REGULATORY UPDATE 5/2011

FDA GLP - no news - the agency is still sorting through the comments

FDA Clinical - a new FR notice regarding disqualification of clinical investigators has been issued. It is attached

EPA GLP - there has been a TON of discussion lately concerning test system/test substance for biotechnology. The North Carolina Chapter of SQA hosted an informal evening with the regulators last week in Raleigh. Mark Lear and Dan Meyer were there and gave brief presentations and then opened the floor to answer questions. Highlights were:

Mark Lear informed us that EPA will be issuing guidance on Plant Incorporated Protectants (PIPs). He further stated that his most common inspection findings were failure to document amendments to protocols and deviations from protocols and SOPs. Another reoccurring issue is failure to provide and/or retain correspondence between the SD and other study personnel, especially in multi-site studies.

During the Q&A Mark stated that EPA does not have any guidance on validation or acceptance/rejection of analytical data.

OPP has defined the test substance as the protein for biotech studies. I ask how EPA was going to get around the test substance to the test system definition of experimental start and Mark said we need to not try to make biotech fit squarely into GLPs and that everyone is on a learning curve. From my view, the TS is defined by the type of study. In many cases (substantial equivalence, etc.) the test substance could be the protein, the seed is the carrier and the plant that grows from the seed the test system. There was some discussion on "fragmenting" of studies. The reiterated, one study, one study director. Again, from my view, the field portion is part of the study except in feeding studies and characterization studies. Then the field growing of a crop becomes very similar to derivitizing/manufacturing the test substance. It would be nice if industry could write a white paper. Even nicer would be if the EPA biotech folks in SQA would forma specific AgChem specialty section focusing on AgChem biotech. I have attached a paper that was recently given to me..

Dan said his most common finding during inspections is labeling of reagents, solutions, and test substances. He gave a great presentation regarding electronic data and reiterated that the original raw data is the electronic signal plus the software it takes to read it and that every modification of that must be saved and secured with an audit trail. One can print the electronic data if they choose, but the official record that must be archived is the electronic version.

Dan also talked about "methods", and feels that methods are uncontrolled

documents not regulated by EPA. However, to make a method an official regulatory document, all one must do is amend it to or reference it in the protocol. Discussion began regarding whether methods should be SOPs. One person felt strongly that they should so that they would have management approval and be controlled. Another person asked who is responsible for assuring the methods used on a study were accurate and reliable. Mark said that the SD is. The next comment was "That is why methods should be part of a protocol not an SOP. If it is an SOP, then the SD is not responsible, management is." I personally feel that methods should stay "uncontrolled" and become official regulatory documents when they are used in a study by amending them to the protocol (or at a minimum referencing them).

EPA is down to three inspectors (plus Francesca Liem). This is no where near enough inspectors to service the labs in the US. With OECD member countries expecting that labs be inspected at least every 2 years in order to utilize the MADs and MOUs, the US is caught between a rock and a hard place. This system is unsustainable and could easily lead to US studies not being accepted by other countries. SQA has written a letter to EPA encouraging them to fund the inspection program and allow the hiring of additional inspectors.

As a final note it was reiterated that is you are a company in the US following EPA GLPs, there is no need to reference OECD GLPs in a protocol. Studies conducted in the US in accordance with either EPA or FDA GLPs will be accepted for review in the other member countries as long as the facility has been inspected by the agency and found to be in compliance.