Draft EMA Policy

Publication and access of clinical-trial data

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Relevance of CDISC Standards for Submissions to EMA

- So far, datasets and metadata are not included in submissions

- Draft Policy: Publication and access to clinical-trial data (24-Jun-2013)
  - based on full transparency requests by many different stakeholders
  - Final Goal: allow for independent meta-analysis or re-analysis
  - Difficulties
    - → Need to protect confidential information
    - → Standard formats for data+metadata are needed for efficient further analyses
  - Currently differentiates between different types of data
    - → e.g. summarized results vs. "raw data“

- "In future, CDISC shall be the required standard, in line with future guidance from the Agency"
  (http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/06/WC500144730.pdf)

Summary of Draft Policy

- Level of proactive publication depends on “data” category
  - Commercially Confidential Information (CCI),
    e.g., details on the investigational product
    → Will not be made available under this policy
  - Open Access (O),
    all data without protection of personal data concerns,
    e.g., summary tables presenting only aggregated data
    → Will be available as downloads from the Agency’s website
    at the time of European Public Assessment Report (EPAR)
  - Controlled Access (C),
    all data with protection of personal data concerns,
    e.g., “raw data” on subject level
    → Will be granted to requesters if a set of requirement are fulfilled
    at the time of EPAR
- Elements of eCTD for registration/CSR are categorized accordingly in Annexes I an II of the draft policy

Definition of Raw data

- For the purpose of the policy, raw CT data shall mean
  - individual patient data sets,
  - individual patient line-listings,
  - individual Case Report Forms (CRFs),
  - and documentation explaining the structure and content of data sets (e.g. annotated CRF, variable definitions, data-derivation specifications, data-set definition file).
- It also includes supporting documents, such as
  - test outputs (if not contained in the statistical analysis plan (SAP)),
  - Statistical Analysis Software logs
  - and SAS statistical programs (if code not included in the SAP).

Summary of Draft Policy (continued)

- Expected effective date: 01-Jan-2014
- Expected applicability: all EMA submission at or after 01-Mar-2013

- "Marketing-authorisation holders/applicants shall provide the Agency with an additional set of 'O' documents that are appropriately de-identified to ensure protection of personal data, as per Annexes I and II."
- "Particular care should be taken by the sponsor to ensure that no personal data are included in this section. Key codes, dates of birth and any other indirect identifiers shall not be included unless adequately de-identified (e.g. date of birth transformed to age group), particularly if many indirect identifiers appear jointly for the same individual."

Further Quotes of Interest to CDISC Users

- “Wherever technically possible, analysable, de-identified raw CT data shall be made available for downloading in the format in which they have been analysed by the applicant, submitted and evaluated. For the time being, this can be according to CDISC (Clinical Data Interchange Standards Consortium) or other appropriate standard. In future, CDISC shall be the required standard, in line with future guidance from the Agency. No conversion of formats is recommended, either by the marketing-authorisation holder or the Agency.”
- “The Agency is committed to making 'C' data available as early as is practical. However, in light of the paramount importance of ensuring patient confidentiality, preparatory steps are required to put in place appropriate standards, rules and procedures for de-identification. The Agency will work with sponsors and other concerned parties towards this goal, and expects to publish a guidance document no later than 31 October 2014, with a view to making available all 'C' data submitted by sponsors on or after 1 January 2015.”

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Discussion Topics

- Do informed consent forms include the additional review/analysis by 3rd parties? Does that have to be included?
- Does the applicant have a choice not to submit electronic data, etc. and by doing so avoid that data can be accessed by third parties because the EMA can only grant access to data they received as part of an application?
- If datasets are required but subsets of data are acceptable, who defines the relevant subset?
- Will the datasets be used to aid in the review process of an application by the agency, e.g. to recalculate the main results?
- Will the datasets just need to be provided so that access can be granted to third parties when requested?
- The appropriate de-identification of the data would be a new extra step in the process of analyzing and filing CT data.