

Remarks of Ms Helen Winkle, Director, Office of Pharmaceuticals, Center
for Drug Evaluation and Research at the ASTM Committee E55 Workshop
on Application of PAT to the Pharmaceutical Industry
May 15th, 2006, Toronto, Canada

It's my pleasure to be here to meet with you today. I want to start by saying that I think what has been done in E55 is phenomenal. It indicates the persistence and tenacity of all involved. And I personally want to thank each of you. And I especially want to thank Don Marlowe for all of his work and support.

I must tell you before I came today I had several different folks at FDA weigh in on what I should say and what message I should deliver from FDA. Various individuals within the agency have various perspectives about E55 and how it should function. I want you to know though that my decision to come today was based on CDER's desire, based on conversations with Dr. Steven Galson & Dr Doug Throckmorton, CDER Center Director and Deputy Director, to share its support of PAT and standards development. I want to be upfront with you though – standards development may be a rocky road at times and we will have to work together to get over the bumps.

There are several things I want to cover today. I want to talk about PAT and its importance to the changing paradigm for quality regulation in FDA. I want to talk about standards development in general and the process of implementing standards in the new FDA environment. And I want to talk about the future and where we'd like to go and how standards fit into that future.

In order to talk about PAT, I must go back to September 2004 when the FDA guidance on Process Analytical Technology was first issued. As you know, this extremely important guidance was intended to describe a framework that would encourage the voluntary development and implementation of innovative pharmaceutical development, manufacturing, and quality assurance. Unlike many of FDA's guidances, which are extremely prescriptive, this guidance is general and does not provide any specifics on how to implement it. It was always envisioned that standards would be the mechanism for developing those specifics, and, in less than one and a half years, ASTM E55 has moved decisively in that direction.

Over the last six months, I've had several folks imply that FDA doesn't support PAT any more. They have perceived that, since Dr. Ajaz Hussain left the Agency, our focus on PAT has diminished. Well, maybe that is true in one sense. Dr. Hussain is not out promoting PAT for FDA any more. However, in other ways, if you truly understand FDA's new paradigm, you'd understand that PAT is really the underpinning of the entire concept of Quality by Design, that is understanding process. To quote from the PAT guidance "The Agency considers PAT to be a system for designing, analyzing and controlling manufacturing through timely measurement of critical quality and performance attributes of raw and in-process materials and processes, with the goal of

ensuring final product quality.” I want to go on the record here by saying that any rockiness that we have encountered with E55 has in no way to do with Agency’s lack of support for PAT, the role of consensus standards, and their future in the regulatory scheme.

With that said, I’d like to talk about standards development in general. As I said earlier FDA supports the development of voluntary consensus standards. There are various activities in which the Agency can participate with regard to standards development that can be extremely valuable to us now and in the future. This includes:

- utilizing standards in place of guidances,
- promoting standards development for certain functions, etc., to help support regulation,
- participating on standards committees, and
- implementing standards to help in understanding.

The current activities of E55 are just the start.

The pathway to participation in the development of consensus standards was established through the NTTAA of 1996 and the OMB Circular A119. ASTM has been actively involved in standards development for a long time. Many of our sister Centers at FDA – most notably the Center for Medical Devices and Radiological Health – have used ASTM over the years to develop and promote standards for medical device regulation. However, the Center for Drug Evaluation and Research and the pharmaceutical regulators have only recently realized the advantages of working with voluntary standards organizations. In the past we only focused on USP. The cGMP Initiative for the 21st Century brought about a number of changes in how FDA regulated, but mainly it empowered industry to be more responsible for product quality. This change requires a shift in thinking at the Agency about making information available more expeditiously to facilitate the development of appropriate submissions, and, actually, dictates the need for standards development and support.

So how do standards in general fit into the overall future strategy at FDA? Basically we see standards, as currently being developed by voluntary consensus groups, as an optional way to describe how a certain function will be implemented to meet requirements. FDA describes *what* needs to be done to meet the requirements and the companies may use standards to describe *how* it is done. However, standards are not policy. In using a standard to describe the how, if the standard doesn’t meet our regulatory needs – either because it is inadequate in general or because it doesn’t apply to the particular product FDA does not need to accept its use. Having said this, FDA’s first responsibility is to the American public and will always operate within existing law and regulation.

It is important as standards are being developed that they are not confused with setting regulatory requirements. The language is important, and important to getting FDA support. FDA’s role can take several forms. We might actively drive a standard, suggesting that it be taken up by a committee, or we may not participate at all. This decision can be driven by priorities as well as resources. However, FDA’s role isn’t the only driver to making this process work.

For FDA, although in theory standards development is practical, in the real world it will take time to implement. We ask for your patience. Again, the pharmaceutical regulators have little experience working with voluntary standards groups other than USP and this change comes at a time when resources are stretched to the limit. There are a number of things we can do internally to start with to improve upon the standards process. This includes:

- Development of an internal process
- Focusing our resources on priority items
- Development of an internal education program
- Improving communication with standard setting organizations

The Council on Pharmaceutical Quality within FDA has established a standards working group, which I chair, to tackle these issues.

I am open to comments and recommendations from any of you here. Many here have vast experience in working with standards groups and might have some excellent suggestions as to how we can overcome some of the barriers that exist.

We all understand that the objective of the NTTAA is for Federal agencies to adopt private sector standards, whenever possible, in lieu of creating proprietary non-consensus standards. I'm not here to tell you what standards to write and which ones not to. That is your choice. I can't even tell you right now FDA's priorities. I will tell you, however, that I think that E55 is too narrow in scope. Although PAT is an important factor in moving FDA forward, it is only a subpart of the overall initiative at the agency. I would like to see the scope of E55 apply to pharmaceutical manufacturing in general. I don't know how flexible the structure is in ASTM but it seems that the current structure somewhat limits future standards development.

Developing standards requires hard work and dedication. It is a partnership of the various stakeholders, working together to make standards a reality. This is essential in today's world. And it requires patience!