Forwarded message from Dr. McCormack:

1. Does FDA accept that stability testing and characterization analyses of test/control article are conducted under GMP* in GMP-compliant facility?
Test and control article characterization and stability testing conducted as part of a nonclinical laboratory study must be conducted in compliance with the provisions of the FDA GLP regulations. [21 CFR Part 58]. However, this does not mean that a facility which normally conducts characterization or stability testing under cGMPs (21 CFR Part 211) could not also perform characterization and stability testing in compliance with the requirements of the GLP regulations. If a facility that normally conducts testing under cGMPs is organized and operates in a manner that satisfies the requirements of the GLPs, we would not object. However, you should be aware that there are two critical differences between FDA GLP and cGMP regulations. First, the cGMPs requires a quality control unit (?211.22), not a quality assurance unit as required by FDA GLPs (58.35). The GLP regulations require that the QAU "[f]or any given study, the quality assurance unit shall be entirely separate from and independent of the personnel engaged in the direction and conduct of that study." There is not an analogous requirement under FDA cGMPs. The quality control unit may be comprised of individuals engaged in or directing the testing. Second, cGMPs.(211.100) require that there be written procedures and that the procedures and any changes to the procedures are to be approved by "appropriate organizational units and reviewed and approved by the quality control unit." In contrast, GLPs require that there be standard operating procedures "that management is satisfied are adequate to insure the quality and integrity of the data [...]" [58.81(a)].

2. In other words, does FDA have no objection to that certificates of analysis (COA) or results of analysis (ROA) of GMP-compliant analytical results are used for GLP studies, as long as the test /control article batches of animal studies (under GLP) would also be used for human clinical trials (under GCP)?
58.185(a)(12) requires that a final report contain "[t]he signed and >dated reports of each of the individual scientists or other professionals involved in the study." COAs or ROAs from the scientist conducting characterization or stability testing for a GLP study would not satisfy the requirement for reporting of individual scientists or other professionals.

3. In case of no GLP organization at the sponsor company, our interpretation for the above statement from the FDA regulation is that FDA accepts stability testing of test/control articles under GMP. Is our understanding correct? And may we also understand that characterization analyses of test/control articles and stability testing of their mixture with a carrier could also be conducted under GMP?
FDA would require that characterization and stability testing for nonclinical laboratory study to be conducted in compliance with FDA GLP regulations. Analytical methods used to test mixtures of test or control articles with carriers must also be conducted in compliance with the provisions of the FDA GLP regulations. A facility that typically conducts testing under cGMPs may be able to conduct the required testing if it also satisfies the requirements of GLPs.

4. Is there any FDA publication that allows characterization and stability testing of test/control articles and stability testing of their mixture with a carrier under GMP in a GMP-compliant facility? If there is, would you please tell us how we could obtain it? Or may we ask you to send it to us by e-mail or fax? We believe that this will help us to have clear understanding about this matter.
No.

5. In case where characterization analysis and stability testing of test/control articles are conducted under GLP separately from toxicology studies, should analytical protocols and reports contain the items required as content of study protocol and final report requested by GLP regulation(58.120 and 58.185 of FDA GLP)?
We assume that the statement "separately from toxicology studies" means that the analytical work is performed under contract or grant by individual scientists or other professionals. The approved protocol for a nonclinical laboratory study must clearly indicate all methods >for the conduct of the study and contain the type and frequency of tests, analyses, and measurements to be made. [58.120(a)]. Therefore the protocol should contain the methods for analytical testing or specific and unambiguous reference to the methods that will be used. The GLP regulations do not specify the content of the reports of individual scientists or other professionals, but the reports should provide sufficient information to permit the study director to prepare an accurate and complete final report.

6.. Are we right to understand that results of such analyses could be included as certificates of analysis (COA) or results of analysis (ROA), instead of preparing full analytical reports?
No, that would be incorrect. See the answer to question #2.

James F. McCormack, Ph.D.
Bioresearch Monitoring Program Coordinator
Division of Compliance Policy, HFC-230
Office of Enforcement