DRUGS CONTROL ADMINISTRATION
GOVERNMENT OF ANDHRAPRADESH
Inspection Check List as per WHO Guidelines
Separate comments sheets may be used if space is inadequate

Date of Inspection	Name of Licensee	Address of firm
Firm's representative		License No.
Inspected by	M. Amrutha Rao- Dy. Director K. Anil Kumar- DI-Jinnaram M. Vara Prasad- DI-Bollaram	Telephone No. Fax No. : E-mail :

Constitution of the Firm	
Purpose of Inspection	
Any Certificates held by the firm (ISO, WHO etc,)	
Categories of drugs manufactured and production capacity	
Last two years turn over of the firm (1) Govt. Supply (2) Trade	
Details of export, if undertaken already	

Technical Personnel	Manufacturing	
	Quality Control	

	Quality Assurance	
Products to be certified		
Products Licensed		
Comments on the Site Master File (SMF) Whether all the relevant information covered in the SMF. (Check whether Quality Policy is incorporated in SMF or not)		

S. No.		
I. General points		
1) Personnel		
	Nominative job description (regarding quality responsibilities [3.11]	
	Training (GMP, record, assessment) [3.12]	
	Personnel hygiene [3.20 to 3.24]	
2) Quality management		
	Quality unit independent from production should exist [2.11, 2.12, 2.13]	
	Responsibilities [2.20 to 2.22]	
	Releasing procedure and delegations (Raw materials, intermediates and finished products) [2.14, 2.17, 2.18, 2.22-1]	
	Reviewing of batch records and delegation [2.22-3, 6.70, 6.71, 6.73]	
	Deviation, OOS reports reviewed before release [6.72]	
3) Documentation system		
	Management rules (procedure management system, approval) [6.10, 6.11]	
	Documentation storage [6.12, 6.13]	
	Data recording at once after activities performed [6.14]	
	Availability of data and retrieval [6.15, 6.16]	
	Electronic signatures [6.18]	
4) Complaints, return, recall		
➢ **Complaints, return, recall**		
	All complaints recorded and retained (trends evaluation [2.22-11, 15.10, 15.12]	
	Complaint record content [5.11]	
	Written procedure defining API recall [15.13]	

	Recall procedure content (responsibilities, who should be informed, recalled material treatment) [5.14]	
	National authorities informed in life threatening situation [15.15]	
➢ **Returns**		
	Identification and quarantine of returned intermediates or API [14.50]	
	Separate storage or alternative system [10.11]	
	Reworking or destruction if doubt regarding shipping conditions[14.51]	
	All returns recorded and content of the record [14.52]	
5) Internal audits (self inspection)		
	Regular internal audit performed in accordance with an approved schedule [2.22-7 and 2.40]	
	Deficiencies and corrective actions recorded [2.14]	
	Corrective actions completed in a timely and effective manner[2.14]	
6) Product quality review		
	Periodicity [2.50]	
	Key points reviewed: critical IPC and critical API test results and production parameters, out of specifications batches, critical deviations or non conformance and related investigation, process and analytical changes, stability program monitoring, complaints and recall, corrective actions [2.50]	
	Assessment of review results in order to decide necessary corrective actions and / or revalidation [2.51]	
7) Contract manufacturers		
	Compliance of contract manufacturers with GMP[16.10]	
	GMP compliance of the sub-contractor evaluated by the contract given [16.11]	
	Written and approved contract including responsibilities of each party [16.12]	
	GMP audit of the contract acceptor permitted by the contract given [16.13]	
	No subcontracting to a third party without approval of the contract given's [16.14]	

