FDA cGMP Medical Device Quality: Targeting Excellence

Through years, ATL has emerged as a leader in the manufacture of disposable medical devices. ATL is an FDA-registered medical device company whose custom disposable medical components are manufactured and shipped worldwide. Services range from master roll distribution of medical foams and tapes to custom die-cut components with tight tolerances. The company's success is largely predicated upon adherence to the strict FDA regulations of cGMP compliance to 21 CFR 820 for the manufacture, packaging, and storage of all medical devices.

As a registered medical device manufacturer, quality is paramount. To ensure quality, ATL is also cGMP compliant to: 21 CFR 210 and 211. As such, a thorough understanding of the importance of strictly adhering to FDA regulations for the safety of consumers and end users is inherent. To ensure quality and safety, our Quality Management System (QMS) and continuous "Systems Validation Protocol" monitor all major product lines and our engineers use the principles of Quality Function Deployment (QFD) and other preventive quality assurance techniques to ensure the highest possible conformance to quality.

Vision of Quality

Quality is a mindset, a broad and pliable term that in some entities can challenge companywide acceptance. At ATL quality encompasses every aspect of the organization: the work we perform, the services we provide, the information we disseminate, all processes, our various divisions, the staffing continuum (workers, engineers, managers and executives), our many objectives and the entire system. Our overall commitment and basic approach to business are control of quality in every manifestation.

Quality begins with a series of questions and ends with complex solutions and successful completion of an assigned task. At the outset we question our customers about the myriad relevant aspects of a project, including end-user application and critical quality characteristics. As this process continues, a clear approach comes into sharp focus. From here we proceed to manufacturing—with quality always at the forefront.

Quality defined

Within the industry, each manufacturer adheres to the many quality standards that exist and evolve in unique ways. At ATL, quality is the cornerstone of our existence and we extend every effort to define and ensure quality as far upstream as possible. To that end we advise customers when a more practical, efficient and quality-effective approach to production of their product may exist.

There are many avenues to high quality, and ATL has identified a road map to unequivocal success. Advanced Product Quality Planning (APQP) identifies the characteristics that are Critical to Quality (CTQ). Failure Modes & Effects Analysis (FMEA) identifies applicable Risk Priority Numbers (RPN). Our New Product Development (NPD) test run form, comprised of 131 questions, requires a sign-off from each participant.

When a CTQ measurement is variable, our engineering and manufacturing staff are provided with real-time data on Cpk (process mean, sigma and defects per million). This in-process data enable justification of sampling frequency based upon an Operating Characteristics Curve. If a job duration is extended, a Control Plan, FDA-mandated Performance Qualification or Quality Traveler is established. During production, processes are measured to assure that Cpk consistently remains at optimal levels. When applicable, assignable cause is identified for any increase in variation. In each instance, quality is established up front—where it is easiest to control.

Aspects of quality

Key to successful manufacturing are our problem solving hypothesis tests, either a t-distribution test or Analysis of Variance (ANOVA) evaluation to determine whether our population means and standard deviations are equal over time. When Cpk is calculated during in-process production, we calculate a confidence interval for the power of our prediction. In this fashion we minimize the likelihood of experiencing a false sense of security about a process if the mean and sigma do not exhibit complete stability. All hypothesis evaluations require a minimum 95% confidence interval, and stability in measurement must be

assured. Gages are calibrated and gage repeatability and reproducibility tests performed to assure that no measurement errors are induced into Cpk and other data.

Establishing goals

Customized engineering: ATL offers sophisticated and extensive custom engineering designed to meet any unique requirement. The overriding goal is to remain within specification limits while constantly reducing process variation in order to reduce alpha risk and Type 1 error. The target never varies—zero defects—and continuous improvements enable us to approach or reach this target. The FDA validation cycle is a useful tool to help us achieve our goal.

Tight-tolerance production: Tight tolerance holds the permissible measurement deviation from a specification to its minimum value. Tight-tolerance jobs require Cpk at 1.66 (assuming a defect would mean a catastrophic failure). In-process inspection is based upon the nature of possible defects, their likelihood of occurrence, and ability to detect the quality characteristic in question. Our essential technology is among the most sophisticated anywhere and capable of measuring die cut critical characteristics to 1/10/000 of an inch, enabling increased sensitivity in the calculation of Cpk.

Track-and-trace: Track-and-trace is a critical operations tool used to assure the authenticity of each product in the process chain and the delivery of promised goods. Track-and-trace methodology includes holograms, serialization and color-shifting inks.

