Comments on European Commission consultation document *„Risk proportionate approaches in clinical trials“*.
Submitted by Dr. Ingo Rath of CliPS - Clinical Project Services®, Malvenweg 51, 48163 Münster, Germany.

Line Number (s)	Comment(s)	Proposed Action(s)
54	The wording *“**Many** clinical trials, however, pose a minimal additional risk…”* overemphasizes the proportion of low interventional clinical trials and gives the impression that such trials are commonly found throughout phases I to III as well. Line 110 uses the much more adequate word “some” instead of “many” to describe the same type of trials.	Replace *“many”* by *“some”*.
387, 388, 394, 398, 452	The option to completely replace on-site monitoring by centralised monitoring is mentioned somewhat in abundance giving the impression that this option could apply to various types of trials. Article 48 of EU Regulation 536/2014 clearly states that monitoring must verify that subjects’ rights are protected and that reported data are reliable and robust. This includes checking the informed consent form and doing at least some degree of source data verification both of which can only be achieved adequately during on-site monitoring. ICH-GCP (5.18.3) is quite clear on this topic: *“In general there is a need for on-site monitoring […]; however **in exceptional circumstances** […] central monitoring in conjunction with procedures […] can assure appropriate conduct.”* EU Regulation 536/2014 in its rationale (43 and 80) clearly acknowledges ICH-GCP. The option to completely replace on-site monitoring by centralised monitoring should therefore remain an exception to the rule.	Use more restrictive wording when describing the possibility to replace on-site monitoring by centralised monitoring. It should become clear from the text that this option (i.e. no on-site monitoring) is an exception to the rule.
388	The wording *“On-site monitoring remains relevant in **certain** types of clinical trials…”* gives the impression that on-site monitoring has become or should become a rare species endemic to a minority of clinical trials. The opposite should be the case (see above).	Replace *“certain”* by *“most”*.
421	The wording *“…should include utilisation of **one or** a combination of approaches listed below…”* would allow that (e.g.) trial oversight by a DMC could be the one and only monitoring approach and that there could be trials with neither on-site nor centralised monitoring.	Alternative wording: *“A risk based approach to monitoring can include multiple monitoring and oversight tools such as: …”*