The CTFG Reference Safety Information Q&A document published on the CTFG website on the 12th of November 2017 (version 1.0). The document was developed to provide clarity to sponsors about the expectations of EU national competent authorities in relation to the reference safety information for determination of SUSARs for expedited reporting and annual safety reporting in clinical trials. The publication of the Q&A followed detailed discussions between national competent authorities and sponsors, which arose from clinical trial application and substantial amendment procedures, as well as GCP inspections.

The CTFG Reference Safety Information Q&A document should be considered as being applicable from the publication date and sponsors are encouraged to update the reference safety information (RSI) section of the Investigator’s Brochure (IB) to comply with the procedures set out in the Q&A at the earliest opportunity. CTFG acknowledges that a number of important changes to sponsor procedures may be necessary in order to comply with the new guideline for RSI. As such, the CTFG advises that a 1-year transition period will apply for the duration of 2018 (i.e. from 1/1/2018 to 31/12/2018) before the recommendations outlined in the Q&A are strictly enforced by national competent authorities. During this period, clinical trial applications and/or substantial amendment dossiers will not be rejected if the RSI is not completely in line the Q&A, and when the IB contains a clear RSI section that is fit for purpose is submitted. Specifically, it should be clear:

- which serious adverse reactions are considered expected. If ‘Suspected’ SARs that have occurred once are included in the RSI, a robust justification based on medical judgement and evidence of a very strong plausibility of a causal relationship with the IMP should be provided;
- that frequency provided is calculated on an aggregated level and based on previously observed ‘suspected’ SARs to the IMP;
- all fatal adverse reactions are considered unexpected, unless IMP has a marketing authorization and these fatal adverse reactions are clearly listed as such in the section 4.8 of the SmPC.

IBs that were completed in 2017 in advance of the publication of the Q&A with an RSI section that do not completely comply with the guideline of the Q&A will still be acceptable for authorisations in Member States in 2018. Nonetheless, comments on the RSI may be raised and the sponsor will be expected to update the RSI section accordingly at the next routine IB update. The national competent authorities represented at CTFG plan to implement the guidance more strictly from 1/1/2019, and submission of an application and/or substantial amendment with an RSI that does not comply with the guidelines outlined in the Q&A risks being rejected.