

## “Navigate GMP with DBA”\*

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Internal auditing – including checklist

Steps for “Plan – RAM” (recognise – action – manage)

### Preparation for an internal audit

#### Define the **Scope of Internal audit**

*Objective*

*Type*

*Depth*

*Timing*

*Inspectors:*

*size of team*

*make-up of team*

#### **Notification**

*The area being inspected*

*Team members*

*expert support*

*other inspectors*

*Other interested parties*

#### **Review documentation from previous audits**

*Company file*

*Site Master File*

*Manufacturing licence*

*Registration dossiers*

*Previous 3rd party reports and CAPA*

*Adverse Drug Reaction reports (ADRs)*

*Previous internal audit reports and CAPA*

*Records*

*Complaints and recalls*

*Regulatory test results (surveillance)*

#### **Program – prepare checklists, aide memoirs and agenda**

*Checklist*

*Aide-mémoire for internal audit*



Develop internal audit programme

Distribute internal audit programme

Company

Team

1. Use checklists with caution – often get distracted by competing the checklist or worse adds multiple journeys to same room, eg first to check all equipment labeling, then records etc. They should not a substitute for understanding of the GMP guidelines.
2. Use a notebook for entries during the audit.
3. Note some questions on the checklist require multiple answers!
4. Combine horizontal audit (room to room) with vertical audit (backward and forward traceability) Choose three batches for eg traceability of components and raw materials (b) records of raw materials, training records, validation, etc
5. Spend more time on major issues less time on trivial issues.

### **Principle**

Ensures that a company's operations remain compliant with GMP

Assists in ensuring continuous quality improvement

Should cover all aspects of production and quality control

Be designed to detect shortcomings in the implementation of GMP

Must recommend corrective action if shortcomings are observed

Set a timetable for corrective action to be completed

Special occasions may demand additional self-inspections. For example

- Recalls

- Repeated rejections

- GMP inspections announced by the National Drug Regulatory Authority

Team should consist of personnel who can evaluate the situation objectively

- No conflict of interest

- No revenge in mind

- Should have experience as observers before becoming team member

Lead self-auditors with experience as team member

### **Scope of Self-Audit program**

Written instructions covering all aspects of GMP:

personnel

premises including personnel facilities

maintenance of buildings and equipment

storage of starting materials and finished products

equipment

production and in-process controls

quality control  
documentation  
sanitation and hygiene  
validation and revalidation programmes  
calibration of instruments or measurement systems  
recall procedures  
complaints management  
labels control  
results of previous self-inspections and any corrective steps taken

### **The Self-Audit Team**

Team leader needs:

authority  
experience  
may be appointed from inside or outside the company

Team members, including local staff who are familiar with the area, and experts in their own field familiar with GMP may be appointed from inside or outside the company

Key points to set in SOP

Frequency  
Report:  
results  
evaluation  
conclusions  
recommended corrective measures, if applicable  
Follow-up action

Company management must evaluate both the report and corrective actions



Aide Memoir for Audit of Non-Sterile Products

**COMPANY:** \_\_\_\_\_

**ADDRESS/Contacts**  
: \_\_\_\_\_

**LICENCE NUMBER:** \_\_\_\_\_

**DATE(s) OF INSPECTION:** \_\_\_\_\_

**AUDITORS**  
\_\_\_\_\_  
\_\_\_\_\_

**Audit ref:** \_\_\_\_\_

Section	Area	Comments
<b>I</b>	<b>General Information</b>	
	Pharmaceutical Activities Approved  Purpose of audit  Inspection Plan  Review of Previous Audit Issues  Pre-audit Comments  Personnel Met  Company Profile  Changes Since Last audit	
<b>II</b>	<b>Quality Management / Quality Assurance</b>	
	Batch Disposition  - Disposition by QA - Declaration of compliance (GMP & MA) - Manufacturing and QC documents complete - Close out of Deviations  Manufacturer's Licence  - Review Accuracy of Licence	

Section	Area	Comments
	<p data-bbox="411 226 520 255">Content</p> <p data-bbox="347 297 636 327">Customer Complaints</p> <ul data-bbox="359 369 805 465" style="list-style-type: none"> <li>- Complaints SOP &amp; Log</li> <li>- Complaint handling (Quality &amp; Clinical)</li> </ul> <p data-bbox="347 508 767 537">Deviations / Non Conformances</p> <ul data-bbox="359 580 799 741" style="list-style-type: none"> <li>- SOP and Log</li> <li>- Completeness of investigation</li> <li>- Close out &amp; QP notification</li> <li>- Validation / Training Implications</li> </ul> <p data-bbox="347 853 743 882">Recall - SOP and Log</p> <ul data-bbox="359 925 799 1391" style="list-style-type: none"> <li>- TGA on circulation list</li> <li>- 24hr contact numbers</li> <li>- Notification of QP</li> <li>- Discussion with IMB before action</li> <li>- Identification of distribution chain</li> <li>- Notification of all concerned authorities</li> <li>- Handling of recalled material</li> <li>- Investigation and Final Report sent to TGA <ul data-bbox="512 1330 791 1391" style="list-style-type: none"> <li>- Challenging of Recall procedure</li> </ul> </li> </ul> <p data-bbox="347 1433 743 1462">Change Control SOP and Log</p> <ul data-bbox="359 1505 810 2000" style="list-style-type: none"> <li>- Ensure compliance with MA</li> <li>- Comprehensive investigation prior to implementation</li> <li>- Evaluation of effectiveness after implementation.</li> <li>- Approval by relevant personnel</li> <li>-</li> <li>- Supplier Evaluation / Auditing – audit log / schedule</li> <li>- Periodic quality evaluation</li> <li>- Notification of quality issues to persons responsible for supplier audits (eg Corporate QA)</li> <li>-</li> </ul>	

