

Guidance Number: 097

Figure 1:

Application description	System boundary	Intended Use	Regulatory Registered Test?	Other Quality Tests as Back-up?	Direct/Indirect/ No Impact	Validation Elements typically required (see PQS V7101)
Example 1: HPLC and data collection system interfacing to a reactor.	PAT system. Boundary does NOT include direct product contact surfaces (i.e. sample loop).	To determine reaction completion: for quality	No	Yes	Indirect	None, Commissioning only
Example 2: Same as above	PAT system, including direct product contact surfaces	Reaction completion: for quality	Yes	No	Direct	Commissioning, Component Level Impact Assessment, User Requirements, Specifications, Validation Plan, Protocols, Validation Report, Approved SOPs, Change Control
Example 3: Same as above	PAT system. Boundary does not include direct product contact surfaces (i.e. sample loop).	Reaction completion: for yield	No	No	No Impact	None, Commissioning only

Appendix 1: Example 1 – Indirect Impact: System Level Impact Assessment

System No.	System Name/ Description	System Impact Assessment	Basis used for Impact Assessment ^A					Commission	IQ	OQ	PQ	Notes
			1	2	3	4	5					
Example 1	<p>PAT System Boundary: HPLC and data collection system, cables.</p> <p>Direct product contact surfaces (e.g. sample loop) are outside of the PAT system boundary.</p> <p>These components are included within the reactor system boundary.</p>	Indirect						Y	N	N	N	<p>Assumption: PAT is a system interfacing to another system (e.g. reactor system).</p> <p>The responses to the questions were based on:</p> <ul style="list-style-type: none"> Product contact surfaces (e.g. sample loop) are assumed to be outside boundary of PAT system. They are within the boundary of the reactor system: 'N' to Q1. There is an independent verification by separate system (e.g. QO lab testing) that critical quality attributes have been met so Q5 is 'N'. Product is withheld from release until the QO lab data are confirmed to meet specifications. This is a test that is not included in a regulatory filing.

^A If the answer is "yes" to any of the questions (page 3) **BOLD** the number(s) that correspond to the question.

Appendix 2: Example 2 – Direct Impact: System Level Impact Assessment

System No.	System Name/ Description	System Impact Assessment	Basis used for Impact Assessment ^A					Commission	IQ	OQ	PQ	Notes
			1	2	3	4	5					
Example 2	<p>PAT System Boundary:</p> <p>HPLC and data collection system, cables, sample loop</p> <p>Direct product contact surfaces (e.g. sample loop) are within the PAT system boundary</p>	Direct						Y	Y	Y	Y	<p>Assumption: PAT is a system interfacing to another system (e.g. reactor system).</p> <p>The responses to the questions were based on:</p> <ul style="list-style-type: none"> Product contact surfaces (e.g. sample loop) are assumed to be within boundary of PAT system. Therefore, they are critical components and direct impact: Y to Q1. (Would at least need material of construction certification for sample loop.) If PAT is used to adjust critical process parameters (e.g. reaction time): Y to Q5. There is no independent verification by separate system that critical quality attributes have been met: Y to Q4 % reaction completion tested on an in-process sample is not a critical quality attribute of the final product. This testing is included in a regulatory filing

^A If the answer is "yes" to any of the questions (page 3) **BOLD** the number(s) that correspond to the question.

Appendix 3: Example 3 – No Impact: System Level Impact Assessment

System No.	System Name/ Description	System Impact Assessment	Basis used for Impact Assessment ^A					Commission	IQ	OQ	PQ	Notes
			1	2	3	4	5					
Example 3	<p>PAT System Boundary:</p> <p>HPLC and data collection system, cables.</p> <p>Direct product contact surfaces (e.g. sample loop) are outside of the PAT system boundary.</p> <p>These components are included within the reactor system boundary.</p>	No Impact						Y	N	N	N	<p>Assumption: PAT is a system interfacing to another system (e.g. reactor system).</p> <p>The responses to the questions were based on:</p> <ul style="list-style-type: none"> Product contact surfaces (e.g. sample loop) are assumed to be outside boundary of PAT system. They are within the boundary of the reactor system: 'N' to Q1. This is a test that is not included in a regulatory filing. Data from this testing are used either to gather process knowledge (For Information Only) to optimize yield, to gain knowledge regarding feasibility of the PAT application, or to gain knowledge about the PAT system's capabilities. There is no impact on product quality if under-reaction or over-reaction takes place.

