HISTORY AND MILESTONES

- DOC S.r.l., Documentation Organization & Consultancy, was established in 1997 by MASCO group C.E.O. Eng. Alberto Borella and Eng. Paolo Curtò who became Managing Director.

- DOC key personnel are active members of relevant regulatory recognized organizations like PDA, ISPE and FIP.
• DOC operates in Italy through offices based in Padua (near Venice) and Settala (Milan).

• 2011: DOC got from Lloyd’s Quality Assurance Register Limited ISO 9001:2008 certification for “cGMP compliance and validation consultancy services”
• 2014: new DOC headquarter opening in Settala (Milan) including offices, Training and meeting rooms

• 2015: DOC service portfolio enlargement in the areas of Process Validation, Product Qualification and Analytical Laboratory tests supporting pharmaceutical manufacturing Companies in compliance with the latest international regulatory requirements.
To play the role of the “System Integrator”, acting as “Communication Platform & Facilitator” between the cGMP Compliance requirements and the final users. The final result is to provide a functional system totally validated.

Be recognised as a qualified provider of Validation Services for pharmaceutical companies on a global scale.
VALIDATION LIFE CYCLE APPROACH

- User Requirement Specification
- Functional Specification
- Design Specification
- System Maintenance
- Change control and Process Revalidation
- Instrumentation Recalibration
- GMP Personnel Training
- Ongoing Qualification and Validation (Maintenance)
- Release to Manufacturing
- Product Performance Qualification
- Operational Qualification
- Instruments Calibration
- FAT/SAT Support
- Installation Qualification
- Personnel Initial Training & SOPs
- Regulatory and GMP reference as per International Standards, EMA, US FDA, WHO, PIC/S ..

Enhanced Design Review (EDR)
Quality Risk Management (QRM)
- Conceptual Design Support and potential vendors evaluation
- User requirements specification preparation (URS)
- Functional & design specification revision (FDS)
- Quality Risk Management (QRM)
- Design qualification (EDR: Enhanced Design Review)
- Traceability Matrix
- Coordination & assistance (witnessing) for the system commissioning activities at supplier factory & at final user site, i.e:
  - F.A.T. (Factory Acceptance Test)
  - S.A.T. (Site Acceptance Test)
• Validation Protocols preparation, “Site” tests execution & validation reports preparation for:
  • Installation Qualification (IQ)
  • Operational Qualification (OQ)
    • Performance Qualification (PQ)
    • Product Process Validation (PPV)

• Computerized control system validation as per GAMP 5 and 21 CFR part 11 requirements.
Production, storage and distribution of:

- Water for Injection
- Purified Water
- Pure steam
- Process gases (compressed air, nitrogen, etc)

HVAC Systems and related controlled classified areas including:

- Unidirectional Air Flow areas (LAFs)
- Environmental monitoring systems (EMS) for critical parameters
SYSTEM QUALIFICATION – MANUFACTURING EQUIPMENT

API
- Syntesis Reactors
- Filter dryers
- Static dryers
- Freeze Dryers
- Centrifuges
- Crystallizers

Bioprocess (API)
- Fermentation Units
- Incubators
- RO/UF purification units
- Centrifuges
- Downstream Units

Solid finished forms
- Powder Mixers
- High Shear Granulators
- Oscillating Granulators
- Fluidized Bed Granulators and Dryers
- Tableting Machines
- Coating Machines
- Capsules filling and sorting Machines
- Blistering and Secondary Packaging Lines
SYSTEM QUALIFICATION – MANUFACTURING EQUIPMENT

**Liquid Finished Forms**
- Solution preparation and filtration units
- Vials and Ampoules washing, depyrogenation and filling line
- Prefilled Syringes lines
- Bags form, fill and seal machines
- Freeze Dryers (Lyophilizers)
- Sterilization Units (Autoclaves and Ovens)
- VHP sterilizers
- Blow fill and seal machines
- Washing Machines for equipment pieces
- Cold Rooms and Warehouse

