an ethical assessment with which its own research ethics committee disagrees.
  - For instance, a comparator treatment considered acceptable by a central research ethics committee in a multinational trial might represent standard care in several participating countries but be inferior to the treatment routinely offered to patients in another country. In such circumstances, exposing participants to the comparator treatment could raise serious ethical concerns in that particular country where stand of care is better than the offered treatment in the comparator arm. Research participants in that country will therefore risk substandard treatment while participating in the trial. This illustrates why a scientific and ethical assessment cannot be entirely separated from national clinical practice and why meaningful national ethical review remains essential.
  - There is therefore a particular concern with arrangements under which a central majority decision could effectively replace the conclusion of an independent national research ethics committee.
  - This is not simply a question of administrative organisation or efficiency. It concerns the protection of research participants, the independence of ethical review and the responsibility of individual Member States for research conducted within their healthcare systems.

    - Ultimately, maintaining public trust in medical research, research ethics committees and the medical profession is essential.
- The proposal for an accelerated and special procedure for the authorisation of multinational clinical trials raises a concern: a central ethics opinion issued on such a short timeline could effectively replace national ethical review, removing the local, independent assessment that protects participants and takes national legal, clinical and cultural contexts into account.
- We have strong reservations regarding this accelerated procedure and the proposed Standing Ethics Panel within EMA for certain ERN-coordinated rare disease trials, where a central ethical opinion would replace national ethical review entirely.
- This procedure fails to meet key international requirements for an independent ethical assessment of research projects in the interests of protection of participants if authorisation can be granted exclusively by a central Standing Ethics Panel at the EMA level.
- Although the importance of facilitating research into rare and ultra-rare diseases is fully recognised, the small number of participants in individual countries is not considered to be a sufficient justification for removing independent national ethical oversight. Such trials are already being conducted through the existing multinational framework.

CPME position

- We see with some concern the proposal to establish an Ethical Assessment Committee within CTAG. It is recognised that representation drawn specifically from national ethics committees, including lay representation, would address some of the concerns associated with combining regulatory and ethical responsibilities in a single Clinical Trials Expert Committee representative. However, important questions remain concerning the practical functioning of such a committee, the resources required and, above all, its relationship with national research ethics committees. In particular, it would be important to clarify whether the committee's conclusions could become binding on Member States, including where a national ethics committee has reached a different conclusion. If national assessments must be undertaken before representatives can participate, it is also unclear how the proposed structure would deliver the intended efficiency gains.