This draft document uses wording throughout that implies that various steps in the validation process are optional, i.e., the use of “should” rather than “shall” or “recommends”. This is especially obvious when discussing inter-laboratory reproducibility. Describing some of the validation steps and procedures as optional can be mis-understood by developers such as those described in the document as research, rather than regulatory or industry oriented, and can be misleading to the developer planning to submit their NAM to a regulatory authority for acceptance.

p. 20, point #5. “interlaboratory evaluation (if needed)” and Figure 2, step 5 “determination of method transferability (if needed)”.

This down-playing of the importance of interlaboratory reproducibility/ transferability (i.e., “if needed”) is concerning. Why, and under what circumstances, would a measurement of interlaboratory reproducibility not be needed? Regardless of its performance in the developing laboratory, a NAM is not useful or trustworthy if it cannot be successfully transferred to an independent laboratory. If the only demonstration of the NAM’s activity is from the developing laboratory, it does not necessarily follow that another qualified laboratory will be able to reproduce those results. The term used in the earlier 1997 ICCVAM document was “reliable”. It goes without saying that the NAM-developer has a personal, professional, and financial stake in its regulatory acceptance and, consequently, there is the potential for a conscious or subconscious bias in its validation for use, not to mention that there are always (considered minor) procedural aspects of the protocol that may not be included in the SOP. The inter-laboratory transferability of a proposed NAM should be a requirement rather than an option.

This is addressed on **p. 21, 1st para.** “Interlaboratory testing can potentially reveal steps in a protocol that are interpreted differently among laboratories and revisions that can be made to improve the NAM technical quality”. This statement effectively contradicts the statements regarding reproducibility made elsewhere in the document.

p. 36, sect. 3.3.2, para. 2. “A submission of a NAM for regulatory evaluation should include a description of any intra-laboratory or interlaboratory studies, if conducted.”

It is not clear how an agency, or any individual, can evaluate a NAM without knowing both its intra- and inter-laboratory responses to substances producing a range of responses. The steps described in this paragraph as “should” must be mandatory, not optional.

p. 43. Sect. 3.3.2.4. If a method is going to be submitted to a regulatory agency, an SOP should be required, not “recommended”.

References, l. 1340. OECD (2005) should be Guidance Document No. 34 not “Test” 34.

The NAM’s requirement for proprietary or patented information or equipment needs to be addressed.

Errol Zeiger Ph.D., J.D.
Errol Zeiger Consulting
800 Indian Springs Rd.
Chapel Hill, NC 27514
1-919-932-3778
zeiger@nc.rr.com