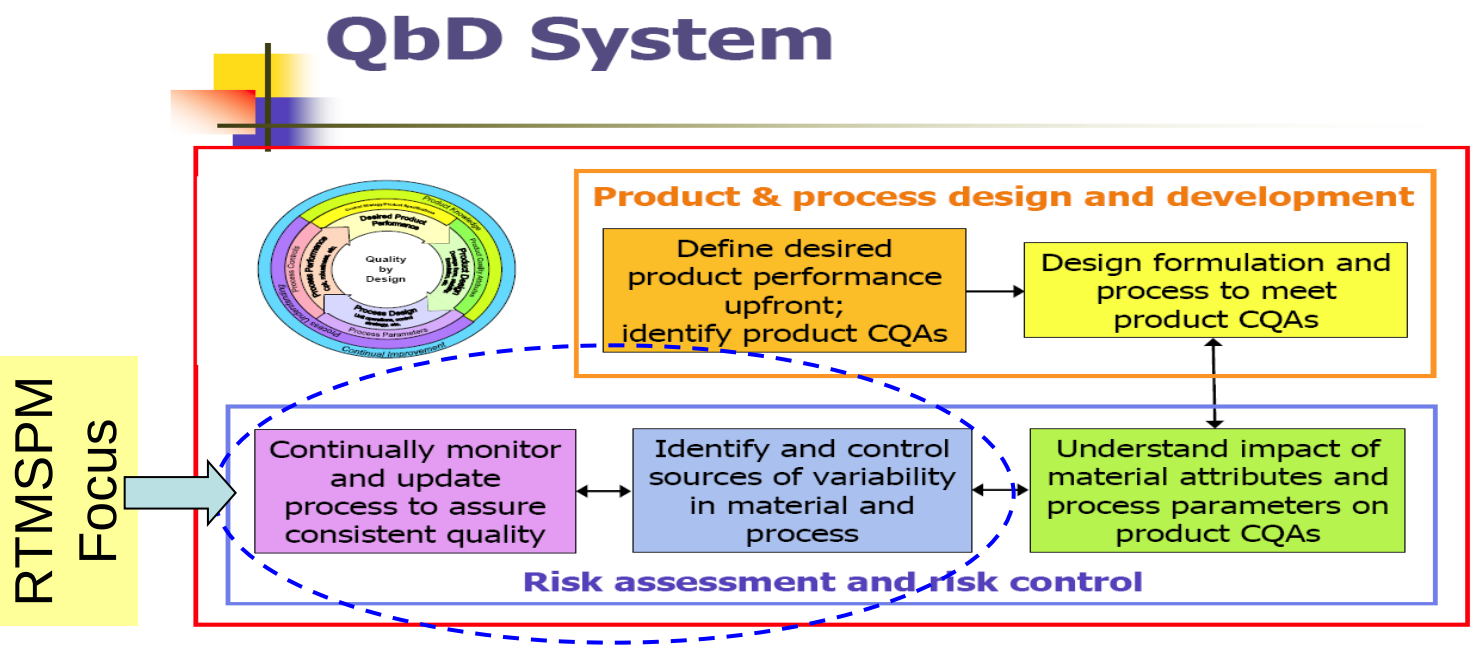
MVDA and Advanced Process Controls

Biologics Mfg Examples

MVDA

- When do we use it?
- Small-scale vs. large-scale data
- DOE/RSD and MVA-based design-space?
- Large-scale postmortem analysis
  - Troubleshooting of mfg
  - Continuous improvement
  - Effectiveness verification of process changes
- RT-MSPM & Soft-sensors

RT-MSPM fits well within the FDA and ICH guidelines



Enhanced Quality by Design Approach (from ICH Q8R1)

- **Lifecycle approach to validation and, ideally, continuous process verification**
- **Use of statistical process control methods**
- **Process operations tracked and trended to support continual improvement efforts post-approval**

A diverse range of monitoring objective(s) is possible via RT-MSPM

1. Fault Detection Based on Historical Data
2. Quality/Performance or Operational Predictions
3. Process Optimization
4. Design Space Monitoring (ICH Q8R1)
5. Real-time Release
   - High standard of Design Space and validated quality prediction methods are required

Adapted from ASTM E55

Needs for New Sensors and Future Challenges for Advanced Control & Monitoring

- Conventional real-time measurements (e.g., pH, pO_2, T, V, P, conductivity) are essential and available
- Open-loop and batch-to-batch control are possible today
- Closed-loop control of CQAs require new measurements or very reliable estimates
- Process Analytical Chemistry tools, new sensors, analyzers are required for measuring CQAs and performance variables (e.g., cell density probes, aggregation measures, amino acid meas. via HPLC)
- Model predictive control technology needs to be adapted to biological processes