Section	Area	Comments
	<p data-bbox="347 230 675 259">Annual Product Reviews</p> <p data-bbox="347 264 775 327">Self Inspection – SOP and Log / Schedule</p> <ul style="list-style-type: none"> <li data-bbox="347 367 719 430">- All relevant areas covered annually</li> </ul> <p data-bbox="347 470 560 499">Site Master File</p> <p data-bbox="347 539 691 568">Accurate reflection of Site</p> <p data-bbox="347 609 533 638">PIC/S Format</p> <p data-bbox="347 752 655 781">Documentation Control</p> <p data-bbox="347 822 719 851">Reproduction of BMR / BPR</p> <p data-bbox="347 891 727 954">Issue / Change of Controlled Documents</p> <p data-bbox="347 994 564 1023">Revision History</p> <p data-bbox="347 1064 751 1093">Security of Storage / Archiving</p> <p data-bbox="347 1133 738 1162">SOPs available at site of use.</p> <p data-bbox="347 1276 812 1305">Contract Manufacture and Analysis</p> <p data-bbox="347 1346 568 1375">Written Contract</p> <p data-bbox="347 1415 632 1444">Auditing of contractor</p> <p data-bbox="347 1485 668 1514">Responsibilities Defined</p> <p data-bbox="347 1554 576 1583">QP Role Defined</p> <p data-bbox="347 1624 679 1653">Notification of Deviations</p>	
	<ul style="list-style-type: none"> <li data-bbox="347 1742 544 1771">- Personnel</li> <li data-bbox="347 1776 363 1805">-</li> <li data-bbox="347 1809 703 1839">- Company Organogram</li> <li data-bbox="347 1843 363 1872">-</li> <li data-bbox="347 1877 751 1939">- Independence of Quality &amp; Production</li> <li data-bbox="347 1944 807 1973">- Key Job Descriptions – Signed</li> <li data-bbox="347 1977 363 2007">-</li> <li data-bbox="347 2011 727 2040">- Training</li> </ul>	

Section	Area	Comments
	<ul style="list-style-type: none"> <li>-</li> <li>- Training Assessment</li> <li>-</li> <li>- GMP at Induction /Ongoing GMP training</li> <li>-</li> <li>- Documenting of Skills Training</li> <li>- Training Time Appropriate for Skills</li> <li>-</li> <li>- SOP training</li> <li>-</li> </ul>	
<b>III</b>	<b>Premises &amp; Equipment / Production</b>	
	<p><b>Warehouse</b></p> <p>Building facility</p> <p>Pest Control</p> <p>Temperature Mapping &amp; Ongoing Monitoring</p> <p>Receipt of Materials, Checking &amp; Batch Numbering</p> <p>Material Segregation &amp; Labelling</p> <p>Computer Control of Material Status</p> <p>Storage of Rejected Materials</p> <p>Storage of Printed Packaging Materials</p>	
	<p><b>Sampling</b></p> <p>Location</p> <p>Facility – Air Handling, Area Classification, Air locks</p> <p>Garbing Facilities</p> <p>Sampling Equipment</p> <p>Cleaning Procedures for Room and Equipment</p> <p>Room Status Labelling</p>	

Section	Area	Comments
	<p><b>Dispensing</b></p> <p>Facility &amp; Air Handling</p> <p>Sequence of Operation / Cleaning</p> <p>Room Status Labelling</p> <p>Weighing Equipment</p> <p>Computer Controlled Dispensing</p> <p>Bagging and Labelling</p> <p>Cleaning Procedure</p> <p>Documentation for the Weighing Process</p> <p>Dispensing Tolerances</p>	
	<p>Manufacturing Process</p> <p>Garment Appropriate for Area Classification</p> <p>Garment Facility – Washing Facilities</p> <p>SOP displayed</p> <p>Step over bench / clear demarcation</p> <p>Procedure for laundering factory garb</p> <p>Personnel Flow / Material Flow</p> <p>Material Transfer Via Pipelines – Auto./ Manual Controls</p>	
	<p>Processing Equipment</p>	

Section	Area	Comments
	<ul style="list-style-type: none"> <li>- Condition and Calibration Status</li> <li>- Logbooks</li> <li>SOPs for Operation &amp; Cleaning</li> <li>Manufacturing Process</li> <li>Detailed instructions</li> <li>Equipment checks (eg screens)</li> <li>Specifications for Variables</li> <li>Critical Data Recorded</li> <li>In-Process Controls</li> <li>Yield Calculations / Specifications</li> <li>Computerised System Control</li> <li>Reworking - &lt; 10 % rework incorporated</li> <li>Criteria for allowing rework</li> <li>Stability and Shelf Life implications</li> <li>Written justification by QP</li> <li>Increased QC</li> <li>Compliance with MA</li> </ul>	
	<ul style="list-style-type: none"> <li>Packaging Clearance - Detailed Line</li> <li>- Automated Security Mechanisms On-line</li> <li>- On-Line Challenges</li> <li>- Statistical basis for FP sampling</li> <li>Samples of Printed Packaging Attached</li> <li>Reconciliation of Packaging</li> </ul>	

