

_____ Workshop on Extractables and GMP for Components of
Inhalation & Nasal Drug Products - Sept 25, 2007, Basel

Managing Change Together -
Panel Discussion with Suppliers and Pharma

_____ What does a “change” mean to you?

Material change definition from Pharma Industry point of view

Any change in raw material/ composition, manufacturing processes and/or equipment that affects material properties.

- Mechanical properties
- Chemical properties (i.e. identity, purity)
 - extractables profile
 - IR spectra or other chemical testing parameters
- Process properties
 - e.g. MFR
- Changes in production site
- All other changes affecting DMF or fulfilling regulatory requirements

_____ What is the impact of a "change" and how do you assess its impact?
Material change impact from Pharma Industry point of view

Unplanned changes might cause:

- ↪ Deviation in quality regarding the material properties
- ↪ Out of specification results (OOS)
- ↪ Rejection of the packaging batch
- ↪ **The drug product cannot be delivered to our patients.**

What is the impact of a "change" and how do you assess its impact? Material change impact from Pharma Industry point of view

Consequences of a change notification:

- ↪ All changes in packaging materials must be justified to the regulatory body
- ↪ Any material changes may have the effect of new material/ new supplier
- ↪ Qualification process for new materials
 - Production process Safety Stability
 - Test runs - Extractables studies - Stability studies
 - Modification (e.g. tools) - Leachables studies - Compatibility tests
 - Process revalidation - Toxicological evaluation
 - Testing of component - Routine testing
- ↪ Takes several years (minimum 36 months) to qualify new materials for a critical component

Tools to enhance communications between suppliers and pharma when a change occurs

- Quality and supply agreement incl.
 - Specifications, acceptance criteria
 - Monitoring of the extractable profile at the beginning of the supply chain
 - Definition of changes
 - Controlled change procedure, i.e. changes must be notified at least 3 years before and can only be implemented after approval by pharma
 - 3 years availability of unchanged material
 - Minimum shelf-life of 36 months
 - Last-call option previous to production discontinuation

⇒ **In order to guarantee supply to patients**