	Documentation (Production and control) kept at the site where the activity occurs [16.15]	
	And documentation readily available [16.14]	
	Contract giver's must be informed and must approved any changes [16.16]	
	Contract giver's responsible for the quality of materials supplied.	
II. Building and facilities inspection		
8) Warehouse		
➢ **Material reception**		
	Reception area clean in a defined place (cross contamination) [14.11, 4.14-1]	
	Visual examination upon receipt [7.20]	
	Identification and / or test for bulk incoming materials [7.21]	
	Bulk deliveries in non dedicated tankers (certificate of cleaning, pipes used …) [7.22]	
	Identification rules of each container with a unique batch number	
	Unique batch number used to identify each container or grouping of containers [7.24]	
	Batch number used to identify the status and record the disposition [7.24]	
	Quarantine system (electronic or physic) [7.20]	
➢		
	Minimum one identification test of each batch or release after analysis certificate examination if a system in place to evaluate the supplier [7.30]	
	Supplier approval procedure with regular checking of the analysis certificate reliability [7.31]	
	Processing aids, hazardous or highly toxic raw materials cases [7.32]	
	Sampling rules (representative ness) [7.33]	
	Sampling at defined location and risk of contamination [7.34]	

	Containers sampled should be marked [7.35]	
➢ **Storage area**		
	Indoors (location, labeling, FIFO) [7.40, 7.41, 7.42]	
	Outdoors (labeling, protection, cleaning before use) [7.43]	
	Rejected materials under a quarantine system [7.44, 10.11]	
	Appropriate conditions for storage with records (controlled T°, humidity) [10.10]	
	Vermin program [4.72]	
	Re-evaluation of materials before use if necessary [7.50]	
➢ **Material preparation**		
	FIFO [7.42]	
	Location and weighing or measuring conditions [8.10]	
	Suitable accuracy for weighing devices [8.10]	
	Labeling of the material subdivided [8.11]	
	Critical operations subjected to an equivalent control [8.12, 8.13]	
	Material verified prior to use [8.12]	
➢ **Raw material documentation [6.30]**		
	Name of the manufacture, identity and quality information for each batch	
	Name of the supplier	
	Supplier’s control number	
	Name allocated on receipt and date	
	Result of any test performed on the batch	
	Batch traceability (upstream and downstream)	
	Documentation regarding controls performed on labeling and packaging materials.	
	Final decision regarding rejected materials	

9) Production facility		
➢ **Facilities designed to minimize potential contamination [4.10]**		
	Adequate space for orderly placement and to prevent mix-up or contamination [4.11]	
	Closed equipment can be located outdoors [4.12]	
	Flow of personnel and materials design to prevent mix-up and contamination [4.13]	
	Defined areas for each operation (receipt, quarantine, sampling, storage) [4.14]	
	Clean washing and toilet facilities for personnel [4.15]	
	Separation of laboratory area from production areas [4.16] except for IPC tests	
	Drains with anti back-siphon age device [4.24]	
	Containment for highly active products [4.40 to 4.42]	
	Lighting [4.50]	
	Sewage, reuse and other waste [4.60]	
	Procedure for building cleaning [4.70, 4.71]	
➢ **Utilities**		
	Qualification for all utilities impacting on product quality [4.20]	
	Drawing available for these utilities [4.20]	
	Air treatment units and environmental monitoring [4.21]	
	Particular attention when API exposed to the environment [4.21]	
	Specific measures to prevent cross-contamination in case of air recirculation [4.22]	
	Identification of permanently installed pipe work [4.23]	
	Drain with device to avoid back-siphon age [4.24]	

➢ **Water**		
	At least drinking water quality (potable)[4.31]	
	If potable water insufficient, appropriate specification for correct attributes [4.32]	
	Qualification and monitoring of the water treatment system [4.33]	
	Water used for non sterile API production used to produce a sterile drug monitored and controlled for microbial counts, objectionable organisms and endotoxins [4.34]	
➢ **Lighting**		
	Adequate for correct cleaning, maintenance and proper operation [4.50]	
➢ **Sewage and refuse**		
	Disposition of sewage, refuse and other waste in safe timely and sanitary manners [4.60]	
	Containers and pipes for waste clearly identified [4.60]	
➢ **Sanitation and maintenance**		
	Maintenance and sanitation of buildings [4.70]	
	Written procedures for cleaning schedules, methods, equipment and materials [4.71]	
➢ **Process equipment**		
	Identification and contents, cleanliness or processing status [5.13, 5.26, 8.16]	
	Identification of permanently installed processing lines [5.13]	
	Food grade lubricants and oils used [5.14]	
	Closed equipment as often as possible [5.15]	
	Drawings maintained for equipment and critical installation [5.16]	
	Schedules and procedures for preventive maintenance [5.20]	
	Written procedures for cleaning of equipment (responsibilities, complete description of methods and materials including cleaning agents, instruction for dis and reassembling each article of equipment, inspection before use, maximum time) [5.21]	