Section	Area	Comments
	<p>Materials</p> <p>Revision Control for Printed Packaging</p> <ul style="list-style-type: none"> <li>- Expiry Dating</li> </ul> <p>Review of Batch Records (BMR &amp; BPR)</p> <p>Standard of Completion</p> <p>Yields and Reconciliations</p> <p>Data Amendment</p> <p>Process Deviations</p> <p>Samples of Printed Packaging</p> <p>Cleaning Procedures &amp; Cleaning Records</p> <p>CIP Vs Manual Cleaning</p> <p>Dedicated / Non Dedicated Equipment</p> <p>Use of Detergents</p> <p>Rotation of Disinfectants / Detergents</p> <p>Preparation of Disinfectant / Detergent</p> <p>Final rinse with Demineralised Water</p> <p>Washroom Facility</p> <p>Segregation of Clean &amp; Dirty Equip.</p>	
<b>IV</b>	<b>Utilities &amp; Maintenance</b>	
	Process Water	

Section	Area	Comments
	<p>Uses</p> <p>Materials of construction</p> <p>Location</p> <p>Dead Legs</p> <p>Continuous recirculation - Draining / Flushing</p> <p>Resin Beds</p> <p>Monitoring of Generation System – Checks / Frequency</p> <p>Welding</p> <p>Iron Fouling</p> <p>Sanitisation - How / When</p> <p>Regeneration - How / When</p> <p>Passivation - How / When</p> <p>Conductivity Meters – Position / Calibration</p> <p>Monitoring for Leakage</p> <p>Sampling Points – Number &amp; Location</p> <p>Water Quality Tests - Type / Frequency</p> <p>Air Handling</p> <p>Monitoring of Air Handling System</p> <p>Temperature &amp; Humidity monitoring</p> <p>Air Filtering &amp; Recirculation</p> <p>Air Changes / Hour (Recommended Min 15 ac/hr)</p> <p>Differential Pressures (Recommended 10-15 Pa)</p>	

Section	Area	Comments
	<p>Location of air intake &amp; extract</p> <p>Filter inspection/ cleaning/ replacement</p> <p>Compressed Air</p> <ul style="list-style-type: none"> <li>- Contact with Product / 1° Packaging</li> <li>- Filtration to remove oil / particles</li> </ul> <p>Nitrogen</p> <ul style="list-style-type: none"> <li>- Purchased or generated on site</li> <li>- Quality</li> </ul> <p>Drains</p> <p>Sanitary design / gully traps</p> <p>Drain connections between buildings</p> <p>Maintenance Programme</p> <p>Planning and recording of Preventative Maintenance</p> <p>Instrumentation list identifying Critical Instruments</p> <p>Identification / Calibration of instrument loops</p> <p>Approved Instrument Calibration Tolerances</p> <p>Calibration Grace Periods</p> <p>Certification of Instruments used for Calibration</p>	

Section	Area	Comments
	Equipment Handover after Maintenance (Planned & Unplanned)	
<b>V</b>	<b>Validation</b>	
	Validation Master Plan  Facilities Qualification  Air Handling System Validation  Water System Validation  Building Management System    Equipment Qualification  DQ / IQ/ OQ/ PQ  Computer Systems  Inventory and Risk Assessment  System classification  User Requirement Specification  Functional Design Specification  Installation Qualification  Operation Qualification  Performance Qualification  Ongoing system monitoring /assessment   Validation Considerations  Security of Access  Audit Trail  Back-Up Procedures  Disaster Recovery	

Section	Area	Comments
	<p>Training Records</p> <p>Challenges to the System</p> <p>Process Validation</p> <p>Identification of Critical Process Steps</p> <p>Prospective, Concurrent, Retrospective</p> <p>Analytical Methods Validated</p> <p>Unit Dose Sampling (3 x unit dose)</p> <p>Process Capability Studies</p> <p>Deviations from Protocol</p>	
	<p>Cleaning Validation</p> <p>Defined Residues for Actives</p> <p>Defined Residues for Detergents</p> <p>Defined Microbial Cleanliness</p> <p>Product Matrix Established</p> <p>Identification of Worst Case Scenarios</p> <p>Analytical Method Validation</p> <p>Limit of Detection</p> <p>Limit of Quantitation</p> <p>Swab Vs Rinse Method</p> <p>Recovery Studies</p> <p>Validation of Time Limits</p> <p>(Processing – Cleaning – Processing)</p>	

