c) Impact of local regulations to CDM

Changes to global regulations such as ICH E6 generate a lot of attention from Clinical Development stakeholders as Good Clinical Practice defines our foundational principles. While less visible, local regulations may still have significant impact to Clinical Development including CDM activities with the risk of local inspection findings affecting global studies and potentially submissions.

As a first example, new **local German requirements** were introduced in January 2018 regarding the "timely" review of the CRF data by "medically qualified" personnel and the endorsement of the data by the Primary Investigator (PI) at regular/critical timepoints. Some companies may decide to apply these requirements to German sites only; others to all sites. Whatever the decision is, the ability to implement, monitor and demonstrate adherence to these requirements may depend on the flexibility of the EDC system. CDM would likely have to adjust the set-up of eCRF signatures in EDC, document the approach in the Data Management Plan and potentially create custom reports to help monitor the "timeliness" of the review by the Investigator as attested by their signatures on the eCRF. The implementation strategy must be tailored by each company and CDM has a key role to play in in ensuring the compliance to those requirements.

As a second example, the **Chinese Reform on Leading PIs** for Medical Device released in October 2017 further illustrates the impact of local regulations to CDM. The requirement is that Chinese device studies involving more than three (3) sites must have a leading Site/PI assigned. Per local regulations, the leading PI is considered responsible for "clinical data administration and analysis" which includes CDM, Statistical Analysis and Report Writing. Even though individual company interpretations may differ on this, there is no dispute of the fact that the lead PI needs some level of oversight of CDM activities across all Chinese sites. To an extreme, oversight may be understood by some companies as the need for the lead PI to approve CDM Documents (e.g. eCRF Specifications, DM Plan) and/or to manage a CRO performing the CDM activities. To complicate the situation further, this local regulation does not apply to Drug studies conducted in China.

The goal of this reflection paper is not to provide guidance on how to implement local regulations but to raise awareness of the rising complexity for CDM. Local regulations are now going beyond the typical data privacy regulations that CDM has been mostly addressing to date. CDM needs to work closely with regional regulatory and operational teams to assess and implement solutions that comply to local regulations because study level processes and data handling conventions may differ by country.