Summary: 2003 Pharmaceutical Process Analytics Roundtable

Steve Arrivo, Pfizer

Andrew Lange, Merck

Attendees

Location: University of Michigan

Dates: 17-18 September 2003

- Pfizer (host)
- Merck
- GSK
- NIST
- Lilly
- CPAC
- MCEC
- Genentec
- Baxter
- Bayer
- Aventis
- 3M Pharma
- Lundbeck
- Control Magazine

Day 1: 26 attendees

Day 2: 25 attendees

PAT Group Structure by Company

Central PAT Groups	Pfizer, Merck, Lilly, Aventis
Merck (Manufacturing)	PAT in Central Analytical; Site contacts
Pfizer Global Support (PGM)	Central Support group
Lundbeck	Product groups own
Site Support Groups	
Pfizer (Manufacturing)	Several site support efforts
Pfizer (R&D)	Site groups - 4
Merck (R&D)	API (1) and Drug Product (1) groups

Benchmarking Survey

- (see Word document summary)

PPAR Steering Committee

- Rick Cooley – Chair, Eli Lilly
- Steve Arrivo – Pfizer
- Andrew Lange – Merck
- ? – Lundbeck
- David Radspinner – Aventis
- ? – GSK

Working Sub-Teams

- *Publications Team*
- Dave Radspinner (Aventis)
- Steve Doherty (Lilly)
- Andrew Lange (Merck)
- Laurie Berry (Pfizer)
- Line Lundsberg-Nielsen (Lundbeck)
- Steve Arrivo (Pfizer)
- Jim Rydzak (or alternate) (GSK)

- *Vendor Audit Team*
- Steve Doherty, Chair – Eli Lilly
- Rob Guenard – Merck
- Casper Leuenhagen – Lundbeck
- Martin Warman – Pfizer
- David Radspinner – Aventis
- GSK

PAT Organizations

- List of groups working on a formal response to FDA
  - PhRMA expert working group
  - USP PAT committee
  - AAPS committee
  - NIRVWoG
  - ISPE
  - PASG
  - CHPA
  - NAMUR
  - PPAR (no, redundant)

Vendor Auditing

- Vendors, FDA, Industry need to set standards
  - Association to perform vendor audits
  - Risk based
  - Drive Internal Harmonization (?)
- Driver $ savings PDA has a group to audit automation suppliers
  - ARC “audit repository” $5k/audit
  - True cost $20k
- Spin off of IFPAC? PQRI?
- Partner with food industry?

Vendor Auditing

- Deliverables
  - Umbrella organization
  - Presentation back to own companies
  - Compliance Audits, then Specifications
- User Requirement Specification
  - Can companies share this to provide unified front to instrument manufacturers?
  - Would include
    - Data format
    - Automation hooks

Formalizing PPAR

- Wants (do)
  - Guide vendors
  - PAT practitioners
  - Influence/define specs
  - Industrial and academic members
  - Promote science-based decisions
  - ID common needs
  - Provide input to other guidelines
  - Write guidelines as needed
  - Influence PAT organizers
- Do not
  - Endorse vendors
  - Include regulatory membership
  - Include vendors
  - Be political

Formalizing PPAR

- PhRMA
  - Excludes generics, vendors
  - Issue with exclusion of academics and consortia
  - Develops working groups
  - Is recognized by regulators as “political”
- PQRI
  - Specific Project/Problem based
  - Defined starting and end points
    - Bad for us – we’d like this to continue!

“Real” costs of implementation

- Andrew Lange, Merck
  - Presented timelines and FTE requirements for an example PAT implementation
- Martin Warman, Pfizer
  - Survey of >100 installations
  - Actual cost of hardware normally 1/3 to 1/7 of total cost
    - e.g. mobile NIR -- $450,000