Section	Area	Comments
VI	Quality Control	
	<p>Samples - Log in of Samples</p> <p>Generation of Test Record</p> <p>Blending of Composite Samples</p> <p>- Sampling Plan / Representative Sampling</p> <p>- Sample Container Labelling</p> <p>Storage of Samples</p> <p>Retention Periods for active and excipient samples, storage &amp; monitoring</p> <p>Reagents / - Labelling</p> <p>Solutions - Shelf Life</p> <p>Test Data - Laboratory Note Books</p> <p>Presentation of Raw Data</p> <p>Calculation Checks</p> <p>Traceability of Chromatography Solns</p> <p>Chromatography Column Traceability</p> <p>System Suitability</p> <p>Bracketing Standards (e.g. 1 duplicate after 3 duplicate sample injections)</p> <p>Trend Analysis</p> <p>Reference Standards</p>	

Section	Area	Comments
	<p>Source of Primary Standards</p> <p>Preparation of Secondary Standards</p> <p>Storage of reference standards</p> <p>Documenting use of standards</p> <p>Out Of Specification Results</p> <p style="padding-left: 40px;">- Procedure defining course of action</p> <p>Analytical Solutions Retained ?</p> <p>Justifiable Cause ?</p> <p>Non-justifiable cause sufficient number of retests must be carried out (usually 6)</p> <p>Resampling - approval</p> <p>OOS log</p> <p>Equipment</p> <p>Suitability</p> <p>Maintenance</p> <p>Cleaning</p> <p>Validation of Programmed Calculations and Change Control</p> <p>Validation and Ongoing Monitoring of Storage / Test Incubators, Fridges, Freezers</p> <p>Log for use of chromatography columns</p> <p>Glassware</p>	
	<p>Approval</p> <p style="text-align: center;">-</p> <p>Responsibilities defined for approval of</p> <p style="padding-left: 40px;">starting materials, intermediates and</p>	

Section	Area	Comments
	<p style="text-align: center;">finished</p> <p>product.</p> <p>Stability Programme</p> <p>Programme for finished product batches</p> <p>Programme for bulk product (if sold)</p> <p>Storage conditions</p> <p>Stability Chamber Monitoring</p> <p>Stability Tests - Stability Indicating ?</p> <p>Shelf life Vs Release Specification</p> <p>Stability Data Review / Trend Analysis</p> <p>OOS Investigations</p> <p>Reporting of stability failures</p> <p>Environmental Monitoring</p> <p>Methods Used (Air sampling, Contact Plates, Settle Plates)</p> <p>Frequency</p> <p>Trend Analysis</p> <p>Acceptance Criteria (appropriate for area classification)</p> <p>General Microbiology</p>	

Section	Area	Comments
	<p>Choice of culture media</p> <p>SOPs &amp; Batch documentation for media preparation</p> <p>Preparation + Autoclaving</p> <p>Validation of Autoclaving Cycle and Equipment</p> <p>Conditions for Preparation of Media – exposure to open env.</p> <p>Dedicated glassware for media containing antimetabolites, inhibitors etc.</p> <p>Use of +ve controls</p> <p>Media batch number &amp; expiry dating.</p> <p>Rinse Fluids, solubilisers, inactivators</p> <ul style="list-style-type: none"> <li>- Control + Documenting of preparation</li> <li>-Validation of suitability for use at concs. Used</li> </ul> <p>Library of typical organisms</p> <p>Reporting of OOS data</p> <p>Media QC (per batch)</p>	

<b>21 CFR 211 checklist</b>	
1.0	General Controls
	Does the facility and its departments (organizational units) operate in a state of control as defined by the GMP regulations?
1.1	Organizational & Management Responsibilities
1.101	Does this facility/business unit operate under a facility or corporate quality policy?
1.102	§211.22(a) Does a Quality Assurance unit (department) exist as a separate organizational entity?
1.103	§211.22(a) Does the Quality Assurance unit alone have both the authority and responsibility to approve or reject all components, drug product containers and closures, in-process materials, packaging materials, labeling and drug products?
1.104	§211.22 Does the QA department or unit routinely review production records to ensure that procedures were followed and properly documented?
1.105	§211.22(b) Are adequate laboratory space, equipment, and qualified personnel available for required testing?
1.106	If any portion of testing is performed by a contractor, has the Quality Assurance unit inspected the contractor's site and verified that the laboratory space, equipment, qualified personnel and procedures are adequate?
1.107	Date of last internal audit
1.108	§211.22(c) Are all QA procedures in writing?
1.109	§211.22(c) Are all QA responsibilities in writing?
1.110	Are all written QA procedures current and approved? (Review log of procedures)
1.111	Are the procedures followed? (Examine records to ensure consistent record-keeping that adequately documents testing.)
1.112	§211.25 Are QA supervisory personnel qualified by way of training and

