INSIGHTS FROM THE BDO LIFE SCIENCES PRACTICE

THE CONFLICT BETWEEN PROCESS CHARACTERIZATION AND QA

By Michael Glacken, Sc.D.

Lately, I have noticed an undesirable trend of QA wanting to become more involved in process characterization (PC), the laboratory scale work that enhances process understanding and provides the information required to draft Process Performance Qualification (PPQ) protocols. Why do I say this is undesirable?

IMPORTANT DIFFERENCES BETWEEN QA AND PC

The role of QA in assuring the safe and efficacious commercial and clinical manufacturing of pharmaceuticals is essential and unquestioned. But PC is not manufacturing. Manufacturing is or should be repeatable, reproducible and predictable. And as such, manufacturing is amenable to SOPs, protocols and pre-approved acceptance criteria. QA adds value by ensuring SOPs are followed, protocols are faithfully executed, pre-approved acceptance criteria are met, and investigations are faithfully completed.

On the other hand, while PC may have some of the features of a manufacturing activity, such as limited use of SOPs to ensure standardization, it is firmly in the research and development bucket. PC experiments—and that is what they are, experiments—explore the process design space to determine the regions that provide acceptable quality product and process performance as well as regions to avoid. This is essentially unknown territory hardly amenable to rigid pre-approved acceptance criteria.

SDMS AT ISSUE AND WHY A ONE-SIZE-FITS-ALL APPROACH WILL NOT WORK

Imposition of typical manufacturing grade quality assurance policies onto PC activities will needlessly slow down progress without adding value. Worse, decisions by inappropriately applied QA procedures could be counter-productive. I know of a case where QA insisted on pre-approved protocols for qualifying scale-down models (SDMs) before they can be used for PC studies. What's wrong with that?

SDM qualification is not a one-size-fits all for every unit operation for every product and process. For example, in the case in question, all unit operations met the acceptance criteria, except one. For the exception, there was an offset in a critical quality attribute (CQA) between the SDM and the full-scale system. Because of this, QA insisted that the SDM could not be used for PC studies. This was nonsense, of course. Because of this one offset, should we believe this SDM is 100% useless for the purpose of enhancing process understanding? Of course not!

First, there are **case studies** where SDMs exhibiting offsets were indeed used, if not for the CQA in question, at least for exploring other CQAs and process performance attributes. Of course, one needs to make a convincing scientific case both to themselves and to regulators (eventually in 3.2.S.2.6 of the CTD) that the SDM studies are relevant to the at-scale process. Moreover, for the example in question, there was strong scientific data outside of the SDM qualification protocol indicating SDM relevance. For the at-scale process, data existed indicating that increasing process parameter X caused a reproducible change in the CQA. The SDM experiments demonstrated that same effect, only with an offset. The SDM demonstrated the same trend as the at-scale process! That's exactly what we would want, right? Yet, a typical QA approach would needlessly discard such an SDM as being inadequate.

This is not to say a QA-like outlook is of no value to PC activities. It's just that the QA approach needs to be adapted to be more suitable to what is essentially an R&D activity that can't simply be cut and pasted from a typical manufacturing template.

LEARN MORE

CONTACT

LANCE MINOR
Principal
301-354-0711 / lminor@bdo.com

TODD BERRY
Assurance Partner and National Co-Leader, BDO Life Sciences
617-239-4125 / tberry@bdo.com

MICHAEL GLACKEN
Managing Director
325-864-0698 / mglacken@bdo.com

ABOUT BDO LIFE SCIENCES PRACTICE

BDO's Life Sciences Practice provides the guidance that pharmaceutical, biotech, and medical device manufacturers need, when they need it. From understanding the complexities of research and development tax credits and FDA regulations, to licensing agreements and due diligence, we help our clients grow.

ABOUT BDO

BDO is the brand name for BDO USA, LLP, a U.S. professional services firm providing assurance, tax, and advisory services to a wide range of publicly traded and privately held companies. For more than 100 years, BDO has provided quality service through the active involvement of experienced and committed professionals. The firm serves clients through more than 65 offices and over 700 independent alliance firm locations nationwide. As an independent Member Firm of BDO International Limited, BDO serves multi-national clients through a global network of more than 88,000 people working out of more than 1,600 offices across 167 countries and territories.

BDO USA, LLP, a Delaware limited liability partnership, is the U.S. member of BDO International Limited, a UK company limited by guarantee, and forms part of the international BDO network of independent member firms. BDO is the brand name for the BDO network and for each of the BDO Member Firms. For more information please visit: www.bdo.com.