	Cleaning, sanitation or sterilization of equipment and utensils if appropriate [5.22]	T
	Regular cleaning of equipment assigned to continuous production (carry over and contamination risk) [5.23]	
	Cleaning of non dedicated equipment [5.24]	
	Cleaning procedure and agents, acceptance criteria for residues defined and justified [5.25]	
	Identification for its content and cleanliness status [5.26, 8.16]	
	Cleaning of non fixed equipment [5.20 to 5.26]	
➢ **Production operations**		
	Critical activities subjected to an equivalent control [8.13]	
	Comparison of actual yields and expected yields [8.14]	
	Yield ranges established and based on lab, pilot or manufacturing data [8.14]	
	Yield deviations regarding critical process steps investigated [8.14]	
	Any deviation documented, explained and investigated for critical ones [8.15]	
	Time limits for some process steps [8.20]	
	Appropriate storage conditions for intermediate held for further processing [8.21]	
➢ **In process control**		
	Written procedures for processing steps causing variability in the quality of API [8.30]	
	IP controls and acceptance criteria defined and based on development or historical data [8.30]	
	Critical IPD approved by the quality unit [8.32]	
	IPC performed by production personnel and process adjusted within pre-established limits approved by quality unit [8.33]	
	All tests and results documented and part of the batch record [8.33]	
	Written procedures for the sampling of intermediates and APIs [8.34, 8.35]	

	Out of specification investigations unnecessary for IPC tests performed for monitoring and / or adjusting the process [8.36]	
➢ **Blending batches of intermediates or API**		
	Blending of batches coming from an established process after test results as conform to specification [8.40, 8.41]	
	Acceptable blending operation for blending small batches to increase batch size and blending of tailing to form a single batch [8.42]	
	Blending operation documented and adequately controlled [8.43]	
	Traceability for the blended batch [8.44]	
	Validation of the blending process when physical attributes of API critical [8.45]	
	Stability testing of final blended batches if necessary [8.46]	
	Expiry or retest date based on the oldest batch in the blend [8.47]	
➢ **Contamination control**		
	Carry over of residual materials should not result in the introduction of degradants or microbial contamination with an impact on the impurity profile [8.50]	
	Measures for prevention of the contamination of API / intermediates by other materials [8.51]	
	Precaution when APIs are handled after purification [8.52]	
➢ **Packing and identification labeling of APIs and intermediates**		
	Written procedures for the management of the packaging and labeling materials [9.10]	
	Packaging and labeling materials conform to established specifications [9.11]	
	Documentation retained for each shipment receipt, examination testing [9.12]	
	Packaging for adequate protection during transportation or storage [9.20]	
	Containers clean, not reactive, sanitized where indicated [9.21]	
	Cleaning procedure for containers re-used [9.22]	
	Access to the label storage limited [9.30]	

