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EORTC reply to the public consultation on the risk proportionate approaches in clinical trials.

Though EORTC does not have any specific comment to the content of the proposed recommendation, in our view, it does not bring much added value to the subject, already extensively discussed during the last decade and documented by OECD (indeed referred to) and other stakeholders.

EORTC would suggest developing a practical and straightforward tool such as a checklist with predefined risks levels per criteria that would

- help the sponsors
- harmonize risk identification and control across sponsors
- facilitate the review by the Competent Authorities.

Similar tools already exist and can be found in public domain, but they are not validated or otherwise endorsed by any competent authority or other competent bodies. Therefore, an EU guideline would constitute a valuable and practical support to sponsors.
Similarly, the document refers to the risk assessment and mitigation plan and EORTC believes that development of a template for such a document would be helpful.

Though we understand the limits set-up by the clinical trials regulation and despite the fact this document clarifies that risk adaptation is relevant to any clinical trial, it is worded and organized around the marketing authorization time point and its general logic follows the classical drug development timeline. We believe this approach does not fit anymore the clinical research landscape, specifically with regards to the oncology field.When a drugis on the market, verylittleisknown and thisis not a criteria to relax any type of monitoring, specially on safety. In the era of mechanismbased treatment and immunotherapy, challenges such as long termsafety monitoring are crucial and not developed in the propsoed guideline.On the other hand, a well documented drug may be used outside the label within a comparable type of patient population with though a different disease and in our view, despite the fact that this situation will not fit into the low intervention trial definition as per regulation would largely justify risk adaptation.

Reallife and pragmatic clinical trials which are critical to assess the value of treatmentshave not been properly taken into account, though today part of the full landscape.If shorter routes to drug development such as the implementation of MAPPs, further sustained monitoring beyond the marketing authorization will be needed. Last but not least, in the era of mechanism based treatment and immunotherapy, questions such as long term safety monitoring is crucial and not developed in this document.

All these aspects may be taken into consideration within the practical tool(s) we recommend above to be developed.