

AstraZeneca's response to FDA request for comments on 21 CFR Part 11

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The structure of the comments below follows the Part IV- Topics for Discussion and Comment in the notice of public meeting.

TOPIC	COMMENTS
A. Part 11 Subpart A-General provisions	
1. "In the part 11 guidance document...etc. We are interested in comments on FDA's interpretation of the narrow scope of part 11 as discussed in the part 11 guidance and whether part 11 should be revised to implement the narrow interpretation described in the guidance. "	There is wide support in AstraZeneca for the interpretation of scope put forward in the guidance. This is felt to be much more practical than earlier interpretations.
2. " We are interested in comments on whether revisions to definitions in part 11 would help clarify a narrow approach and suggestions for any such revisions. "	Definitions tend to be all-inclusive, so that clarification in line with the guidance, of 'electronic record' in particular, would be useful. Some terms such as 'hybrid system', 'transient data', 'metadata' have come into common use so that recognition of these and definition would be helpful.
3. "In the part 11 guidance...etc. We are interested in comments on the need for clarification in part 11 regarding which records are required by predicate rules and are therefore required to be part 11 compliant? "	It would be helpful if clarification of whether or not records should be explicitly required by predicate rules to be in scope. Some examples of in and out of scope records would be useful.
B. Part 11 Subpart B-Electronic Records	
1. "As mentioned previously, the part 11 guidance identified four...etc. We are interested in comments on whether there are other areas of part 11 that should incorporate the concept of a risk-based approach, detailed in the part 11 guidance (e.g., those that require operational system and device checks). "	Certainly we believe that 11.10 f & h could be risk based. Indeed, in line with current general thinking there seems no reason why any control requirement could not be applied to a degree based on the risks associated with its function.
2. " Is additional clarity needed regarding how predicate rule requirements related to subpart B can be fulfilled? "	In principle, we do not believe the rule should define how requirements are to be fulfilled, rather what is to be fulfilled.

TOPIC	COMMENTS
<p>3. "Under the current part 11, the controls that apply to electronic records that are maintained also apply to electronic records that are submitted to FDA. Should the requirements for electronic records submitted to FDA be separate from electronic records maintained to satisfy predicate rule requirements?"</p>	<p>No. It should be possible to define a single standard, which will avoid further confusion. It is the extent of scope to which this standard is applied that is key.</p>
<p>4. "The controls for electronic records in subpart B distinguish between ...etc. Should part 11 continue to differentiate between open systems and closed systems?"</p>	<p>This differentiation is important but could perhaps be encompassed by risk consideration, with the appropriate application of controls in line with risk assessment.</p>
<p>4.1 "The part 11 guidance identified validation ...etc. Should we retain the validation provision under 5 11.10(b) required to ensure that a system meets predicate rule requirements for validation?"</p>	<p>We support this provision.</p>
<p>4.2 "The part 11 guidance identified record retention Are there any related predicate rule requirements that you believe are necessary to preserve, the content and meaning of records with respect to record copying and record retention? What requirements would preserve record security and integrity and ensure that records are suitable for inspection, review, and copying by the agency?"</p>	<p>In keeping with riskbased principles, we would like to see it left to sponsors to assess risk and document each system's requirements for ensuring that records are suitable for inspection etc by the agency.</p>
<p>4.3 "Should audit trail requirements include safeguards designed and implemented to deter, prevent, and document unauthorized record creation, modification, and deletion?"</p>	<p>In our opinion the audit trail functionality should be focussed on safeguarding business information not as an administrative control in itself. There is a danger that this provision would encourage additional routine access authorizations where system administrator duties only are to be performed</p>
<p>4.4"Section 11.10(k) requires appropriate controls over systems documentation. In light of how technology has developed since part 11 became effective, should part 11 be modified to incorporate concepts, such as configuration and document management, for all of a system's software and hardware?"</p>	<p>Whilst these are important concepts, it should be left to the discretion of the regulated entity to decide how to meet the requirement. Over time these concepts will undoubtedly develop further, or even be superceded.</p>

TOPIC	COMMENTS
C. Part 11 Subpart C-Electronic Signatures	
“Within the context of subpart C... Should part 11 address investigations and followup when these security breaches occur? ”	Again, the principle of limited access authorization is very important. The response of an organization to breaches, essentially of security, should be a matter for internal policy, provided it is effective. A review of effectiveness would be a valid challenge but not against a prescribed process.
D. Additional Questions for Comment	
1. “What are the economic ramifications of modifying part 11 based on the issues raised in this document?”	There is an opportunity to focus and contain effort to those areas where benefit to patient can result. This in turn would reduce the disincentive to introduce new ideas and technology. At the same time, significant alteration or addition to the provisions of the rule could precipitate a further review of all of a company’s computerised systems with an attendant commensurate cost.
2. “Is there a need to clarify in part 11 which records are required by predicate rules where those records are not specifically identified in predicate rules? If so, how could this distinction be made?”	See A3. The differentiation between explicit requirements of the predicate rules, (perhaps ‘direct impact’ requirements?) and implicit requirements (‘indirect impact’?) could be subject to a risk-based assessment defining more or less rigorous control.
3. “In what ways can part 11 discourage innovation?”	Prescribed processes or procedures, and especially specific control methods, limit innovation. Part 11 should be interpreted so as not be a ‘stick’ but rather a ‘carrot’.
4. “What potential changes to part 11 would encourage innovation and technical advances consistent with the agency’s need to safeguard public health?”	The introduction of risk concepts to decision-making and controls is itself a major step forward. The option to use any justified means of achieving a control requirement should be explicitly stated.
7. “Should part 11 address record conversion?”	Only to the extent that the need for it should be recognised and the requirement to protect integrity of the record stated.