experience?	
1.113 §211.25 Are other QA personnel, e.g., chemists, analysts, laboratory technicians) qualified by way of training and experience?	
1.2 Document Control Program	
1.201 §211.22(a) Does the QA unit have a person or department specifically charged with the responsibility of designing, revising, and obtaining approval for production and testing procedures, forms, and records?	
1.202 §211.22(d) Does a written SOP, which identifies how the form is to be completed and who signs and countersigns, exist for each record or form?	
1.203 §211.165(a)(b)(c) Is the production batch record and release test results reviewed for accuracy and completeness before a batch/lot of finished product is released?	
1.3 Employee Orientation, Quality Awareness, and Job Training	
1.301 Check training for new employee: (1) Company brochure (2) Literature describing GMP regulations and stressing importance of following instructions. (3) On-the-job training for each function to be performed (before the employee is allowed to perform such tasks). (4) Other: enter in notebook.	
1.302 §211.25(a) Does each employee receive retraining on an SOP (procedures) if critical changes have been made in the procedure?	
1.303 Indicate how on-going, periodic GMP training is accomplished.	
1.304 §211.25 is all training documented in writing that indicates the date of the training, the type of training, and the signature of both the employee and the trainer?	
1.305 §211.25 Are training records readily retrievable in a manner that enables one to determine what training an employee has received, which employees have been trained on a particular procedure, or have attended a particular training program?	
1.306 Are GMP trainers qualified through experience and training?	
1.307 §211.25(a) Are supervisory personnel instructed to prohibit any employee who, because of any physical condition (as determined by medical examination or supervisory observation) that may adversely affect the safety or quality of drug products, from coming into direct contact with any drug	

component or immediate containers for finished product?	
1.308 §211.28(d) Are employees required to report to supervisory personnel any health or physical condition that may have an adverse effect on drug product safety and purity?	
1.309 §211.25(a) Are temporary employees given the same orientation as permanent employees?	
1.310 §211.34 Are consultants, who are hired to advise on any aspect of manufacture, processing, packing or holding, of approval for release of drug products, asked to provide evidence of their education, training, and experience?	
1.311 §211.34 Are written records maintained stating the name, address, qualifications, and date of service for any consultants and the type of service they provide?	
1.4 Plant Safety and Security	
1.401 Does this facility have a facility or corporate safety program?	
1.402 Are safety procedures written?	
1.403 Are safety procedures current?	
1.404 Do employees receive safety orientation before working in the plant area?	
1.405 Is safety training documented in a readily retrievable manner that states the name of the employee, the type of training, the date of the training, and the name of the trainer and the signature of the trainer and the participant?	
1.406 Does this facility have a formal, written security policy?	
1.407 Is access to the facility restricted?	
1.408 Describe how entry is monitored/restricted:	
1.409 Is a security person available 24 hours per day?	
1.5 Internal Quality/GMP Audit Program	
1.501 Does this business unit/facility have a written quality policy?	
1.502 Is a copy of this quality policy	

furnished to all employees?	
1.503 If "yes" to above, when provided? _____	
1.504 Is training provided in quality improvement?	
1.505 Does a formal auditing function exist in the Quality Assurance department?	
1.506 Does a written SOP specify who shall conduct audits and qualifications (education, training, and experience) for those who conduct audits?	
1.507 Does a written SOP specify the scope and frequency of audits and how such audits are to be documented?	
1.508 Does a written SOP specify the distribution of the audit report?	
1.6 Quality Cost Program	
1.601 Does this facility have a periodic and formal review of the cost of quality?	
1.602 Does this facility have the ability, through personnel, software, and accounting records, to identify and capture quality costs?	
1.603 Does this facility make a conscious effort to reduce quality costs?	
2.0 Design Control	
Not directly related to the Drug Regulation	
3.0 Facility Control	
3.1 Facility Design and Layout	
3.101 §211.42(a) Are all parts of the facility constructed in a way that makes them suitable for the manufacture, testing, and holding of drug products?	
3.102 §211.42(b) Is there sufficient space in the facility for the type of work and typical volume of production?	
3.103 Does the layout and organization of the facility prevent contamination?	
3.2 Environmental Control Program	
3.201 The facility is NOT situated in a location that potentially subjects workers or product to particulate matter, fumes, or infestations?	

3.202	Are grounds free of standing water?	
3.203	§211.44 Is lighting adequate in all areas?	
3.204	§211.46 Is adequate ventilation provided?	
3.205	§211.46 Is control of air pressure, dust, humidity and temperature adequate for the manufacture, processing, storage or testing of drug products?	
3.206	§211.46 If air filters are used, is there a written procedure specifying the frequency of internal audit and replacement?	
3.207	Are drains and routine cleaning procedures sufficient to prevent standing water inside the facility?	
3.208	§211.42(d) Does the facility have separate air handling systems, if required, to prevent contamination? (MANDATORY IF PENICILLIN IS PRESENT!)	
3.3	Facility Maintenance and Good Housekeeping Program	
3.301	§211.56(a) Is this facility free from infestation by rodents, birds, insects and vermin?	
3.302	§211.56(c) Does this facility have written procedures for the safe use of suitable, (e.g. those that are properly registered) rodenticides, insecticides, fungicides, and fumigating agents?	
3.303	Is this facility maintained in a clean and sanitary condition?	
3.304	Does this facility have written procedures that describe in sufficient detail the cleaning schedule, methods, equipment and material?	
3.305	Does this facility have written procedures for the safe and correct use of cleaning and sanitizing agents?	
3.306	§211.58 Are all parts of the facility maintained in a good state of repair?	
3.307	§211.52 Is sewage, trash and other refuse disposed of in a safe and sanitary manner (and with sufficient frequency?)	
3.4	Outside Contractor Control Program	
3.401	§211.56(d) Are contractors and temporary employees required to perform	

