PDA Global Headquarters
Bethesda Towers,
Suite 600
4350 East West Highway
Bethesda, MD 20814 USA
TEL: +1 (301) 656-5900
FAX: +1 (301) 986-0296

PDA Europe gGmbH
Am Borsigturm 60
13507 Berlin
Germany

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Dr. Sabine Kopp
Group Lead, Medicines Quality Assurance
Department of Essential Medicines and Health Products
World Health Organization
CH-1211 Geneva 27
Switzerland

Reference: Draft guideline on data integrity (working document QAS/19.819)

Dear Dr. Kopp:

PDA appreciates the opportunity to comment on WHO's draft guideline on data integrity, working document QAS/19.819. We present our comments in the attached table.

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our comments have been prepared by a committee of PDA members with expertise in data integrity and regulatory issues in pharmaceutical and biopharmaceutical manufacturing on behalf of PDA's Regulatory and Quality Advisory Board and Board of Directors.

If you have any questions, please do not hesitate to contact me via email at johnson@pda.org.

Sincerely,

Richard Johnson
President and CEO

Comments on WHO Working Document QAS/19.819
Title of the document : Guideline on Data Integrity

Comments submitted by : Parenteral Drug Association
Telephone number : +1 301 656 5900
Address : 4350 East West Highway suite 600, Bethesda, Maryland, 20815, USA
Email : johnson@pda.org
Date : January 15, 2020
*Kindly complete the table **without modifying the format** of the document - thank you.*

General comment(s) if any :	**Originator of the comments**
PDA suggests that WHO revise the document to include a section on Rationale and Purpose, which would better allow comment on whether the draft guideline achieves WHO's goal. For instance, if WHO's intent is to provide general guidance on data integrity management, PDA likely would suggest reorienting this document to begin with such steps as identifying data, determining data flow, knowing systems, determining system functionality/architecture, and defining system configuration. That knowledge is critical to numerous other steps including policy/procedure development and training, and to the successful implementation of quality risk management (QRM). If, on the other hand, WHO's intent is to guide the use of QRM in data integrity, PDA would provide different input. PDA looks forward to providing this input in the anticipated second round of comment. The Rationale and Purpose section also could clarify the relationship between this document and the 2016 WHO Guidance on good data and record management practices, published as Annex 5 to WHO Technical Report series No. 996. If this guideline will supersede the 2016 guidance, commenters may suggest the inclusion here of additional information from that guidance. If the two documents will co-exist, this new guideline could reference definitions and other content from the 1996 guidance.	

# section	**Line no.**	**Comment / Rationale**	**Proposed change / suggested text**	**Classification** **L**= low **M**= medium **H**= high	**Originator of the comments (for WHO use)**
1.2	89	"Possible causes for this may include (i) too much reliance on human practices …" PDA cautions against giving the impression that automation is more trustworthy than human practice.	"Possible causes for this may include (i) reliance on inadequate human practices…"	H	

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		Automated practices can be breached by humans.			
2.2	121	PDA agrees that this document should cover GXP situations broadly. To this end, WHO might consider again whether the language throughout the document is broad enough to encompass situations other than GMP. Perhaps WHO might consider a targeted consultation with those knowledgeable in GCP and GLP. Particular attention might be paid to section 13.		H	
2.3	124	PDA recommends citing the documents with which WHO is attempting to harmonize and using identical language if possible. This would ease understanding and implementation.		H	
3	164	"An independent individual designated in GLP who has been..." In a GXP environment, an archivist may not need to be an expert in GLP.	"An independent individual who has been..."	M	
3	176	"Data governance: The arrangements to ensure that data, irrespective of the format in which they are generated, are recorded, processed, retained and used to ensure the record throughout the data life cycle." PDA suggests revising this definition for clarity.	"Data governance: The arrangements to ensure that data are complete, consistent, and accurate throughout the data life cycle, irrespective of the format in which they are generated, recorded, processed, retained, or used."	M	
3	203	PDA is concerned that the definition of "routine data review" may cause confusion, particularly as the term is used in only one other location in the document.	In light of its limited usage, WHO might consider deleting the definition. If WHO retains the definition, WHO might include more discussion of the use of routine data review.	H	
4.9	271	"…regular review of documents and data to identify any DI failures." PDA suggests replacing "DI failures" with more specific language.	"…regular review of documents and data for consistency with ALCOA+ principles." We suggest similarly revising sections 4.10 and 4.11 to refer to ALCOA+ rather than "DI weaknesses" or "DI lapses."	H	
4.12	281	"Significant DI lapses identified should be reported to the national medicine regulatory authority." Reporting requirements are (or should be) detailed in	"Identified data issues must be reported to national medicine regulatory authorities to the extent required by law and regulation."	H	

