ASK THE EXPERT

# Manufacturing with a Quality Mindset

## Role of Automated Visual Inspection

with Mitsutaka Shirasaki

Visual inspection for biopharmaceutical product defects is inherently subjective, a fact acknowledged by regulatory authorities. Although visual inspection alone cannot detect all defective products, it serves as a vital method for ensuring that drug products are free from discoloration, visible particles, unsecured vial caps, and other signs of problems. To address the limitations of manual visual inspection (MVI), automated visual inspection (AVI) has been introduced as an enhancement for those "gray areas" caused by subjective assessments. But using AVI also requires diligent evaluation and qualification. In a December 2025 Ask the Expert webinar, Mitsutaka Shirasaki (principal scientist of drug product at Samsung Biologics) discussed the benefits and drawbacks of AVI systems over traditional MVI systems.

### Shirasaki's Presentation

Defect detectability is influenced by visibility and repeatability. Whereas MVI struggles with repeatability, AVI excels in those two factors and offers consistent performance. Historically, AVI qualification requirements have been minimal, with the primary criterion that automated screening performs as well as or better than MVI. That lack of detailed requirements has led to different approaches among biopharmaceutical companies for AVI qualification.

The process typically involves creating a defect kit with representative defect vials, conducting a probability of detection (PoD) study with manual inspectors, and developing AVI parameters based on those study results. The Knapp method is a prominent approach for qualification, for qualification, filtering out defects at a rate of >70%. That threshold often is adopted in qualification kits. However, variations exist, with some companies using the entire defect kit or targeting specific detection percentages for different defect types.

Defect kit creation requires careful consideration of AVI technology capabilities, including camera resolution, image coverage, and defect detectability. Acceptance criteria also can differ, with defect rates ranging from 10% to 20%. Such rates are significantly higher than actual production defect rates, which are typically <0.01%. That discrepancy introduces bias in PoD studies because manual inspectors might over-reject defects to ensure higher detection rates. Fatigue and focus during PoD studies are critical factors, with a recommended testing period of three to four hours to simulate real-world conditions. Simple documentation is essential to avoid errors and ensure valid data collection.

Detection curves are central to understanding AVI and MVI performance. The curves, often represented by logistic functions, illustrate the relationship between defect visibility and detection probability. Different defect types exhibit distinctive curve shapes, with darker particles generally being easier to detect than lighter ones. The Knapp method compares the reject-zone detection rates of AVI and MVI, aiming for AVI to outperform MVI while minimizing false rejects. AVI's repeatability results in steeper detection curves, indicating higher sensitivity and consistency compared with MVI. However, some companies focus solely on reject-zone data and ignore the acceptance and gray zones, which can lead to incomplete assessments of detection capabilities.

Simulating detection curves with real data provides valuable insights into AVI and MVI performance. Logistic curves fitted to data points reveal accurate representations of detection capabilities, allowing for comparisons between AVI and MVI. For example, AVI often outperforms MVI in detecting stopper particles, silicone particles, and related defect types. However, focusing solely on reject-zone data can skew results, particularly for technologies such as static

division systems, which excel in detecting small particles. Camera-based AVI systems are better suited for meeting qualification criteria with their consistent repeatability.

Particle generation curves modeled using Weibull's function simulate the distribution of particle sizes in production. Those curves demonstrate that smaller particles are more likely to be generated, contrasting with detection curves in which larger particles are easier to detect. Combining particle generation curves with detection curves allows for simulations of real-world detection counts. AVI generally detects a greater number of particles than MVI can, particularly in scenarios with advanced shifts in particle generation. That sensitivity enables AVI to identify process changes earlier than MVI can, enhancing process monitoring and defect detection.

Despite its advantages, AVI has some limitations. Small particle sizes are underrepresented in defect kits, and sub-visible particle generation curves cannot be measured. AVI qualification often combines data from all particle types, which may not reflect real-world conditions. Different technologies, such as static division systems and camera systems, have varying capabilities, with heavier particles being more challenging for static division systems to detect. These limitations highlight the need for tailored qualification approaches based on the technology and production line characteristics.

AVI qualification should prioritize small particle sizes to better represent real-world conditions. Comparing entire detection curves, rather than focusing on reject-zone data, provides an accurate assessment of AVI performance. Fitted detection curves offer a clear representation of detection capabilities, enabling sensitive and repeatable AVI processes. By continuously improving AVI performance, manufacturers can enhance defect detection and process monitoring, ensuring high product quality and reducing the risk of adverse shifts in production.

## Questions and Answers

**Beyond evaluating vendor claims about high-resolution cameras, what specific questions should users ask to verify an AVI system's resolution for <100-µm particles in a product format?** It is important to ask about a camera's object resolution. The ideal for particle detection with a camera is about 9–10 µm/px. With that capability, the resolution is about 5 × 5 px, and a geometry filter can be applied to visualize objects' shapes and then distinguish particles from bubbles.

**How can users practically model normal particle profiles without perfect data?** You can use a mathematical model and change the parameters to simulate different types of particle-generation curves. During such testing, you can determine which inspection system will work for your situation.

**If AVI underperforms with subtle defects such as translucent fibers, should MVI be applied instead? How might users balance AVI's consistency and MVI's flexibility in a hybrid approach?** MVI data generated during a PoD study are skewed. We are talking about approximately 100× more acceptable samples being used for the blinding effect with a 10% defect rate, whereas a real-world defect rate is less than 0.1%. That results in a 100× higher blinding effect in the real world, so MVI detection must be taken with a grain of salt. What AVI provides, however, is repeatability.

AVI detection curves in a simulation are fixed, unlike MVI detection curves. Operator performance will differ from individual to individual and day to day. So MVI detection counts are not reliable and fluctuate frequently.

The variations observed between generation and detection curves constitute the data that we obtain from MVI particle-defect rates. To set a limit on both variations, you must widen your range. AVI is much more consistent compared with MVI, so the fluctuation that you are likely to find in real-world detection counts more closely represents the defect generation curve fluctuations.

Find the full webinar online at www.bioprocessintl.com/webinars.