	Procedures in place to reconcile quantities of labels issued, used [9.31]	
	Investigation in case of discrepancies found [9.31]	
	Management of returned labels or surplus in order to prevent confusion [9.32]	
	Obsolete and out-dated labels destroyed [9.33]	
	Control printing devices [9.34]	
	Examination of printed labels issued for a batch (identity and conformity with master [9.35]	
	A printed labels used included in the batch record [9.36]	
	Written procedure for the packaging and labeling operations [9.40, 9.41]	
	Separation form operations involving other intermediates or APIs [9.41]	
	Minimum information on the labels [9.42, 10.22]	
	Information on the label for API transferred outside the control of the manufacturer [9.43]	
	Expiry date on the label and certificate of analysis [9.43]	
	Retest date on the label and / or the certificate of analysis [9.43]	
	Inspection of packaging and labeling facilities prior to used and removal of all materials recorded [9.44]	
	Checking after operation that APIs have the correct label and examination recorded [9.45]	
	Containers transported sealed if transported out side of the manufacturer's controls [9.46]	
➢ **Distribution**		
	Distribution to third parties after release by the quality unit [10.20]	
	Transfer under quarantine under the company's control [10.20]	

	Transfer without alteration of the APIs quality [10.21]	
	Special transport conditions stated on the label [10.22]	
	Transportation contractor know and follows the appropriate condition [10.23]	
	System in place to follow localization of each batch distributed for potential recall [10.24]	
➢ **Rejected materials**		
	Identification and quarantine for APIs and intermediates failing to met specifications [14.10]	
	Final disposition of rejected material recorded [14.10]	
➢ **Reprocessing**		
	Precaution to avoid unauthorized use of materials to be reprocessed or reworked [8.17]	
	Reprocessing included as par of the standard manufacturing process if done on a majority of batches [14.20]	
	Continuation of an incomplete step after IPC is not a reprocessing [14.21]	
	Introducing un-reacted material back into process is a processing and special attention to the impact of potential formation of by – products or over – reacted material [14.22]	

➢ **Reworking**		
	Non conformance reason investigated before reworking [14.30]	
	Evaluation of reworked batches to demonstrate their quality equivalent to that produced by original process [14.31]	
	Concurrent validation in case of reworking [14.31]	
	"Reduced" report only if one batch to be reworked [14.31]	
	Comparison of the impurity profile between reworked and standard batches [14.32]	
	Additional analytical methods implemented if routines methods inadequate [14.32]	
➢ **Recovery of materials and solvents**		
	Approved procedures for recovery [14.40]	
	Recovery of solvent [14.41]	
	Recovered materials meet specification suitable for their intended use [14.40, 14.41]	
	Mixture of fresh and recycled solvent possible after adequate testing [14.42	
	Use of recovered materials adequately documented [14.43]	
➢ **Calibration**		
	Critical equipment for API's quality calibrated according to written procedures and established schedule [5.30]	
	Equipment calibrations using standard traceable to certified standard [5.31]	
	Records of calibration maintained [5.32]	
	Current calibration status of critical equipment known and verifiable [5.33]	
	Non use of instruments that do not meet calibration [5.34]	
	Impact investigation performed if deviation from approved standard of calibration [5.35]	

III. Laboratory controls and batch record		
10) Laboratory controls		
➢ **General controls**		
	Independent laboratory facilities for QC [11.10]	
	Procedures for sampling, testing approval or rejection of material and data storage [11.11]	
	Specification, sampling plans, test procedures scientifically sound [11.12]	
	Specifications and test procedures consistent to those included in registration file [11.12]	
	Documentation drafted by appropriate organizational unit, reviewed and approved by quality unit [11.12]	
	Specification on APIs including impurities [11.13]	
	If adequate, total microbial counts, objectionable organisms and appropriate actions limits established [11.13]	
	If adequate specification for endotoxins met with action limits established [11.13]	
	Laboratory controls followed and documented at the time of performance [11.14]	
	Any departures from described procedures documented and explained [11.14]	
➢ **Laboratory controls records**		
	Description of samples received for testing [6.60]	
	Statement or reference to each test or method used [6.60]	
	Statement of the weight or measure of sample used for each test [6.60]	
	Data or reference to the preparation and testing of reference standards, reagents and standard solutions [6.60]	
	Complete records of all data generated, graphs, spectra, charts properly identified [6.60]	
	Records of all calculations performed in connection with tests [6.60]	
	Test results statements and comparison with established acceptance criteria [6.60]	

