PolyPeptide GROUP

THE ULTIMATE PEPTIDE PARTNER

GLOBAL SUPPORT FOR A QUALITY SOLUTION

Tim Culbreth

PolyPeptide Group

President - US Operations

Required Disclaimer

- The comments expressed here represent individual perspectives built up over many years experience at multiple firms
- These comments are general in nature and do not reflect any specific product, project or approach
- Other perspectives and approaches are/may be equally valid
  - Can’t we all just get along

PolyPeptide GROUP

Know thy audience – Know thy speaker

- Know thy audience
  - Production?
  - QA?
  - Engineering?
  - Validation?
- Years of experience in the industry?
  - 25 +
  - 20
  - 15
  - 10
  - 5
- I’m in the wrong meeting?

PolyPeptide GROUP

Know thy audience – Know thy speaker

- Know thy speaker
  - Production?
  - QA?
  - Engineering?
  - Validation?
  - QC?
  - Warehouse?
  - Utilities?
  - Hazmat Tech?
- Years of experience in the industry?
  - 25 + (Critical as it relates to Process Validation)
  - 1986
  - Southerner (not SOCAL originally)
- I'm in the wrong meeting?

PolyPeptide GROUP

Know thy speaker

- PDA – (ISPE, ASQ, Lean 6sigma – Greenbelt, RAS, and a few others) – UT Avis
- Habitat for Humanity BOD, Relay for Life Local Chairman, AHA Local Champion, First Robotics Team Sponsor, ….
- Importance – Trade Groups; other groups
- Secret to my success? - Son
- Patient – few comments

PolyPeptide GROUP

Know thy speaker

- I am always asked what is a peptide

- Peptide
  - Between small molecule and biologic in size
  - Chain of AA plus special groups/functional modification
  - Usually trigger or block a response in the body/cells
  - Diabetes, Cancer, Labor, and many other
  - Usually Inj/inf and generally shorter duration than biologics

  - Why I am here AND our industry

PolyPeptide GROUP

Thoughts on Process Validation…(?)

- Ode to Rick Bowles and Bill Mullen – Poetry as a part of Quality

A few core drives and beliefs about New Products and Processes (Process Validation)

“A true vocation calls us out beyond ourselves; breaks our heart in the process and then humbles, simplifies and enlightens us about the hidden, core nature of the work that enticed us in the first place.” – David Whyte

PolyPeptide GROUP

Process Validation

- Brief history
  - 1987 General Principles of PV
  - Concurrent, Prospective, Retrospective
  - IQ, OQ, PQ
  - Multiple (3) batch
  - Worst Case

- Documented evidence, high degree of assurance, a specific process will produce a PRODUCT

- RANDOM INSERTION - Comparison to Airline Safety - Hate it

PolyPeptide GROUP

Initial Reactions

- Can’t be done for certain processes
- Still some hocus pocus and magic in production
- Wax Pencil – who knows what these are???

Failures – that lasted a long time

3 Batch

Worst Case

But we made progress and ushered on

We did a lot of good stuff and actually started learning about our processes

PolyPeptide GROUP

Validation - Other

- Along the way we added
  - Cleaning Validation
  - Computer System Validation (and Part 11 Compliance)
  - Analytical Method Validation
  - Equipment Qualification (Validation)
  - And many other things

PolyPeptide GROUP

PV Update 2008 - 2010

- Life Cycle Approach
  - Process Design (When – early vs late) (just give me my stuff)
    - Development (DOE)
    - Knowledge and understanding
    - Harken back to the Whyte quote
  - Process Qualification
    - Confirm Process Design at Commercial Scale
    - Number of Batches not defined – hmmm?
    - Facility and Equipment Qualified
  - Process Verification
    - Ongoing normal production
    - Learnings based on experience – larger data set
- Final Issued Jan 2011
- We got rid of the “3 batch” and the “Worst Case” aspects
- RANDOM THOUGHT – Eye Lash

PolyPeptide GROUP

PV Guide Issued Jan 2011

- What has happened since:
- Rapid advances in gene technology and analysis
  - I am Irish, Scottish with a little UK/Danish (who knew?)
- Rapid advances in computing power
- Giant increases in prices for some drugs
  - (especially for key fields)
- Stock Market and Venture Capital is living large

PolyPeptide GROUP

FDA – Cancer Focus

- NCI and FDA Oncology Biomarker Qualification Initiative
- FDA Critical Path Initiative (slow at first)
- VP Cancer Moon Shot
- FDA Oncology Center for Excellence

- Side Comment on ritual for current melanoma survivors

PolyPeptide GROUP

Individualized Antigen ImmunoTherapy

- The advances covered in the last two slides lead us to this point and treatment approach – for melanoma

- Biopsy cells removed patient
- Genetic analysis of mutations
- Identify 24 to 36 Patient Specific Neoantigens (Small Peptides)
- Produce each of these Neoantigens in 40 to 50 mg qty (RT)
- Combine Neoantigens in specific groups of five 20 to 30 mg ea (RT)
- Completed sterile fill of 10 to 30 vials (patient specific) (RT)
- Deliver to Hospital
- Administer to patient
- All in less than six to eight weeks (target four weeks)
- 2 to 5 patients every week
- Update computer algorithm based on outcomes

PolyPeptide GROUP

Individualized Antigen ImmunoTherapy

- Validation concepts – Traditional
  - Product specific
    - Process Design
    - Process Qualification
    - Process Verification
    - Analytical Method Development (Many – some general)
    - Full Release Testing (ICH – Impurities, Residual Solvents, Micro, others)
    - Cleaning (Many – some general)

PolyPeptide GROUP

Individualized Antigen ImmunoTherapy

- Validation concepts – New
  - Process Approach – not Product specific but Process Specific
    - Process Design
    - Process Qualification
    - Process Verification
    - Analytical Method Development (Many – some general)
    - Full Release Testing (ICH – Impurities, Residual Solvents, Micro, others)
    - Cleaning (Many – some general)
    - Computer System (algorithms constantly updated)
    - Stability, Sterility
  - What does this look like?
    - Some general thoughts

PolyPeptide GROUP

PV – for Patient Specific Therapies

- Are we as group/organization ready to take the next step?
- Are we ready to partner with the regulatory bodies to move this forward in the coming years to make this viable?

PolyPeptide GROUP

Closing

"To have a firm persuasion in our work – to feel that what we do is right for ourselves and good for the world at exactly the same time – is one of the great triumphs of human existence." – David Whyte

- Thank you for listening
- Questions

PolyPeptide GROUP

www.polypeptide.com