

Process Analytical Technology (PAT) and its Applications in the Pharmaceutical Industry

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Overview

- ◆ **Pharmaceutical Industry**
 - Purpose
 - Challenges
 - Impact
- ◆ **Pfizer Sydney – Facing the Challenges**
- ◆ **Process Analytical Technologies**
 - What is it?
 - Benefits
 - Applications at Pfizer - Sydney
 - Future
 - Our Vision

Pharmaceutical Industry

◆ Purpose

- An industry dedicated to humanity's quest for longer, healthier, happier lives through good quality medicines

◆ Why are we different to other industries?

- The lives of people are at stake, we only get one chance to get it right. Their health is already compromised. To prevent the risk of compromising their health even further, we must provide safe, proven, high quality product.
- Consumer has no choice but to have 100% trust in our products.

Pharmaceutical Industry

◆ What are some of the challenges?

- High tech drug discovery vs low tech manufacturing techniques
 - Lag behind many other industries
 - Higher percentage of rejected product compared to other industries
 - Long product cycle times
- Tough Regulations
 - Make change difficult and costly (Validation)
 - Require intense sampling and testing
 - Suppress manufacturing innovation

Pharmaceutical Industry

◆ What is the impact?

A manufacturing industry that is

- Regulated more than any other industry
- Very conservative
- Usually unwilling to make change due to “red tape”
- Slow to adopt new technologies
- Reactive instead of proactive

Pfizer Sydney Facing the Challenges

◆ Our Approach

- Learn “best practice” from other industries
- A belief in ourselves, to effect change within the industry
- Look for and implement innovative technologies

◆ Our Solution

Process Analytical Technologies (PAT)

Process Analytical Technologies

◆ What is PAT?

- Bringing laboratory instrumentation into a production environment either “at-line” (beside manufacturing equipment) or “in-line” (incorporated into manufacturing equipment)

◆ The types of PAT’s under Development at Pfizer Sydney

- “At-Line” Near Infrared (NIR)
- “At-Line” Density Meter
- Particle Size Imaging System
- Rapid Micro assessment

PAT - Milestones

◆ Late 1980’s – Getting it off the Ground

- Purchased first Near Infrared Spectrophotometer (NIR)
- Early focus was on NIR applications aimed at replacing QC Compliance Testing
- Early methodology and the technology was tested on animal health products due to regulatory constraints
- Considerable difficulties in implementation

◆ 1990’s – Development Years

- Purchased 2nd generation NIR (powerful software)
- Development of Blend Assay / Uniformity methods
- Took a collaborative approach with regulatory authorities (TGA)
- Success with registration of raw material methods

PAT - Milestones

- ◆ **Early 2000's – The Defining Period**
 - Quantitative methods for some of our tablet products were developed and registered
 - Our focus had changed from replacing QC compliance testing to process knowledge and understanding beyond normal testing parameters
 - Process Analytical Technology (PAT) had evolved
- ◆ **2001 and Beyond – Industry Revolution**
 - Continuing PAT development and implementation, areas such as; Validation, Material vs Process Correlations, Counterfeiting etc.
 - FDA Stance
 - Recently the FDA distributed a draft guidance document on PAT

PAT - Benefits

- ◆ **True process understanding - as opposed to “blind” compliance**
- ◆ **Cornerstone of process validation and continuous improvement initiatives**
- ◆ **Provide greater quality control and assurance**
- ◆ **Inventory Savings**
- ◆ **EH&S and Waste Reduction**
- ◆ **Increased process effectiveness through less variation and cycle time reduction**
- ◆ **Improved basis for process investigations**

PAT Applications - Pfizer Sydney

- ◆ Raw and Packaging Materials (ID and Conformance testing)
- ◆ Cleaning Validation / Verification
- ◆ Material Change Evaluations
- ◆ Blend and Tablet Validation
- ◆ Routine Blend and Tablet Testing
- ◆ Process Optimisation
- ◆ Investigations
 - Troubleshooting
 - Counterfeit

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PAT Application Raw and Packaging Materials

