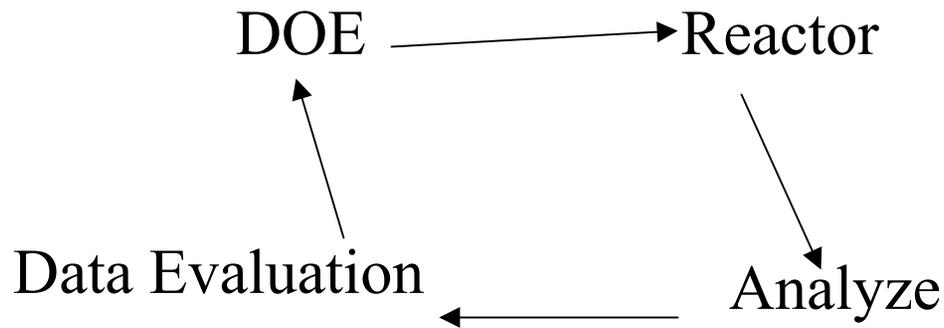


Chemometric Working Group

Recommendations
and Summary of Discussion

Introduction to Justify Paradigm Shift



Experimental
Design (DOE)

Preprocessing
Calibration
Diagnostics

Prediction
Validation

The role of chemometrics in the application of PAT

- Application of sound mathematical and statistical tools requiring chemical knowledge.
- Implies that the chemist understands the statistics, rather than the statistician trying to understand the chemistry

Role of Chemometrics in PAT

Modeling - deterministic

Identifying and deriving the state of the process

Monitoring

Calibration

Supporting the use of process analyzers and sensors

Controls

Actively manipulating the process to maintain or obtain a desired condition

****Diagnostics (essential part of each of the above)**

instrument

chemometrics to evaluate the process

feed forward

Chemometric tools needed for the use of PAT

- Preprocessing
- Regression tools
- Classification / Discrimination
- Outlier detection
- Homogeneity checking
- DOE
- Data visualization
- Terminology

What is needed for successful PAT / Chemometrics

- | | |
|-----------------------------------|-------------------------------|
| 1. Adequate measurements | Knowledge, <u>experiments</u> |
| 2. Representative samples | Knowledge, DOE |
| 3. <u>Adequate analysis</u> | Clarity, “Reproducibility” |
| 4 Adequate data
management | Pilot, production |
| 5. Validation | |
| 6. Standard (reference)
sample | |
| 7. <u>Auto-diagnosis</u> | |

What is needed to develop, validate, and maintain chemometric based PAT

- QUALITY DATA
 - Need reference samples (as a result of DOE)
 - Data from routine production
 - Data from faults

Currently accepted tools in Industry

- Reference ASTM E1655 – 00
- On going initiatives
 - COLI Chemometric on-line initiative (CPAC)
 - EMEA/CVMP/CPMP
 - PASG

Initial and on-going validation

- DOE leads to representative data
- Measurement is adequate
- Process is OK
- Sampling is OK
- Algorithm is OK
- Model validation
- All measurements can be made in predictive mode

Q8 Training approaches

- On-going conferences, symposium, workshops, etc., for chemometrics
- FDA have chemometrics short course that is case study based in-house and field.
- Direct involvement with consortium and participating in focus groups
- COLI - Chemometric on-line initiative
- Industry perspective on background and training for person doing chemometrics

Recommendations

- General exemption from reporting PAT data to the batch records collected for the purposes of investigating new technologies
- A recommendation is that guidance to evolve from simple model to a complex model; that is chemometrics as a tool for the FDA reviewer should be explained as what its role is the guidance
- Audit function versus review function