Japan Society of Pharmaceutical Machinery
and Engineering (JSPME)

October 31, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration (FDA)
5630 Fishers Lane, rm. 1061
Rockville, MD 20852
U.S.A.

Re: Docket No. 03D-0380, CDER 2003136

Dear Sir/Madam:

We, Japan Society of Pharmaceutical Machinery and Engineering are pleased to submit you our offers and comments concerning "Draft Guidance for Industry: Process Analytical Technology-A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance" (Docket No. 03D-0380, CDER 2003136). We hope that you will consider our comments, and this guidance will be a very fruitful guidance for PAT. This document prepared by using Microsoft® Word 2002 is also sent to FDA(coryj@cder.fda.gov) by e-mail today.

We would be much obliged if you give us FDA review of our comments by letter or by e-mail.

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For your references, we, Japan Society of Pharmaceutical Machinery and Engineering (JSPME) are nonprofit industry group which is operated mainly in Japan with approx. 810 members, and we were established Oct. 1990 in order to seek the ideal pharmaceutical production through the research, development and discussion based on both theoretical and practical concept in cooperating with industry, government and academia.

Sincerely,

Katsuhide Terada

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Comments concerning the PAT Guidance

Japan Society of Pharmaceutical Machinery and Engineering

[I] Outline

1. This guidance remains in conceptual description which is described on it, and therefore, this is not exact and appropriate guidance for industrial firm. We offer that this information should not be called as guidance, but such as proposal.

2. If this information will be named as guidance,

a) Each pharmaceutical and related company should have conferences for each cases. It is necessary to show the concrete examples or publish the case study book in addition to the guidance in order to support the operating directional decision.

b) The final purpose of PAT should be clarified (For example; Parametric Release or Control the section of production which is overlooked in terms of statistical quality control), and government direction for the above purpose should be described clearly. This guidance will herewith, be achieved to higher understandings for industry.

c) This guidance does not show clearly how this is linked to existing guidance. For example, different approaches may be necessary for existing production line under operation or brand new line which will be established. Therefore, concrete examples should be described. Especially, government's prompt correspondences for such as simplification of change approval is required.

d) The relationship between PAT and GMP is not clarified. It is not clear that PAT and GMP will be treated separately or PAT will be included in GMP.

e) There is a possibility that it may take relatively long time to receive the approval in case that it is not clear how much back data is necessary, and each cases should be consulted to the government.

f) It should be clearly described that PAT is adopted for either process assessment or administrative standard.

g) Feature of this quality control technology is basically understanding of production process, however, some cases are shown that physical, chemical, and drug formulated explanation cannot be necessarily applied even if clear correlations between product quality and process parameter are found by current analytical technology. Even in this case, it should be described that these examples can be applied to PAT.

h) Decision making standard whether PAT can be applied or not should be clarified. For example, a standard when multiple linear regression analysis is used to decide whether it is applied or not should be shown.

1) It should be clarified how long the data should be retained for inspection regarding PAT. Many experiments which prove the bases of data have been obtained during research or development phases.

3. It is better to add glossary in guidance, not as references.

[II] Comments for each sections

① Statistical analysis should be added. (Line 163)

② Micro-biological characteristic should be added. (Line 174)

③ It is better to add the word "Statistical". (Line 177-179)

④ PAT framework describes that this guideline is used for small size equipments (in order to eliminate a certain issue of scale-up) and exclusive production equipments. However, 1) scale up issue of drug formulation equipment which is combined with small sized fluidized-bed corning dryer as semi-continuous type which is used in batch process as usual has been eliminated. Please clarify whether this equipment is included in PAT framework without mounting any special sensor or not. 2) Please kindly confirm whether product name of semi-continuous fluidized-bed corning dryer such as Tectransor of Freund / Vector can be described on reference documents of FDA's homepage or not. 3) Please clarify whether these types of equipment can be added on specific point of PAT guideline as examples or not.

⑤ We offer you to change the words "new tools" to "current and new tools". (Line 284)

⑥ We offer you to adduce practical and concrete examples or reference data. Especially, clear notification of software is necessary. (Line 291-355)

⑦ Mechanism of absorption is not necessary. (Line 350-351)

⑧ It is almost impossible to adopt the PAT from development phase (Line 356) since it is very difficult to determine the risk factor since only small number of lots are produced in development phase.

⑨ It may be easy to understand that these two sections are compiled as in-line measurement, and divide it to invasive and noninvasive. (Line 375-379)

⑩ Concrete example how to determine the parameter for validation regarding PAT may be described. (Line 468-474)

⑪ Please clarify whether re-validation is necessary or not in case that analytical instrument is mounted since PAT needs to find out the end point on real time of production. Clear notification of validation concept should be necessary. (Line 475-479)