their work under sanitary conditions?	
3.402 ¶ 163 Are contractors qualified by experience or training to perform tasks that may influence the production, packaging, or holding of drug products?	
4.0 Equipment Control	
4.1 Equipment Design and Placement	
4.101 §211.63 Is all equipment used to manufacture, process or hold a drug product of appropriate design and size for its intended use?	
4.102 Are the following pieces of equipment suitable for their purpose? Blender(s), Conveyor(s), Tablet, Presses, Capsule Fillers, Bottle Fillers, Other (specify).	
4.103 Are the following pieces of equipment suitable in their size/capacity? Blender(s), Conveyor(s), Tablet, Presses, Capsule Fillers, Bottle Fillers, Other (specify).	
4.104 Are the following pieces of equipment suitable in their design? Blender(s), Conveyor(s), Tablet, Presses, Capsule Fillers, Bottle Fillers, Other (specify).	
4.105 Are the locations in the facility of the following pieces of equipment acceptable? Blender(s), Conveyor(s), Tablet, Presses, Capsule Fillers, Bottle Fillers, Other (specify).	
4.106 Are the following pieces of equipment properly installed? Blender(s), Conveyor(s), Tablet, Presses, Capsule Fillers, Bottle Fillers, Other (specify).	
4.107 Is there adequate space for the following pieces of equipment? Blender(s), Conveyor(s), Tablet, Presses, Capsule Fillers, Bottle Fillers, Other (specify).	
4.108 §211.65(a) Are machine surfaces that contact materials or finished goods non-reactive, non-absorptive, and non-additive so as not to affect the product?	
4.109 §211.65(b) Are design and operating precautions taken to ensure that lubricants or coolants or other operating substances do NOT come into contact with drug components or finished product?	
4.110 §211.72 Fiber-releasing filters are NOT used in the production of injectable products?	
4.111 § 211.72 Asbestos filters are NOT used in the production of products?	

4.112 Is each idle piece of equipment clearly marked "needs cleaning" or "cleaned; ready for service"?	
4.113 Is equipment cleaned promptly after use?	
4.114 Is idle equipment stored in a designated area?	
4.115 §211.67(a)(b) Are written procedures available for each piece of equipment used in the manufacturing, processing or holding of components, in-process material or finished product?	
4.116 Do cleaning instructions include disassembly and drainage procedure, if required, to ensure that no cleaning solution or rinse remains in the equipment?	
4.117 Does the cleaning procedure or startup procedure ensure that the equipment is systematically and thoroughly cleaned?	
4.2 Equipment Identification	
4.201 §211.105 Are all pieces of equipment clearly identified with easily visible markings?	
4.202 §211.105(b) Are all pieces of equipment also marked with an identification number that corresponds with an entry in an equipment log?	
4.203 Does each piece of equipment have written instructions for maintenance that includes a schedule for maintenance?	
4.204 Is the maintenance log for each piece of equipment kept on or near the equipment?	
4.3 Equipment Maintenance & Cleaning	
4.301 §211.67(b) Are written procedures established for the cleaning and maintenance of equipment and utensils?	
4.302 Are these procedures followed?	
4.303 §211.67(b)(1) Does a written procedure assign responsibility for the cleaning and maintenance of equipment?	
4.304 §211.67(b)(2) Has a written schedule been established and is it followed for the maintenance and cleaning of equipment?	

4.305	Has the cleaning procedure been properly validated?	
4.306	§211.67(b)(2) If appropriate, is the equipment sanitized using a procedure written for this task?	
4.307	§211.67(b)(3) Has a sufficiently detailed cleaning and maintenance procedure been written for each different piece of equipment to identify any necessary disassembly and reassembly required to provide cleaning and maintenance?	
4.308	§211.67(b)(3) Does the procedure specify the removal or obliteration of production batch information from each piece of equipment during its cleaning?	
4.309	Is equipment cleaned promptly after use?	
4.310	Is clean equipment clearly identified as "clean" with a cleaning date shown on the equipment?	
4.311	§211.67(b)(5) Is clean equipment adequately protected against contamination prior to use?	
4.312	§211.67(b) Is equipment inspected immediately prior to use?	
4.313	§211.67(c) Are written records maintained on equipment cleaning, sanitizing and maintenance on or near each piece of equipment?	
4.4	Measurement Equipment Calibration Program	
4.401	§211.68(a) Does the facility have approved written procedures for checking and calibration of each piece of measurement equipment? (Verify procedure and log for each piece of equipment and note exceptions in notebook with cross reference.)	
4.402	§211.68(a) Are records of calibration checks and internal audits maintained in a readily retrievable manner?	
4.5	Equipment Qualification Program	
4.501	§211.63 Verify that all pieces of equipment used in production, packaging, and quality assurance are capable of producing valid results.	
4.502	§211.68(a) When computers are used to automate production or quality testing, have the computer and software been validated?	