	Signature of the person who performed the analysis and date [6.60]	
	Signature of the person who reviewed original records for accuracy [6.60]	
	Records for any modification to an established analytical method [6.61]	
	Records for periodic calibration of instruments and devices [6.61]	
	Records for all stability testing performed on APIs [6.61]	
	OOS investigations [6.61]	
➢ **OOS treatment**		
	Written procedure for OOS results treatment [11.15]	
.	Analysis of the data, assessment of the problem corrective actions, conclusions [11.15]	
	Re-sampling and retesting [11.15]	
➢ **Reagent and standard solutions**		
	Written procedures for the preparation and labeling of reagents and standard solution [11.16]	
	"Use by" dates applied [11.16]	
	Primary standard source documented [11.17]	
	Records maintained for primary standard storage and use [11.17]	
	Testing and documentation regarding "In-house primary standard" [11.18]	
	Qualification of secondary reference standard against primary one prior first use [11.19]	
	Periodic re-qualification in accordance with written procedure [11.19]	
➢ **Testing of APIs and intermediates**		
	Laboratory test conducted for each batch of intermediate and API [11.20]	
	Impurity profile established for each API (identified and non-identified) [11.21]	

	Regular comparison of the batch impurity profile against the one submitted in the marketing authorization or against historical data [11.22]	
	Microbiological tests conducted on each batch where μ biological quality specified [11.23]	
➢ **Certificate of analysis**		
	Authentic certificates issued for each batch on request [11.40]	
	Information provided on the certificate (grade, batch number, date of release, expiry date, name address and phone of the original manufacturer [11.41, 11.43]	
	Each test performed listed with specifications (acceptance limits) and numerical results obtained [11.42]	
	Certificates dated and signed by authorized personnel [11.43]	
	Name and address of the manufacturer if analysis carried out externally [11.43]	
➢ **Stability monitoring APIs**		
	Documented on going program designed to monitor stability characteristics of API [11.50]	
	Results of the above program used to confirm storage conditions [11.50]	
	Results of the above program used to confirm expiry or retest date [11.50, 11.60]	
	Test procedures used in stability testing validated [11.51]	
	Stability samples stored in containers that simulate the market one (smaller scale) [11.52]	
	Stability monitoring program on the first three commercial production batches [11.53]	
	At least one batch per year added to the stability program with an annually test [11.54]	
	If APIs with short shelf lives [11.55]	
	Stability storage conditions consistent with ICH guideline [11.56]	

➢ **Reserve / retention samples**		
	Identified reserve samples retained and variable storage time [11.71]	
	Storage in the same packaging system or equivalent or more protective [11.72]	
	Sufficient quantities retained for two analyses [11.72]	
11) Production instructions and batch production records		
➢ **Production instructions**		
	Prepared dated signed by one person and checked dated and signed by Q unit [6.40]	
	Include name of the product manufacture with a reference identifying code [6.41]	
	Names and codes of all starting materials used (specific to identify any quality characteristic)[6.41]	
	Accurate statement of the quality of materials to be used and unit measure [6.41]	
	Calculation where the quantity is not fixed [6.41]	
	List of production equipment and location [6.41]	
	Sequences to be followed [6.41]	
	Ranges of process parameters to be used [6.41]	
	Sampling instructions and IPC plus acceptance criteria [6.41]	
	Time limits for completion of steps [6.41]	
	Expected yield ranges [6.41]	
➢ **Batch production record issued**		
	Checking before issuance that it's the correct version, accurate reproduction of master [6.50]	
	These records with a unique batch or identification number [6.51]	
	Date and time together with product code for continuous production [6.51]	

