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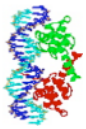

## GMP and Your Company

GMP refers to the Good Manufacturing Practice Regulations promulgated by the US Food and Drug Administration, and followed around the world. These regulations are written into US Code of Federal Regulations (21 CFR Parts 210 and 211) and have the full force of law. They require that manufacturers, processors, and packagers of drugs, medical devices, some food, and blood take proactive steps to ensure that their products are safe, pure, and effective. GMP regulations require a total quality approach to manufacturing. They enable companies to minimize or eliminate instances of contamination, mixups, and errors. Failure of firms to comply with GMP regulations can result in very serious consequences including recall, seizure, fines, and jail time.

GMP regulations apply to recordkeeping, personnel, sanitation, cleanliness, equipment and test method validation, process validation, and complaint handling, to name a few. Most GMP requirements are very general and open-ended, allowing each manufacturer to decide individually how to best implement the necessary controls. This appears to allow flexibility, but in practice, auditors and regulators look for proven, industry-wide practices and procedures to ensure quality in the process.

GMP is also sometimes referred to as "cGMP." The "c" stands for "current," reminding manufacturers that they must employ technologies and systems that are up-to-date in order to comply with the regulation.

GMP is not only a requirement for production and testing; it is also a good business tool that improves performance at your company. GMP requirements lead to a quality approach using a system of continuous improvement.

However, before your company embarks on the path to GMP, it is necessary to establish a QA system, such that all of your company's efforts on the path to GMP are approved, implemented and documented in a traceable way that will hold up to inspection by regulatory agencies and future clients.

All departments in the company should be trained (to varying degrees) on GMP and other standards. This includes top executive management, managers, supervisors, operators, technicians, and support staff. All training must be documented for each individual. Testing is frequently applied in order to determine the individual employee's level of performance.

Enforcing GMP requires auditing to ensure that your efforts have been successful in establishing a GMP culture in the company. Audits can be internal, when performed by the quality assurance department as required by GMP, and external, which can consist of an FDA audit, a consultant checking your compliance status, a potential client's audit

to establish your suitability as a contractor or supplier, or you performing a supplier audit. The results of audits will determine if you need to modify your standards of performance. Of course, no procedures should be changed without a documented change control system and approval from quality assurance. AQS can perform audits and mock inspections to help you prepare for inspections by regulatory agencies. If for example, you are inspected by the FDA, they will issue a series of ”483 Citations,” and will expect a prompt response to each issue. AQS can help defend your company when inspectors find areas in need of improvement.

Here are some examples of cGMP Requirements:

Requirement for a QC unit responsible for releasing or rejecting lots, procedures, specifications.

Personnel should be trained (including in cGMP) and training is documented.

Facilities should be suitably designed, cleaned, maintained.

Facility design allows segregation and flow that prevents mix-ups and cross-contaminations.

Floors, walls, and ceilings must be smooth, hard, and easily cleanable.

HEPA-filtered air handling under positive pressure is usually required.

Systems must be in place for cleaning, disinfecting, and aseptic handling, including written procedures.

Environmental controls must be in place and monitored.

Plans must be free from vermin, including written procedures for use of suitable methods for this control.

**Equipment:**

Designed so surfaces contacting the drug are not reactive, additive, absorptive, and do not alter the drug's specifications.

Cleaned, maintained, and sanitized regularly, including written procedures for doing so and records (logs) kept.

Calibrated and inspected, including written procedures and records kept.

Computerized systems must be controlled so that records cannot be altered and must be validated for accuracy (Audit Trail – 21 CFR Part 11).

Filters don't release fibers into the product.

**Containers and Closures**

Stored to prevent contamination.

Clean, sterilized (if appropriate), and pyrogen-free.

Not reactive, additive, or adsorptive.

Raw materials are quarantined until tested and released or rejected, based on prospectively defined specifications.

Segregation of components of different status (quarantined, released, rejected).

Rotation of stocks of components.

Production and process controls.

**Written procedures (SOPs).**

Deviations recorded and justified.

Yield calculated and calculations verified for each batch.

Equipment used per batch identified and documented.

In-process controls and tests done on representative samples.

Time limits for steps established and deviations documented and justified.

Environmental controls in place (microbiological contamination, dust, etc.).

Prospective SOPs for re-processing.

SOPs for labeling and packaging controls.

Records kept for labels accepted or rejected.

Controls to reconcile quantities.

Segregation to prevent mix-ups and cross-contamination during labeling.

Inspection to ensure accuracy.

Expiration dating determined by stability testing and must appear on labels.

Written stability plan, results determine expiration dating.

Written sops for warehousing and distribution.

Lab procedures, sampling plans, specifications.

Written procedures.

Deviations recorded and justified.

**Controls on:**

Components.

Containers/closures.

Labeling.

In-process testing.

Sampling.

Calibrating instruments.

Batches must meet prospective specifications before being released.

Test methods validated for accuracy, sensitivity, specificity, and reproducibility.

Reserve samples must be retained for specific time-frames.

Lab animal use is controlled and documented.

Records maintained for specific time-frames, including raw data.

Complaints, recalls, returns, investigations documented and reviewed according to written procedures.

Master production records to ensure uniformity batch to batch.

Batch records.

Prepared for each batch documenting.

Dates.

Equipment used.

Batches of components used.

Personnel.

Control results.

Yield.

Samples taken

Deviations and investigations.

Records must be reviewed.

Lab records documenting methods, personnel, etc.

**Records maintained on:**

Deviations and reasons.

Standardization of reference standards.

Calibration of equipment.

Stability.

Distribution records maintained.

Closing Thoughts

Commitment to GMP and quality is critical at all levels of the organization, starting with top management. If you champion and foster commitment, you will help make GMP a lifestyle in your company. No company can achieve cGMP unless its staff has the necessary training and experience to handle the job. AQS retains the necessary talent and expertise needed to get your company to its goals quickly.