**QC Laboratories and Warehouse**
- Sterilization Autoclave
- Washing Machines
- Incubators
- Dry Heat Oven
- LAF and Bio Safety Cabinet
- Freezer
- Dispening Booth
- Warehouse
- Cold Rooms
DOC product process validation services can cover the following typologies:

- **Products as:**
  - Active Pharmaceutical Ingredients (APIs)
  - Antibiotic drug formulations
  - Controlled drug substances and their precursors
  - Cytotoxic drugs
  - Radiopharmaceutical drugs

- **Manufacturing processes as:**
  - Clinical, R&D or small scale pilot batch
  - Stainless steel or Single Use System
  - Long Process campaign
  - High/Low temperature processes
  - High Pressure/Flow
PRODUCT AND PROCESS VALIDATION

VALIDATION STUDIES

PROCESS

PRIMARY PACKAGING

FINISHED PRODUCT
In process material qualification studies on
  • Tubes
  • Connections
  • Process equipment material

Single Use Technology Qualification and Validation

Process Optimization Study
  • Screening, filterability and scale-up studies

Product and Process Filter Validation
  • Compatibility
  • Extractables and Leachables
  • Adsorption Studies
  • Viability Studies
  • Bacterial Retention Studies
• Extractables and Leachables Studies

• Toxicological Evaluation and Assessment

• Cleaning Validation
  • Validation Master Plan
  • Risk Assessment
  • S.O.P. Development and Review
  • Cleaning Validation Protocol and Report
  • Grouping & Bracketing Approach
  • Toxicological Assessment (PDE)

• Sanitizing Efficacy Validation

• Analytical Method Development, Validation and Transfer

• Particle Release Testing and Foreign Matters
PRODUCT VALIDATION

- Material Qualification Studies
  - Compatibility
  - Adsorption Studies

- Extractables and Leachables Studies on
  - Elastomeric closures
  - Containers Glass
  - Containers Plastic

- Toxicological Evaluation Assessment

- Container Closure Integrity Test
PRODUCT VALIDATION

- Sterility Test Studies
- Endotoxin Limit Test (LAL test)
- Stability Studies
  - Accelerated and Real Stability
  - Photo stability
  - Oxidation Studies
- AD/Mix Studies
- Antimicrobial Effectiveness Testing
- Antimicrobial Susceptibility Testing
- Leachables Studies
- Analytical Method Development
Validation maintenance services supplied by DOC include the implementation of the following Support Systems, able to maintain the “Validated State”:

- Standard operating procedure (SOP) for:
  - Operation and cleaning
  - Instruments calibration
  - Preventive maintenance
  - Change control & re-validation
- Process and System re-validation
- Periodical instruments calibration
- Preventive maintenance program
- Change control management
• Delivered by qualified trainers and active members of PDA, ISPE
• Duration Customized from Half a day to Two days standard modules
• Available upon request as totally tailored modules
• Deliverables at DOC site (30 attendees as ideal number for interaction) or at customer site
• Each Training includes a group/individual final evaluation session
• Official Attendance Certificate
CONSULTANCY

- New Facility Conceptual Design
- Pharmaceutical Manufacturing Systems Design Review
  - Quality Risk Analysis (as per ICH Q9)
  - FAT/SAT. support
  - Automated System Development, Change Control and Revalidation (SCADA/DCS)
  - GMP Process & System review
  - Existing Facility Audit
- Validation Master Plan
- SOP /Documentation Preparation
- Single Use Systems Design
- SOP /Documentation Preparation
- GMP Process & System review
- Existing Facility Audit
- Automated System Development, Change Control and Revalidation (SCADA/DCS)
- Quality Risk Analysis (as per ICH Q9)
- FAT/SAT. support
- Pharmaceutical Manufacturing Systems Design Review
- New Facility Conceptual Design
- Consultancy
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