ADVICE FOR BELGIAN ETHICS COMMITTEES ON THE ASSESSMENT OF SAFETY REPORTS AFTER CTR ENTERING INTO APPLICATION

The role of the Belgian ethics committees recognized under the law of 7 May 2017 (ECs) in safety assessment for the clinical trials evaluated under the CTR was unclear for the ethics committees represented in the working group (WG) CTR-MDR. The WG asked for a clear position of the Board members of the College.

Abbreviations used below

ASR: Annual safety Report, previously DSUR
College: the College as described in the law of 7 May 2017 on clinical trials on medicinal products for human use
CT: Clinical Trial
CTA: Clinical Trial Application
CTIS: Clinical Trials Information System
CTR: Clinical Trial Regulation, Regulation (EU) No 536/2014
DSUR: Development Safety Update Reports
EC: Belgian ethics committee recognized under the law of 7 May 2017
IMP: Investigational Medicinal Product
saMS: safety assessing member state
SUSAR: Suspected Unexpected Serious Adverse Reaction

Question addressed in this advice

MUST THE ECS EVALUATE, OR BE INVOLVED IN THE EVALUATION OF, THE ANNUAL SAFETY REPORTS (ASRS) AND SUSPECTED UNEXPECTED SERIOUS ADVERSE REACTIONS (SUSARS) FOR INVESTIGATIONAL MEDICINAL PRODUCTS USED IN CLINICAL TRIALS THAT WERE SUBMITTED VIA THE CLINICAL TRIALS INFORMATION SYSTEM (CTIS)?

Context

For IMPs used in clinical trials that are **evaluated under the CTR**, sponsors have to submit SUSARs via the EudraVigilance database, and the ASRs via the dedicated module in CTIS. The evaluation of SUSARs and ASRs by the member states will be coordinated by the **safety assessing member state** (saMS). Per IMP one saMS is selected. An Implementing Regulation for Safety cooperation will be prepared.

In article 44 of the **CTR** is mentioned that the responsible ethics committee is to be involved in the safety assessment if required per national law.

The **Belgian Law of 7 May 2017 concerning clinical trials with medicinal products for human use does not stipulate** that the ECs must be involved in the evaluation of SUSARs and ASRs, therefore, there is no legal obligation under the CTR for the ECs to be involved in the evaluation.

In the current **CTIS** model for Belgium, the ECs and the College do not have access to SUSARs and ASRs. Only the FAMHP has access to the ASRs in CTIS, and the SUSARs in EudraVigilance. When Belgium is assigned saMS for an IMP, the national contact point of the FAMHP will coordinate the safety assessment.

The evaluating EC, however, does have access in CTIS to **other safety related information that is CT-related, which can be consulted if considered necessary.** It concerns a.o. serious adverse events, serious breaches, urgent safety measures. If ECs have questions for the sponsor or concerns regarding this information they can transfer them, via the College, to the FAMHP. More details are given at the end of this document, in the Annex.

The ECs will also receive for assessment all updates of the **Investigator's Brochure** via substantial modifications.

Advice

The College Board considers the Ethics Committees do not have a formal role in the assessment of ASRs and SUSARs as this responsibility is not assigned to them via the current Belgian legislation.

Annex

Other safety related notifications **per CT** uploaded in CTIS by the sponsor are

a) Temporary halt
   Notification to inform an interruption of the trial, applied by the sponsor and not foreseen in the protocol. The hold is on temporary basis with the intention to resume the trial. It can be related to subject safety and/or benefit-risk balance or not.
b) Serious breach
   Notification to inform of a breach likely to affect to a significant degree the safety and rights of a subject or the reliability and robustness of the data generated in the CT.
c) Unexpected events
   Notification of an incident that might influence the benefit-risk assessment of the medical product or that would lead to changes in the administration of a medical product or the overall conduct of a CT (e.g. a significant hazard to the patient population).
d) Urgent safety measure (USM)
   Notification of an unexpected event that is likely to affect the benefit-risk balance of a CT significantly, and the appropriate urgent safety measures to protect the subjects that have been taken by the sponsor and/or the investigator.
e) SUSAR-related notification
   For the definition of SUSAR, please refer to article 2 and article 42 of the CTR.
f) IMP class and mode of action
   A safety issue affecting medicinal products with a similar mode of action.
g) Other
   Relevant information to the supervision of a trial.