European Federation of Pharmaceutical Industries and Associations

Draft ☐ Final ☒

Submission of EFPIA comments on Public consultation on detailed arrangements for clinical trial inspection procedures including the qualification and training requirements for inspectors pursuant to Article 78(7) of Regulation (EU) No 536/2014

Author: EFPIA **Date:** 24 November 2015 **Version:** Final

1. General comments

Comment nro	General comment (if any)	Outcome (if applicable)
1.	EFPIA welcomes the opportunity to provide comments on the Commission detailed arrangement for clinical trials inspection procedures including the qualifications and training requirements for inspectors.	
2.	EFPIA finds it very important that the document guides towards harmonization of inspection procedures and training throughout the EU, in order to ensure consistency of inspectors' expectations and assessments across member states. We suggest several amendments to be made in the document, which can be found in more specific comments.	

2. Specific comments on text

Line number(s)	Comment and rationale; proposed changes *(If changes to the wording are suggested, they are highlighted)*	Outcome (if applicable)
26-27	**Comment**: Edit proposed. **Proposed change (if any):** Inspectors should verify that principles *of* good clinical practice and requirements of Regulation (EU) No 536/2014 are implemented effectively.	
68-70	**Comment:** It should be added that inspectors should have practical field experience. **Proposed change (if any):** "Inspectors shall have completed education at university level, or have equivalent experience, in medicine, pharmacy, pharmacology, toxicology or other fields relevant to Good Clinical Practice principles. *In addition, inspectors should have previous practical field experience before being trained as inspectors. "*	
86-87	**Comment:** It is welcomed that a degree of risk assessment is applied by the inspectors. However, this relies on the consistency of approach and understanding of inspectors. Risk assessment should be clarified to focus on risks that have significant impacts on subject safety or data integrity. It is expected that training is undertaken by the EMA to ensure that inspectors have a consistency of understanding of this aspect. **Proposed change (if any):** Training of inspectors on on-site risk assessment considerations should be included in annual training with examples brought forward annually to ensure consistency. *Inspectors shall also be able to apply an appropriate degree of risk assessment, in particular relating to findings having an impact on subject safety and/or data integrity versus findings having no such impact.*	
97-99	**Comment:** 1. It should be stated that inspector should not only access, but also follow standard operating procedures.	

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	2. We propose inspection procedures and training requirements to be harmonized and standardised across the EU. **Proposed change (if any):** "Each inspector shall have access to *and comply with* standard operating procedures and details of their duties, responsibilities and ongoing training requirements. Member States shall *harmonize and* maintain those procedures up to date."	
116-118	**Comment:** It is understood that a number of inspectors have previously worked in the pharmaceutical industry. Although not having a current interest, it is expected that there is a definitive time period before which they are allowed to return to a company where they previously worked to inspect. **Proposed change (if any):** Inspectors should not inspect an organisation where they were previously employed until a period of 5 years has elapsed.	
129-131	**Comment:** This appears to indicate that non-EU trials will be assessed according to requirements established directly under Regulation (EU) No 536/2014. **Proposed change (if any):** Inspectors shall verify the compliance of the inspected party with principles of good clinical practice and with the requirements of Regulation (EU) No 536/2014, and with relevant national legislation. Where the trial is conducted in a third country, equivalent standards of GCP are expected and will be assessed.	
138-143	**Comment:** It is not clear whether the third country authority will be informed that an inspection is taking place, and whether they will have access to the report. **Proposed changes:** Member States shall establish national procedures for at least the following actions: (a) appointing experts to accompany inspectors in case of need, and who will be bound by the same rules of confidentiality and conflict of interest as inspectors; (b) arranging inspections in third countries; *third countries authorities shall be informed accordingly*	

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151-154	**Comment:** The extent of documentation that can be shared should be clarified. **Proposed change (if any):** To verify compliance with the principles of good clinical practice, the inspectors shall be entitled to inspect the sites, documents, facilities, records, quality assurance arrangements (*but not audit reports, as a routine*), data and any other resources that are deemed by the competent authority to be related to the clinical trial.	
164-168	**Comment:** Provision of sufficient resources is very subjective. Article 78 of Regulation 536/2014 indicates that inspections should be performed in order to supervise compliance with the legislation. However, no guidance is included. One of the concerns about resources is the timely issuance of inspection reports. **Proposed change (if any):** It is proposed that the GCP IWG determine what an appropriate level of supervision is and work together to avoid duplication of effort. For example if an organisation has a particular trial inspected by ANSM, and the same company gets inspected by MPA, the latter inspection should take into consideration the earlier conducted inspection and choose another trial unless there are grounds for repeated inspections of a particular trial. If this is the case, then a CHMP request would be appropriate. The inspections undertaken at a local level should be taken into consideration when inspection requests are made by CHMP. "In particular an adequate number of inspectors shall be appointed to ensure effective verification of compliance with good clinical practice and with the requirements of Regulation (EU) No 536/2014 *and to allow timely reporting of inspection findings".*	
175-183	**Comment:** Consider adding a review process to ensure harmonization, or at least an escalation mechanism in case an inspected party disagrees with an inspection finding or its criticality in a given MS.	
185-191	**Comment:** For GCP inspections conducted on behalf of the EU, e.g. CHMP	

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	requested inspections, it is essential that there is consistency in the grading of inspection findings and in the overall assessment of the impact of the findings. **Proposed change (if any):** It is recommended that the EMA should implement a process to formally review Inspection Reports for inspections conducted on behalf of the EU, where critical inspection findings are identified, in order to verify the consistency of the grading(s) in comparison to findings of the same type from other inspections and the robustness of the conclusions reached by the inspection team (in particular where the inspection relates to a marketing authorisation application). This process also applies in case multiple minor findings lead to a major finding. This review would go beyond validating that the correct report template has been used. For example, a sub-group of the GCP IWG could act as a panel to review such inspection reports and to make recommendations to the EMA. This may help to promote quality and consistency across the EU GCP inspection network. If the sponsor's answer to this proposal is rejected, then it is recommended that an appeals procedure is implemented whereby sponsors can request a GCP IWG panel to re-examine the grading of critical GCP inspection findings, in circumstances where evidence exists that the grading or conclusions reached may be inappropriate. Consideration should be given on the appropriateness of breaking down findings into individual critical findings when they are clearly a systemic failure in one area.	
194-198	**Comment:** It is not clear whether the inspection report to be uploaded to the portal will include the inspected party's responses to findings. **Proposed change (if any):** "Without prejudice to the obligation to submit the inspection reports**,** *including responses,* via the EU Portal….." The inspected party shall have the right to respond to inspection findings before the report is finalised.	