

SST COMMENTS ON OCT '06 OOS FDA GUIDANCE  
Docket No. 1998D-0777 (formally Docket No. 98D-0777)

1. Page 6, Footnote 7: The referenced Draft Guidance should be dated 2006, not 2004.
2. The Guidance is badly in need of a Decision Tree. This would make the entire subject matter much easier to understand.
3. Page 7, Section IV.B.1 Retesting

The section lacks any comment on how many retests would be acceptable to overturn an original OOS result. Understandably, the Agency wants the Firm to decide this. However, given the existence of the Barr Decision (wherein it states in footnote 9, " Such a conclusion cannot be based on 3 of 4 or 5 of 6 passing results, but possibly 7 of 8, Mulligan, 804:17-25), there is already a very strong statement out there originating in the Courts. It would seem appropriate then for the Agency to at least acknowledge this and comment on it. Every company worth its salt knows that one cannot test into compliance and knows that the number of retests needs to be predetermined. This issue is how many retests overrule the OOS result and can the retests themselves contain a failure? This is what Industry is looking to the Agency for their thinking. Unfortunately, the silence is deafening on this point.

4. Page 8, Section IV.B.1 Retesting; the following statement appears, "If no laboratory or calculation errors are identified in the first test, there is no scientific basis for invalidating initial OOS results in favor of passing retest results." I offer that this is not true. The scientific basis for invalidating the initial OOS result, regardless of whether one understands the reason for the OOS, is that subsequent retesting showed that the OOS result was not reproducible. Therefore, the initial OOS result is invalidated on that basis. Whether one understands the reason for the OOS is an entirely separate matter. If the OOS result were valid, it would be reproducible.

5. Page 8, second paragraph: The concept that a decision to retest can be based on not initially finding an identified laboratory should be included since, in my experience, some companies reject all retesting unless the cause of the OOS has been identified.

6. Page 11, Section C.2. The addition of a few actual examples would make this very important section on Outliers much easier to understand.

7. Page 13 Section V.A; the statement, " For inconclusive investigations.....the OOS result should be give full consideration in the batch or lot disposition decision." Again, as above, if retesting has shown that the OOS result is not reproducible, then, regardless of whether one has identified a cause, the OOS result should be invalidated and not considered in deciding the disposition of the batch.

8. Page 14, Section V.B Cautions

I offer that this section is misplaced, since it essentially contradicts section IV.C.1.a on Averaging (page 9). It should be discussed in the context of the latter section, not as what seems to be an afterthought, by placement at the end of the Guidance.

That said, I suggest this section, due to its far reaching consequence, be completely removed from this version of the Guidance until a separate Forum can be convened to discuss it. As written, the section completely changes the philosophy used for defining a "reportable result," a philosophy widespread in Industry for many years and dramatically raises the bar for the characteristics of a reportable result. Further, it recommends that one should "treat the reportable average of these values as an OOS result, even if that average is within specifications." I suggest this will cause significant confusion and needs considerable discussion before implementation.

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