[S1-3] [10/10/2003(Fri) 13:00-13:30/ Grand Ballroom 102]

Control of Uniformity in the Drug Industry

By focusing on solid dosage forms for internal use

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The present topic in pharmaceutical industry is to establish Quality Assurance System for medicinal product.Therefore, the most important and urgent subject to be solved in the field of the manufacturing industry is to establish, implement and maintain the control system for ensuring uniformity of medicinal product.

In case of solid dosage forms for internal use, its quality was controlled by disintegration test, etc. but at present bioavailability could be predicted with dissolution test and so the assurance of its uniformity should be prerequisite to preserve suitable dissolution of the manufactured medicinal product.

According to Annex 15 on EU-GMP Guidance and PR 1/99-1 on PIC document, it is mentioned that any aspect of, including significant change to, the premises, the facilities, the equipment or the processes, which may affect the quality of the product, directly or indirectly, should be validated and qualified. Therefore, for ensuring the uniformity of a medicinal product as like above mentioned, in the field of the manufacturing industry there should be Quality Assurance System for a medicinal product through qualification and validation.

The relevant information for qualification and validation are stated on *chapter 5 and 6 in EU guide to Good Manufacturing Practice, FDA 21 CFR 210 and 211 of Guideline on General Principles of Process Validation in FDA Regulations and Annex 15(PIC-document PR 1/99-1) and 18(ICH GMP practice guide for APIs)in EU guideline.*

It is considered that the most important thing of in-process parameters, which may affect the uniformity of a medicinal product, is blend uniformity and dose uniformity, and for ensuring this the thorough validation for medicinal product should be performed preferentially in the field of manufacturing industry.

Product validation will assess each definitive unit process within the entire process train, as governed by Critical Process Parameters (CPP's) and Critical Quality Attributes (CQA's). Critical Process Parameters are those processing variables which must be maintained in order to produce

material consistently meeting certain quality characteristics. These quality characteristics, which may include but not limited to measurements of appearance, potency, and in-vitro performance, are termed Critical Quality Attributes. The demonstration of consistency of the CPP's and CQA's at each unit process step, coupled with consistent in-process monitoring, is ultimately consolidated to depict a validated process for manufacture of the candidate dosage in its entirety.

Once a product manufacturing process has been validated, the validated system must be maintained through implementation of operating procedures, preventive maintenance programs, calibration programs, and change control procedures. Any change to process must be evaluated through the Process Change Request system to determine if the validated state will be compromised and if additional validation testing is warranted.

Furthermore, in combination with qualification and validation for uniformity of medicinal product in the filed of manufacturing industry and by conducting annual trend analysis for each medicinal product in the middle and long term, as allowing internal specification to reduce more and more through control, i.e. 3σ, 2σ bout major control parameter, ultimately we could make Quality Assurance System settle by ensuring and managing optimal uniformity for a medicinal product continuously and through use as feed-back data it is possible for us to realize quality as well as process development.