Guideline CTIS trial submission

Date: 16-07-2023

Impact ECTR: Active involvement of coordinating investigators and pharmaceutical company during the development phase of the trial until authorization (approval)

Per 31st January 2022 the European Clinical Trial Regulation (ECTR) became effective.
It aims to ensure the EU offers an attractive and favourable environment for carrying out clinical research on a large scale, with high standards of public transparency and safety for clinical trial participants. All participating countries in EU (also called member states (MS)) need to adhere to the ECTR.
As the ECTR dictates very strict timelines during the development phase of a trial, HOVON as sponsor of the trial, has summarized the most important aspects where the input and feedback of the several parties is required in order to avoid a delay in starting all sites.

INPUT COORDINATING INVESTIGATOR OF THE MS TO HOVON:

- *Between first contact global clinical project manager HOVON and final protocol*
  - List of participating sites in MS
  - Signed collaboration Agreement including Document of Responsibilities (DoR) between HOVON - MS
  - List of required part II documents MS
  - Confirmation from MS if IMP and/or axMP can be used commercially and if labels are required
  - CVs of participating investigators (HOVON/EMA template)
  - Signed Declaration of Interest (HOVON template)
  - Site suitability (MS template)
  - Review of label text
  - Overview of third parties (monitor, central lab etc)

At moment of final protocol: HOVON will inform MS about submission date. After this the timelines are very sensitive!

- *At moment of final protocol* *~Time sensitive~*
  - Translation of required documents in MS
  - Collection of part II required documents in MS

Please note: If the deadline is not met, the submission will proceed without the MS and the MS can only be added afterwards by means of a so called Substantial Modification. This will cause a delay of at least 6 months before the first site of the MS concerned can be activated.

- *Submission and evaluation* *~Critical timelines determined by EMA~*
  - MS needs to be available for Request For Information (RFI) during validation and/or assessment
  - MS needs to provide and/or collect changed docs if requested

<u>Please note:</u> Short timelines for responses (10-12 calendar days). If deadline is missed the application of MS is withdrawn, see third phase for consequences MS concerned

A redacted/public version needs to be available of every document (no signature, no personal data) as required by EMA.

INPUT PHARMACEUTICAL COMPANY TO HOVON (SPONSOR)

- *During protocol development*
  - Signed collaboration agreement HOVON-company
  - Provide IB, SmPC, SUSAR line listings
  - Together with HOVON determine if IMP and/or axMP can be used commercially and if labels are required
  - Batch release certification docs
  - Label design review
  - Supply chain documentation
  - Overview of third parties used by pharma if applicable
  - Shipment of drug to vendor if applicable

At moment of final protocol: HOVON will inform company about submission date. After this timelines are very sensitive!

- *At moment of final protocol ~Time sensitive~*
  - Updated SUSAR line listings for IB and/or statement if IB > 1year old
  - QP declaration

<u>Please note:</u> If deadlines are not met the trial can't be submitted causing a delay of trial start

- *Submission and evaluation ~Critical timelines determined by EMA~*
  - Submission of IMPD
  - Company needs to be available for RFI during validation and/or assessment
  - Company needs to provide and/or collect changed docs concerning the IMP

<u>Please note:</u> Short timelines for responses (10-12 calendar days). If deadline is missed the application of the trial is withdrawn and the whole submission process starts again!

A redacted/public version needs to be available of every document (no signature, no personal data) as required by EMA.