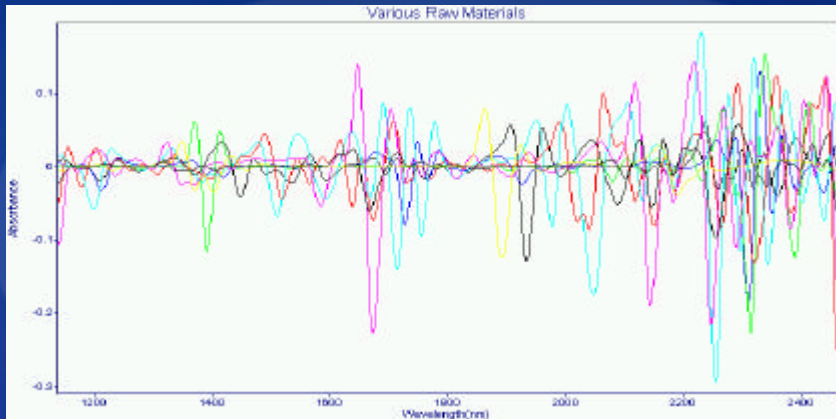
- ◆ **Current Regulatory Situation**
 - Identification (ID) testing of every container of raw material delivery received
- ◆ **Traditional Approach**
 - Raw Materials remain in quarantine (max up to 3 days) until Laboratory have completed ID testing
- ◆ **Pfizer Sydney's Approach**
 - To use NIR to Identify all containers of Raw Materials – Very quick
 - Gives both Chemical and Physical information.
 - Conformance Trending to determine Process-ability
 - Conducted rapidly at-line by warehouse operators.

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Material Identification

- ◆ Chemical ID - Does a sample overlay with known material in the library?

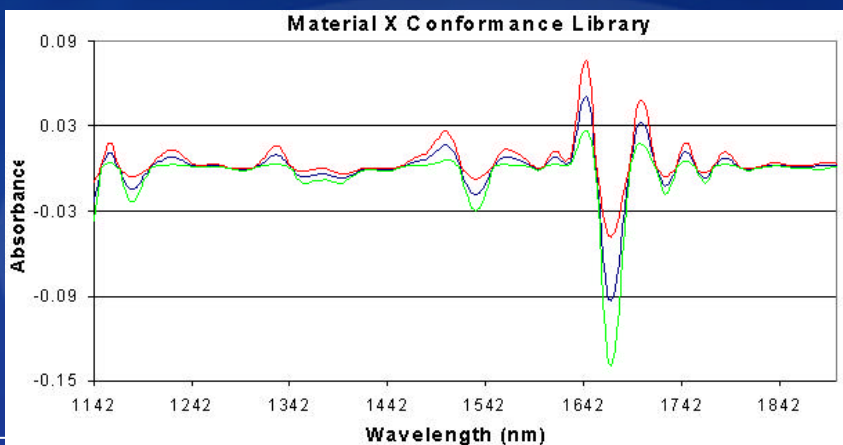


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Material Conformance

- ◆ How well does a sample conform to the library?

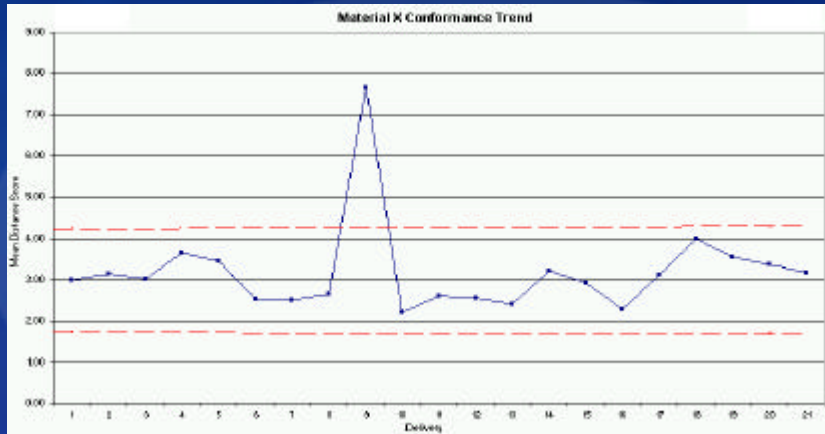


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Material Conformance (cont)

- ◆ How well does a sample conform to previous deliveries?

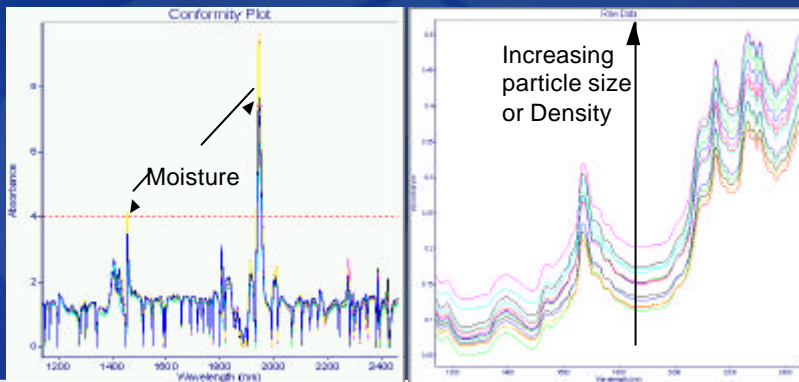


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Material Conformance (cont)

- ◆ What makes the sample Different?
- ◆ Will it affect production?