➢ **Batch production records**		
	Dates and times [6.52]	
	Identity of major equipment used [6.52]	
	Raw materials, intermediates, reprocessed materials used with weighs, measures, batch number [6.52]	
	Actual results recorded for critical process equipment [6.52]	
	Any sampling performed [6.52]	
	Signatures of persons performing and checking each critical step [6.52]	
	Inprocess and laboratory test results [6.52]	
	Actual yield [6.52]	
	Description of packaging and label intermediate and label [6.52]	
	Representative label [6.52]	
	Any deviation noted, its evaluation, investigation conducted [6.52]	
	Results of release testing [6.52]	
IV. Other points		
12) Validation		
➢ **Validation policy**		
	Documentation regarding validation company's overall policy [12.10]	
	Critical parameters identified and ranges for reproducible operation defined during development [12.11]	
	Validation extended to determined critical operation to the quality and purity of API [12.12]	
➢ **Validation documentation**		
	Written protocol specifying how validation of process will be conducted [12.20]	
	Protocol reviewed and approved by Quality unit [12.20]	
	Validation protocol includes critical process steps, acceptance criteria, type of validation	

	and the number of process run [12.21]	
	Report validation with summaries of results obtained, deviations observed and comments, conclusions including recommending changes to correct deficiencies [12.22]	
	Any variations from the validation protocol should be documented and justified [12.23]	
➢ **Qualification**		
	Appropriate qualification of equipment before starting process validation activities [12.30]	
	Major qualification steps [12.30]	
➢ **Process validation**		
	Process validation definition [12.40, 12.41]	
	Prospective validation definition [12.42]	
	Concurrent validation definition [12.43]	
	Retrospective validation and conditions for its use [12.44]	
	Batches selected for retrospective validation representative and included batches failed to meet specification [12.45]. In that case retained samples can be used to obtain data.	
➢ **Process validation program**		
	Number of process runs for validation depends on the complexity and types of validation [12.50]	
	Monitoring and control of critical process parameters [12.51]	
	Parameters unrelated to quality not be included in the process validation [12.51]	
	Confirmation that the impurity profile is within the limits established or better [12.52]	
➢ **Periodic review of validated systems**		
	Evaluation to verify that systems and processes still operate in a valid manner [12.60]	
	When no significant changes and quality review confirms that the produces API meeting specifications, no need for revalidation [12.60]	

➢ **Cleaning validation**		
	Cleaning validation reflects actual equipment usage patterns [12.70]	
	Cleaning validation protocol content (description of equipment to be cleaned, procedures, materials, acceptable cleaning levels, analytical method, samples and methods for their collection [12.72]	
	Sampling methods determination [12.73]	
	Swabbing sampling efficiency if used [12.73]	
	Sensitivity of the validated analytical method sufficient to detect acceptable level of residue [12.74]	
	Microbiological contamination and endotoxin levels taken into account if necessary [12.75]	
	Regular monitoring of cleaning procedures by analytical testing and visual examination of equipment cleanliness [12.76]	
➢ **Validation of analytical methods**		
	Validation compulsory unless the method is included in the pharmacopoeia [12.80]	
	Validation including recommendations of the ICH guideline[12.81]	
	Qualification of the analytical equipment before starting validation [12.81]	
	Records maintained for any modification of a validated method [12.83]	
13) Change control		
➢ **General points**		
	Change control system established to evaluate all changes concerning API [13.10]	
	Procedures for identification, documentation, appropriate review and approval of changes for raw material, specification, analytical methods, facilities, equipment, processing steps, labeling computerized systems[13.11]	
	For any change, proposals must be drafted, reviewed and approved by the appropriate unit and reviewed and approved by the quality unit [13.12]	

➢ **Change management**		
	Potential impact on the quality of the API evaluated [13.13]	
	Level of testing, validation and documentation needed to justify changes [13.13]	
	Classification of changes as minor or major [13.13]	
➢ **Change consequences**		
	Revision of documentation affected by the change [13.14]	
	Evaluation of the first batches produced or tested under the change [13.15]	
	Evaluation of potential changes affecting established expiry date [13.16]	
	Notification of the dosage form manufacturer of changes [13.17]	