4.503	Have on-site tests of successive production runs or tests been used to qualify equipment?	
4.504	Were tests repeated a sufficient number of times to ensure reliable results?	
4.505	§211.63 Is each piece of equipment identified to its minimum and maximum capacities and minimum and maximum operating speeds for valid results?	
4.506	Have performance characteristics been identified for each piece of equipment? (May be provided by the manufacturer, but must be verified under typical operations conditions.)	
4.507	Have operating limits and tolerances for performance been established from performance characteristics?	
5.0	Material/Component Control	
5.1	Material/Component Specification and Purchasing Control	
	Although purchasing is not specifically addressed in the current GMP regulation, incumbent upon user of components and materials to ensure quality of product, material or component.	
5.101	Has each supplier/vendor of material or component been inspected/audited for proper manufacturing controls? (Review suppliers and audits and enter names, material supplied, and date last audited in notebook.)	
5.2	Material/Component Receipt, Internal audit, Sampling, and Laboratory Testing	
5.201	§211.80(a) Does the facility have current written procedures for acceptance/rejections of drug products, containers, closures, labeling and packaging materials? (List selected materials and components in notebook and verify procedures.)	
5.202	§211.80(d) Is each lot within each shipment of material or components assigned a distinctive code so material or component can be traced through manufacturing and distribution?	
5.203	§211.82(a) Does internal audit start with visual examination of each shipping container for appropriate labeling, signs of damage, or contamination?	
5.204	§211.82(b) Is the number of representative samples taken from a	

container or lot based on statistical criteria and experience with each type of material or component?	
5.205 §211.160(b) Is the sampling technique written and followed for each type of sample collected?	
5.206 Is the quantity of sample collected sufficient for analysis and reserve in case retesting or verification is required?	
Verify that the following steps are included in written procedures unless more specific procedures are followed:	
5.207 §211.84(c)(2) Containers are cleaned before samples are removed.	
5.208 §211.84(c)(4) Stratified samples are not composited for analysis.	
5.209 §211.84(c)(5) Containers from which samples have been taken are so marked indicating date and approximate amount taken.	
5.210 Each sample container is clearly identified by material or component name, lot number, date sample taken, name of person taking sample, and original container identification.	
5.211 §211.84(d)(1)(2) At least one test is conducted to confirm the identity of a raw material (bulk chemical or pharmaceutical) when a Certificate of Analysis is provided by supplier and accepted by QA.	
5.212 If a Certificate of Analysis is not accepted for a lot of material, then additional testing is conducted by a written protocol to determine suitability for purpose.	
5.213 §211.84(d)(6) Microbiological testing is conducted where appropriate.	
<b>5.3 Material Component Storage and Handling</b>	
(Verify that materials and components are stored and handled in a way that prevents contamination, mixups, and errors.)	
5.301 §211.42(b) Are incoming material and components quarantined until approved for use?	
5.302 Are all materials handled in such a way to prevent contamination?	
5.303 Are all materials stored off the floor?	
5.304 Are materials spaced to allow for	

cleaning and internal audit?	
5.305 §211.122(d) Are labels for different products, strengths, dosage forms, etc., stored separately with suitable identification?	
5.306 Is label storage area limited to authorized personnel?	
5.307 §211.89 Are rejected components, material, and containers quarantined and clearly marked to prevent their use?	
5.4 Inventory Control Program	
5.401 §211.142 Are inventory control procedures written?	
5.402 Does the program identify destruction dates for obsolete or out-dated materials, components, and packaging materials?	
5.403 §211.150(a) Is stock rotated to ensure that the oldest approved product or material is used first?	
5.404 §211.184(e) Is destruction of materials documented in a way that clearly identifies the material destroyed and the date on which destruction took place?	
5.5 Vendor (Supplier) Control Program	
5.501 Are vendors periodically inspected according to a written procedure?	
5.502 Is the procedure for confirming vendor test results written and followed?	
6.0 Operational Control	
6.1 Material/Component/Label Verification, Storage, and Handling	
6.101 §211.87 Do written procedures identify storage time beyond which components, containers, and closures must be reexamined before use?	
6.102 §211.87 Is release of retested material clearly identified for use?	
6.103 Are retesting information supplements originally obtained?	
6.104 Do written procedures identify steps in the dispensing of material for production?	
6.105 Do these procedures include (1) release by QC, (2) Documentation of correct weight or measure, and (3) Proper	

identification of containers?	
6.106 Does a second person observe weighing/measuring/dispensing and verify accuracy with a second signature?	
6.107 §211.101(c) Is the addition of each component documented by the person adding the material during manufacturing?	
6.108 §211.101(d) Does a second person observe each addition of material and document verification with a second signature?	
6.109 §211.125(a) Does a written procedure specify who is authorized to issue labels?	
6.110 §211.125(a) Does a written procedure specify how labels are issued, used, reconciled with production, returned when unused, and the specific steps for evaluation of any discrepancies?	
6.111 §211.125(d) Do written procedures call for destruction of excess labeling on which lot or control numbers have been stamped or imprinted?	
6.2 Equipment/Line/Area Cleaning, Preparation, and Clearance	
6.201 §211.67(b)(5) Do written procedures detail how equipment is to be checked immediately prior to use for cleanliness, removal of any labels and labeling from prior print operations?	
6.202 §211.67(b)(3) Do written procedures detail any disconnection and reassembly required to verify readiness for use?	
6.3 Operational Process Validation and Production Change Order Control	
6.301 Have production procedures been validated? (Review selected procedures for validation documentation. Adequate?)	
6.302 §211.100(a) Does the process control address all issues to ensure identity, strength, quality and purity of product?	
6.303 §§211.101(a) Does the procedure include formulation that is written to yield not less than 100% of established amount of active ingredients?	
6.304 §211.101(c) Are all weighing and measuring performed by one qualified person and observed by a second person?	
6.305 §211.101(d) Have records indicated preceding policy been followed by presence	