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		the laws of each relevant country. PDA is concerned that this sentence, as written, could confuse users. We believe that it is preferable to direct users to the specific law of each relevant country.			
5.1	319	"... produce data, or where data are obtained..."	Please clarify and expand on this thought.	H	
5.6	339	"Risks include deletion of, changes to, and excluding data and results from data sets without written authorisation and detection of those activities and events." PDA suggests revising this sentence for clarity and to indicate that authorization may not always be necessary.	"Risks include deletion of, changes to, and exclusion of data or results from data sets without written justification, authorisation where appropriate, and detection."	H	
6.2	348	PDA suggests expanding on the discussion of "quality metrics and performance indicators," with a focus on ensuring that the use of such measurements does not inadvertently encourage falsification, and on maintenance of a strong culture of quality and integrity. In addition, PDA suggests revising and clarifying what WHO means when it refers to "lapse in DI rates." If WHO is referring to reductions in identified data integrity issues, PDA cautions that such reductions should not always be taken as an indicator of positive data management practices.		H	
10	409	PDA suggests that WHO consider whether the information in Section 10 is adequately addressed earlier in the document, allowing this entire section to be deleted.	Consider deleting section 10.	H	
11.2	451	Certain of the controls identified in section 11.2 are standard in Good Documentation Practices and should not be subjected to risk assessment prior to implementation.	Omit the following: • No use of pencils or erasers; • The use of single-line cross-outs; • No use of correction fluid or otherwise	H	

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			obscuring the record. PDA also recommends carefully considering whether the other items in the list are baseline Good Documentation Practices expectations for which a risk assessment is not necessary. Consider whether it may be preferable to omit section 11 entirely and refer users to a more comprehensive discussion of Good Documentation Practices elsewhere, to avoid the perception that this discussion is complete. We note that section 4 also covers Principles of Good Documentation Practices.		
12.6	490	"All records that are defined by the data set should be reviewed and retained. Reduced effort and/or frequency may be justifiable." Review of "all records" is impractical and unnecessary.	"All records that are defined by the data set should be reviewed and retained according to the risk assessment."	H	
12.15	529	"Proof of enabling and verification during the life cycle of data should be maintained." PDA suggests revising this sentence for clarity.	"The enabling of the audit trail should be documented, and its activation should be periodically verified and documented throughout the data life cycle."	H	
Annex 1	633	PDA wonders whether readers will clearly understand how to translate 3-axis input (Occurrence, Detection and Severity, all with H/M/L options) into a 2-dimensional grid. With the 3 inputs, there are 27 possible combinations of H/M/L, but the text does not clearly guide the reader in identifying which of the 27 combinations require action. It also does not guide users through the scenario in which both severity and detection are considered to be "high" or "low."	Consider providing additional discussion regarding application of the table.	H	
Annex 1	672	"Entries of data and results (electronic and paper records) should be free from mistakes." PDA encourages WHO to delete this sentence. Human error is and will remain a fact of life. PDA is concerned that,	Consider deleting this sentence.	H	

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		by stating that date entry must be free of errors, WHO will inadvertently encourage individuals to falsify entries to ensure perfection.			
Annex 1	755	"Original data should be reviewed." As noted above regarding line 490, this is impractical and not necessary in all cases.	"Original data should be reviewed according to the risk assessment."	H	