IV C 2	569	It is unclear if this is applicable only to packaging and labeling or to all manufacturing operations. Labeling should be discussed as a system, including its general inputs and outputs, and the critical interfaces to other systems.	This will then serve as an example for other systems not covered in this guidance.
IV C.2	589	Please add the phrase it italics: Change controls should be maintained throughout the design of the "commercial packaging" process.	To reinforce change management is a continuum throughout the life of the product
IV C 3	593	Inputs should not be used in a narrow way to define raw materials. This will only serve to confuse a general term with an area where we already have the term raw material.	
IV C 4	628	Include change management as a separate quality system not as a paragraph under manufacturing processes.	Change management should be one of the quality systems reviewed in this paper not included as a paragraph in the section on manufacturing process.
IV C. 3	628	Change "recommended" to "shall" and rearrange sentence	Use of the word "recommended" implies that it may not be necessary to apply change management in the examples given. However to assure appropriate control change control must be employed in these instances
IV C 4	634	Please state that "Perform and monitor operations" is not a quality system but a manufacturing system.	In this case monitoring of operations is only one part of running a quality and compliant manufacturing system. What are the other parts? Inputs, outputs, value added steps, controls, metrics?
IV C 3	636	Delete the first sentence: "Core purpose of implementing a quality systems approach is not to enable a manufacturer to more efficiently and effectively perform and monitor operations."	The core purpose is to produce a product that meets all requirements in an effective and efficient manner
IV C 4	644	Please add in the potential role of PAT.	
	646	Change from "process weakness" to areas of "higher risk"	The concept of higher risk is consistent with this document
	651	Change "validate" to "assure conformance"	Assure consistency with PAT guidelines
	666	Change "change control" to "change management"	Please refer to Item B in our cover letter.
IV C 4	689	Please delete paragraph on using process data to improve manufacturing control.	The idea of static process parameters – that should always be meet – is not consistent with process control.
	708	Change "change control" to "change management"	The term change management contains the concept of inter-relatedness of process, specification, software changes in a multi-disciplinary approach.
IV C 4	725	Please add in phrase in italics: if implemented "and operated well, will…."	It is necessary for the quality systems to be operated well for the statement to be correct.
	730	Delete word "statistically" from "invalidation of test results should be scientifically and statistically sound and justified."	Statistics should not be used to justify invalidation of a test result. This additional requirement is not consistent with other draft guidances and should be removed.
	734	Please add in the phrase in italics: ..the manufacturer should consider shipment "and storage" requirements…	Storage of pharmaceutical products can impact the quality of the products.