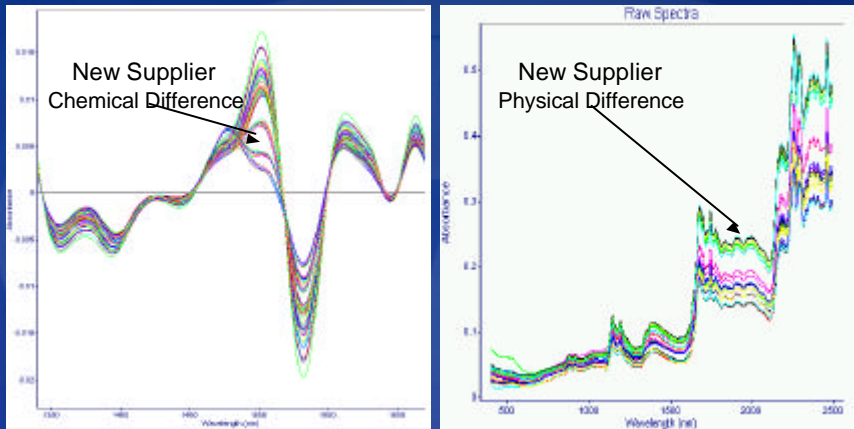


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Material Change Evaluations

- ◆ All material changes are evaluated by NIR



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PAT Application Cleaning Validation / Verification

- ◆ **Current Regulatory Situation**
 - Cleaning validation must be performed to validate the consistent removal of product, microbiological matter and cleaning agents, to an acceptable level, from production equipment.
- ◆ **Traditional Approach**
 - Product has to be extracted from the swab
 - Long sample preparation
 - Destructive testing
 - Limited ability to test for all ingredients

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PAT Application Cleaning Validation / Verification

◆ Pfizer Sydney's Approach

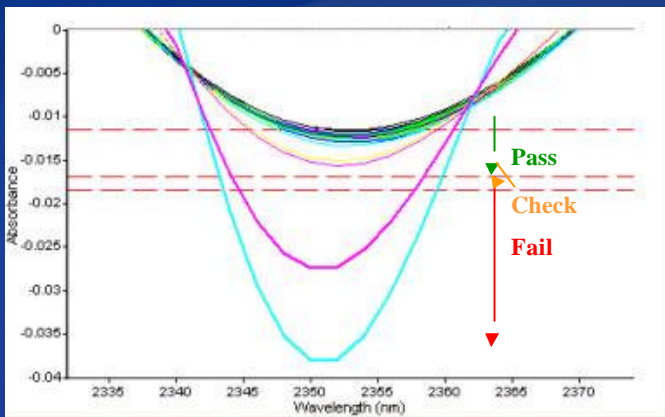
- Developed a method based on direct scanning of swabs by NIR
- Method uses alcohol as solvent
 - Increases number of ingredients that can be tested
 - Rapid sample preparation
- Method does not require the extraction step from swab into test solution (large source of error and time)
- Decreased turn-around time due to greatly reduced sample preparation and analysis time (~60% reduction)
- Developed an easy to use interface for use in the plant by operators

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Cleaning Validation / Verification

◆ Rapid Assessment of non water soluble residue



Swab Holder

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Summary of PAT Benefits

- ◆ True process understanding - as opposed to “blind” compliance
- ◆ Cornerstone of process validation and continuous improvement initiatives
- ◆ Increased process effectiveness through less variation and cycle time reduction
- ◆ Inventory Savings
- ◆ Provide greater quality control and assurance
- ◆ EH&S and Waste Reduction
- ◆ Improved basis for process investigations

Future Directions

- ◆ Extend current PAT applications to other products & materials
- ◆ Further registration of PAT methods with the TGA and Asian authorities
- ◆ Continual focus on material vs process relationships (Process-ability)
- ◆ Rapid micro analysis
- ◆ Move from “At-line” to “In-line” NIR blend analysis

Our Vision

“In the future by determining true process capability we will be able to predict and control the nature of our products, by predicting/controlling the nature of our raw materials, components, processes etc. This will be achieved in “real-time” through process knowledge gained by the use of technologies such as PAT”.