Bridge Associates International LLC

"Partners for Quality and Manufacturing Excellence"

Holistic life cycle model checklist for particulate and physical defect prevention and control

A comprehensive checklist of key focus areas within the product life cycle specifically for control of particulate matter and other container or closure defects are listed below:

- ☐ Supplier auditing, raw material and component defect attribute descriptions and criticality categories in alignment with finished product particulate and defect control requirements
- ☐ Supplier specifications, testing or inspection methods evaluated for effectiveness in controlling particulates and defects
- ☐ Supplier quality agreements include finished product particulates and defects quality requirements
- ☐ Primary packaging component specifications alignment with finished product particulate and defect requirements
- ☐ Primary packaging component specifications to assure minimum siliconization levels for machinability
- ☐ Active Pharmaceutical Ingredient (API) specifications alignment with finished product particulate quality requirements
- ☐ Raw materials and excipients specifications alignment with finished product particulate quality requirements
- ☐ Physical defect and particulate descriptions and library for incoming materials
- ☐ Establish Incoming product contact materials particle control, washing or cleaning requirements, such as gaskets, filters, sieves/screens, polymeric tubing, connectors, sterilization wrapping/bags, rigid and flexible plastic process vessels, etc.
- ☐ Particulate controls for process related clean room supplies including gowns, gloves, goggles and wipers
- ☐ Process gasses and point of use filtration for particulate control
- ☐ Process water and point of use filtration for particulate control
- ☐ Raw material weighing/handling processing area particulate controls
- ☐ Formulation/compounding processing areas particulate controls
- ☐ Cellulose free wiping and cleaning materials (synthetic materials) used in processing areas
- ☐ Cellulose free wrapping materials (Tyvek) used in processing areas
- ☐ Appropriate personnel gowning and goggles to reduce extrinsic particle contamination for equipment cleaning and wrapping in grade D(100,000) and grade C(10000) processing areas
- ☐ Equipment/parts washing, wrapping and storage under HEPA laminar flow post-cleaning until sterilization
- ☐ Glass container washing reduction studies using membrane filtration microscopic particle counting for visible particle (glass, fibers) evaluation
- ☐ Glass container washing reduction studies light obscuration or membrane filtration microscopic reserved for sub-visible particle counting evaluation
- ☐ Stopper/elastomer washing reduction studies using membrane filtration microscopic particle counting for visible particle (especially fibers) evaluation
- ☐ Stopper/elastomer washing reduction studies using light obscuration or membrane filtration microscopic for sub-visible particle evaluation.
- ☐ Processing areas –Depyrogenation tunnel or oven maintenance and cleaning routine schedule

- ☐ Processing areas –Filling (routine pump components inspection/maintenance, needle alignment checks, aseptic procedure for component/stopper replenishment, aseptic operator positioning/movement and component handling, etc.)
- ☐ Defined and documented clearance of glass breakage events in all processing steps (after tunnel, filling and stoppering.
- ☐ Physical defects (container-closure) critical, major and minor descriptions and library for finished products
- ☐ Finished Product appearance descriptions and Library
- ☐ Defect standards or test set development, qualification, maintenance
- ☐ Test set matrix and inspector qualification schedule related to the product portfolio
- ☐ Manual inspection work stations with contrasting black and white backgrounds, stabilized illumination, delineated sample inspection position and human ergonomic considerations
- ☐ Manual inspection method development and inspector visible particle size threshold sensitivity qualification
- ☐ Inspector vision screening
- ☐ Inspector training program
- ☐ Training specifically for Stability and Retention inspectors for product, container and elastomer degradation detection
- ☐ Inspector qualification with blinded characterized defect test sets (worst case fatigue scenario)
- ☐ Inspector fatigue breaks and documentation
- ☐ Semi-automated manual inspection method development and inspector defect detection comparison to the qualified manual baseline inspection
- ☐ Semi-automated manual inspection work station with stabilized illumination, magnification, 360^0 sample rotation speed, defined, point of inspection, sample viewing area dwell time, belt speed and machine maintenance
- ☐ Automated inspection equipment method development/tuning, particulate and physical defect detection comparison to the qualified manual 100% and or AQL baseline inspection
- ☐ Statistical manual AQL inspection at time of release (prior to labeling)
- ☐ Database, trending and limits or action level evaluation of test or inspection data from:
    - Suppliers certificate of analysis or conformance to specifications
    - Incoming components or raw materials testing
    - Statistical or periodic in-process manufacturing checks
    - 100% in-process manufacturing inspection
    - Finished product AQL inspection
    - Retention sample inspection
    - Stability sample inspection
    - Customer or field complaints
- ☐ Feedback loop of shared trending and data review across the product life cycle departments
- ☐ Formalized re-inspection practices
- ☐ Reject unit classification and defect population monitoring from 100% in-process inspection
- ☐ Reject unit classification and defect population monitoring from AQL inspection
- ☐ Investigation process of root cause for non-conformance or out of trend data
- ☐ Establishing appropriate corrective or preventative actions