of two signatures?	
6.306 §211.103 Are actual yields calculated at the conclusion of appropriate phases of the operation and at the end of the process?	
6.307 §211.103 Are calculations performed by one person? Is there independent verification by a second person?	
6.4 In-Process Internal audit, Sampling, and Laboratory Control	
6.401 §211.110(a) Are written procedures established to monitor output and validate the performance of manufacturing procedures that may cause variability in characteristics of in-process materials and finished drug products?	
6.402 §211.110(c) Are in-process materials tested at appropriate phases for identity, strength, quality, purity and are they approved or rejected by Quality Control?	
6.403 §211.160(b) Are there laboratory controls including sampling and testing procedures to assure conformance of components, containers, closures, in-process materials, and finished product specifications?	
6.5 Reprocessing/Disposition of Materials	
6.501 §211.115(a) Do written procedures identify steps for reprocessing batches?	
6.502 §211.115(b) Are quality control review and approval required for any and all reprocessing of material?	
6.503 Does testing confirm that reprocessed batches conform to established specification?	
6.504 Does a written procedure outline steps required to reprocess returned drug products (if it can be determined that such products have not been subjected to improper storage conditions?)	
6.505 Does Quality Control review such reprocessed returned goods and test such material for conformance to specifications before releasing such material for resale?	
7.0 Finished Product Control	
7.1 Finished Product Verification, Storage, and Handling	
7.101 §211.30 Do written procedures indicate how and who verifies that correct containers and packages are used for finished	

product during the finishing operation?	
7.102 §211.134(a) In addition, do written procedures require that representative sample of units be visually examined upon completion of packaging to verify correct labeling?	
7.103 §211.137(a) Are expiration dates stamped or imprinted on labels?	
7.104 §211.137(b) Are expiration dates related to any storage conditions stated on the label?	
7.105 §211.142(a) Are all finished products held in quarantine until QC has completed its testing and releases product on a batch to batch basis for sale?	
7.106 §211.142(o) Is finished product stored under appropriate conditions of temperature, humidity, light, etc.	
7.2 Finished Product Internal audit, Sampling, Testing, and Release for Distribution	
7.201 §211.166 Has the formulation for each product been tested for stability based on a written protocol? (Containers must duplicate those used in final product packaging.)	
7.202 §211.166 Are written sampling and testing procedures and acceptance criteria available for each product to ensure conformance to finished product specifications?	
7.203 §211.170(a) Is a quantity of samples equal to at least twice the quantity needed for finished product release testing maintained as a reserve sample?	
7.204 §211.167(a) Are sterility and pyrogen testing performed as required?	
7.205 §211.167(b) Are specific tests for foreign particles or abrasives included for any ophthalmic ointments?	
7.206 §211.167(c) Do controlled release or sustained release products include tests to determine conformance to release time specification?	
7.3 Distribution Controls	
7.301 §211.150(a) Does a written procedure manage stocks to ensure that oldest approved product is sold first?	
7.302 §211.150(a) Are deviations to the policy above documented?	

7.303 §211.150(a) Does a written procedure identify the steps required if a product recall is necessary?	
7.304 Is the recall policy current and adequate?	
7.4 Marketing Controls	
7.401 The current regulation does not address marketing controls per se except that all finished products must meet their specifications.	
7.5 Complaint Handling and Customer Satisfaction Program	
7.501 §211.198(a) Are complaints, whether received in oral or written form, documented in writing and retained in a designated file?	
7.502 §211.198(a) Are complaints reviewed on a timely basis by the Quality Control Unit?	
7.503 §211.198(b)(1) Is the action taken in response to each complaint documented?	
7.504 §211.198(b)(3) Are decisions not to investigate a complaint also documented and the name of the responsible person documented?	

7.505 §211.198(b)(2) Are complaint investigations documented and do they include investigation steps, findings, and follow-up steps, if required? Are dates included for each entry? The David Buckley & Associates' (DBA) web site is provided to you free of charge, "as is" without warranty of any kind, either expressed or implied, including, but not limited to, the implied warranties of merchantability, fitness for a particular purpose, or non-infringement. In no event shall DBA be liable for any damages whatsoever, including special, indirect, consequential or incidental damages or damages for loss of profits, revenue, use, or data whether brought in contract or tort, arising out of or connected with any DBA web site or the use, reliance upon or performance of any material contained in or accessed from any DBA web site. All information in this article is intended for your general knowledge only and is not a substitute for expert advice. Neither David Buckley & Associates Pty Ltd nor any of their employees or associates, makes any warranty, express or implied, including warranties of merchantability and fitness for a particular purpose, or assumes any legal liability for the accuracy, completeness, or usefulness of any information from this document. The opinions expressed are those of the author. The article is intended as a general discussion of legal and other issues concerning due diligence. Advice given on issues is not legal advice or a legal opinion. It is suggested all persons seek independent counsel to act upon any laws discussed in this article.