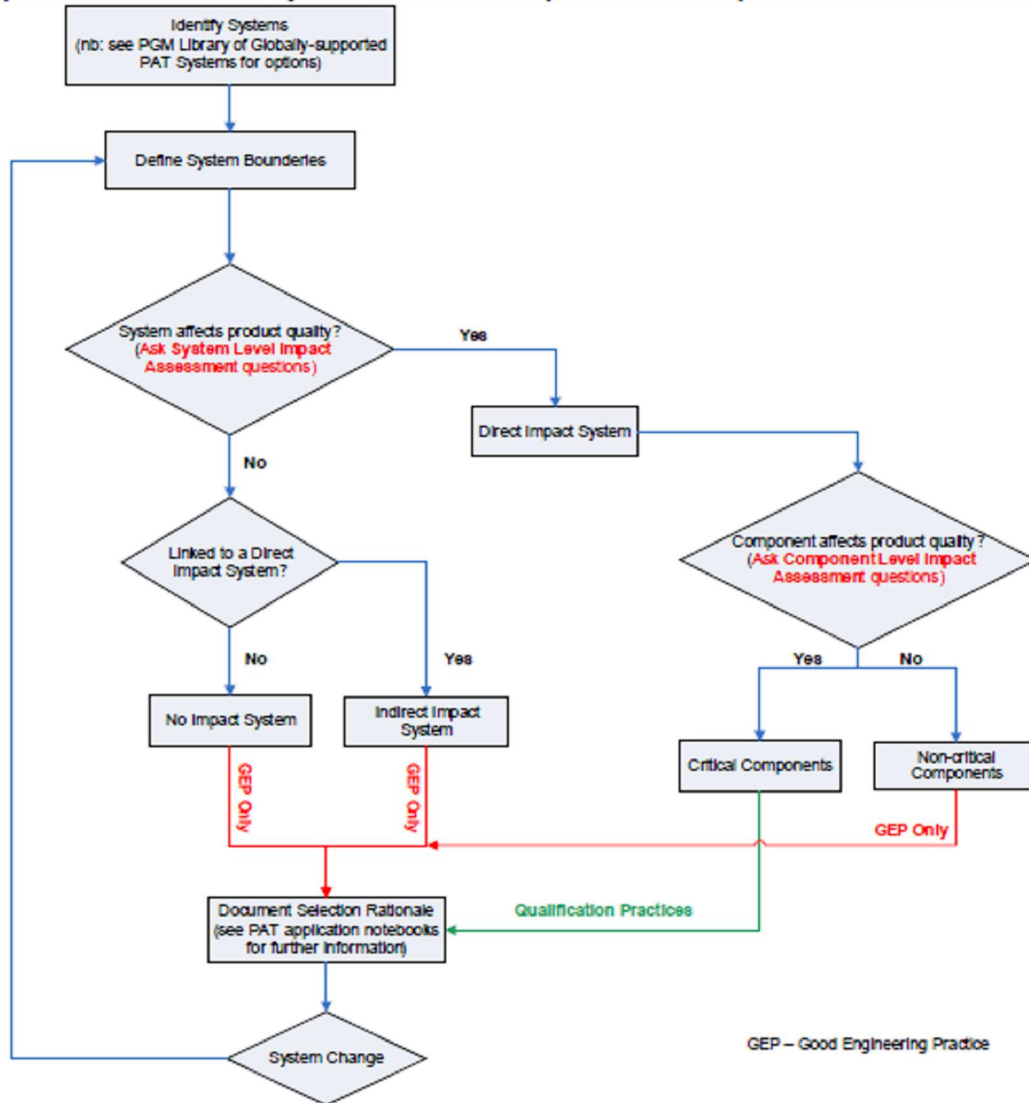
^A If the answer is "yes" to any of the questions (page 3) **BOLD** the number(s) that correspond to the question.

Appendix 4: Example 2 – Direct Impact System: Component Level Impact Assessment

Component Tag / ID #	Component Description	Component Impact Assessment	Basis used for Impact Assessment ^A		Commission	IQ	OQ	Existing IA on file?	Notes
XXX	Sample loop	Non-Critical	1	2	Y	Y	N		Materials of construction must be verified for qualified manufacturing systems
YYY	Cabling	Non-Critical	1	2	Y	Y	N		
ZZZ	HPLC Black-box (inc. computerized system and field device I/O calibration and testing)	Critical	1	2	Y	Y	Y		
WWW	Waste handling components associated with on-line HPLC (Nitrogen used to clear probe surface)	Non-Critical	1	2	Y	N	N		

^A If the answer is "yes" to any of the questions (page 4) **BOLD** the number(s) that correspond to the question.

Appendix 5: Overview of System Level and Component Level Impact Assessment Process



Appendix 6: Increasing Levels of Commissioning & Qualification Related to System Use