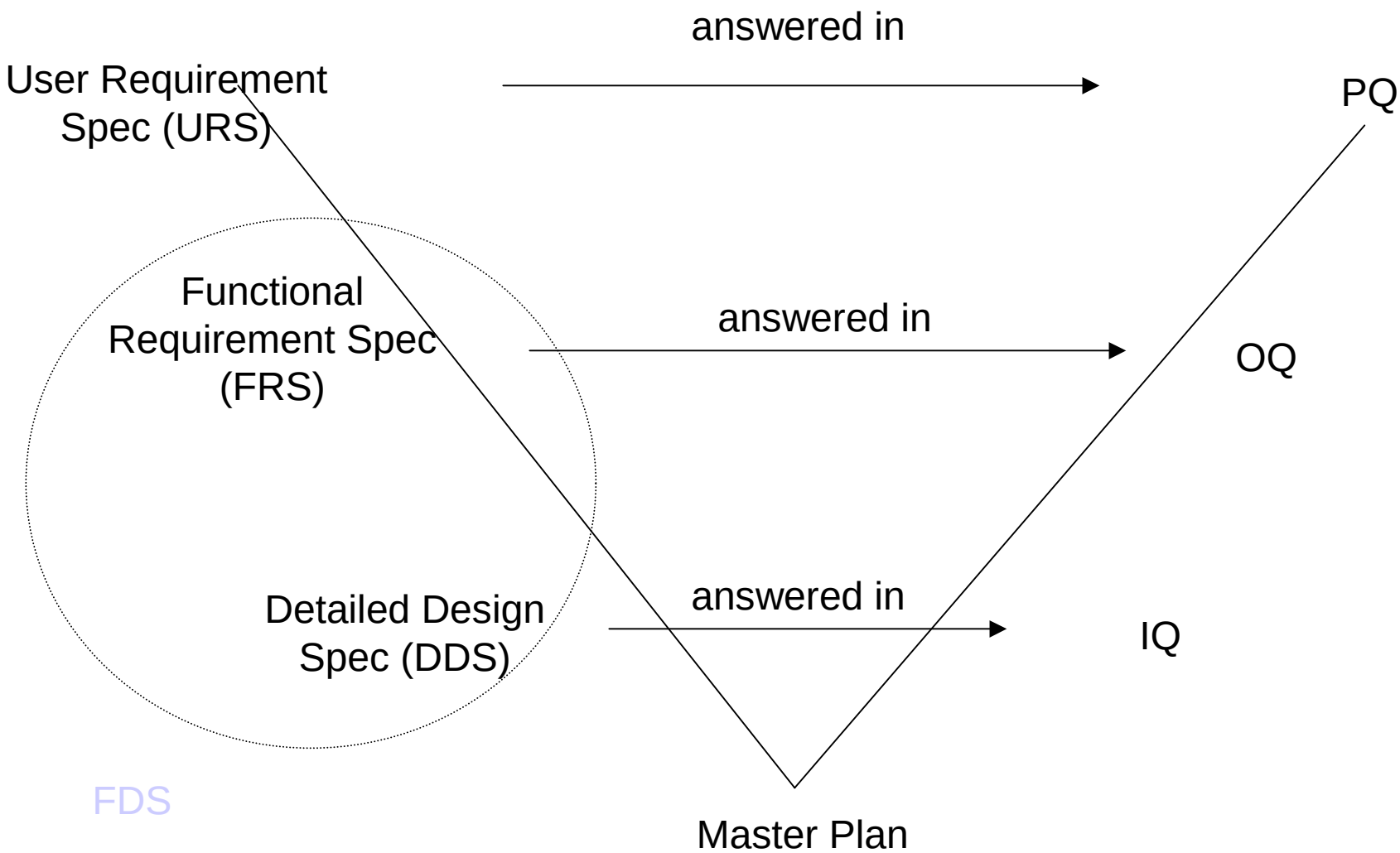
Levels of Qualification

- Level 1 – developer
- Level 2 – for information only
- Level 3 – cGMP
- These levels are decided up front in the “process matrix”

Instrument Qualification

- User Requirement Specification (URS)
- Poling of PPAR companies URS's
  - Sharing for this purpose
  - Blinded USR's
- Define standards for on-line applications

Validation “V”



Levels of Automation

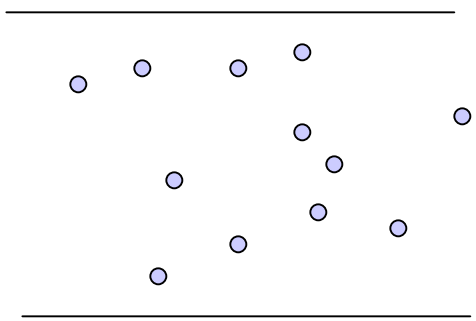
- Level 1 – stand –alone
- Level 2 analog via PLC -- $20k
- Level 3 digital via OPC -- $20k – $160k

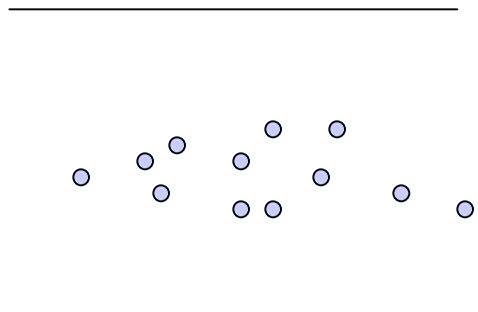
Test Case

- Aventis/Merck/Lilly/Pfizer
- Joint paper(s) using hypothetical cases along the lines of a “mock submission”
- Purpose: drive consistency, define terms, test the waters for actual submission
- API & Drug Product

Six Sigma

- Discussion of specifications versus control limits
  - Never get to 6 sigma if specs are set at process capability





Instrument Diagnostics – USP, etc.

- System suitability
  - Measure sample as suitable and not full wavelength linearization, etc?
  - (chromatography approach)

Action Items

- Working Group for Vendor Audits
  - Focus on Compliance aspects first
  - Collect companies ideas on this – collate
- Working group for publication(s)
  - Series of publications to drive consistency, define terms, set position for PAT
- Generic Manufacturer's Association PAT position presentation – Attached to message
- 10 Minute presentation at FACSS by Arrivo

Going Forward…

- Genentec has agreed to host 2004 edition of PPAR
- Meeting will continue to rotate through the “member” companies
- Sub-teams or groups get together at IFPAC & FACSS (or other) during the year

Going Forward…

- Potential topics for PPAR IV
  - Student Training
  - Infrastructure issues
  - Joint Programs with CPAC, MCEC, UM, etc.
  - Specification setting -> PAT Pharma Team
  - FDA & Pharma Manufacturing (Mel idea – publication?)
  - Contract Manufacturing? How is this covered?
  - Generic Involvement?

Appendix I: Generic PAT Position

- Presentation: See file from message

Appendix II: Questions to Ponder

- "HL7" Electronic stability standards?
- How will PATRIOT review applications?
  - Just PAT parts of NDA or entire dossier?
- How does PAT changes fit into "continuous improvement"?
- Case study – Risk Assessment
  - Publication of positive implementations of PAT – Sharing – Implementation, data storage, etc.
  - helps FDA – e.g. how effective has FDA been in implementing this initiative?
- We need consistent Reviews and Inspections