Good Manufacturing Practice

Good Manufacturing Practice (GMP) encompasses the systems and practices that must be adhered to in pharmaceutical products and manufacturing, quality control, quality systems, diagnostics, and medical devices. GMPs are the guidance that outlines the many aspects of production and testing that can impact the quality of products that are manufactured.

Our GMP is unique because we produce clinical trial booklets that are distributed worldwide. Because our work is often of short-run duration, our Systems Validation Protocol is constructed to account for multiple sizes and shapes of products. In this manner we can validate stability and conformance over a broad operating range.

Our successful validations have spanned a decade or more and our conformance level approaches six sigma quality. When production of a job that was produced considerably earlier is resumed, we perform designed experiments to assure that critical values, such as t critical, F critical, P critical or X Bar critical, remain static. This measure enables us to prove that overall production quality remains consistently high over longer periods of time.

Auditing and validation

ATL has established an FDA validation cycle that was performed for several medical devices, and the company passed multiple audits for the GMP items listed below. Here is an example of 43 quality validation steps:

1. **Delta Press Validation IQ-OQ-PQ**
2. **Installation Qualification Delta Press # 2371**
3. **Delta Press Drawings (4)**
4. **Installation Qualification Delta Press # 2371 (#2)**
5. **Operational Qualification Delta Press # 2371**
6. **Operational Qualification Delta Press # 2371 (#2)**
7. **Performance Qualification Delta Press # 2371**
8. **Performance Qualification Delta Press # 2371 (#2)**
9. **Installation Qualification Delta Press # 2485 – Part One**
10. **Installation Qualification Delta Press # 2485 – Part Two**
11. **Operational Qualification Delta Press # 2485**
12. **Performance Qualification Delta Press # 2485**
13. **Drawings, Device Master Record, Work Inst., Materials (Title)**
14. **Customer Drawings (XXXX Rev. 1) (ZZZZ Rev. 1)**
15. **Work Inst., Mtrl, DMR (XXXX Rev. 1) (ZZZZ Rev. 1)**
16. **Standard Operating Procedures**
17. **SOP QA-21 Rev. 0 "Medical Device Processing"**
18. **SOP MP-06 Rev. 1 "Preventive Maintenance – Delta Press"**
19. **SOP MP-07 Rev. 0 "Prev. Maint. – Twin Carton Sealer"**
20. **Control Plans (Title Page)**
21. **Control Plan: Complete Product**
22. **Control Plan: Production 1**

23. **Control Plan: Production 2**

24. **Control Plan: Packaging 3**

25. **Control Plan: Quality Assurance 4 (Final Insp. & Release)**

26. **Training Records (Title Page)**

27. **Training Records (Objective Evidence)**

28. **Maintenance Records**

29. **Maintenance Records (Objective Evidence)**

30. **Twin Carton Sealer I.Q. – O.Q.**

31. **Twin Carton Sealer I.Q. – O.Q. (#2)**

32. **Twin Carton Sealer P.Q.**

33. **Medical Device #1**

34. **Medical Device #1 – P.Q. Validation**

35. **Medical Device #2 - P.Q. Validation**

36. **Medical Device #3 - P.Q. Validation**

37. **Medical Device #4 – P.Q. Validation**

38. **Software Validation – Delta Programs & Cold Seal - #1**

39. **Software Validations – Delta Programs & Cold Seal – #2**

40. **Software Validations – Delta Programs & Cold Seal – #3**

41. **P.Q. Quote System / Barcodes/ Template/ UPS**

42. **P.Q. Quote System / Barcodes/ Template/ UPS #2**

43. **P.Q. Inspection Frequency Validation**

Conclusion: Quality trumps

As globalization advances and rapid improvements in technology proliferate, manufacturing is becoming increasingly competitive. To many vendors, that means tightening their focus on finding new and better ways to design, produce and deliver medical devices. At ATL, such focus has always existed—with quality the essential ingredient.

The FDA is renowned for its strict enforcement of controls on quality in the production of pharmaceuticals and medical devices. However, ATL goes beyond federal standards to ensure quality at all levels of production and beyond. There are many measures of manufacturing excellence, but ATL believes overall quality is the only true measure of successful product development.

While Good Manufacturing Practice is the cornerstone of successful medical device manufacturing, we go a step further: great manufacturing, framed by quality at all levels, is the standard of care.