



# Enhancing Tablets, Pills, Capsules, and Caplets in Bio-Pharmaceutical Manufacturing with Instrumental Color Measurement

## Introduction

Color is a critical quality attribute in the manufacturing of solid oral dosage forms, including tablets, pills, capsules, and caplets, serving both as a visual indicator of product consistency as well as an indirect measure of formulation integrity and process control. In modern pharmaceutical production, color differences are not just aesthetic; they may reflect variations in coating thickness, blend uniformity, or thermal exposure during processing and handling. While visual inspection has historically been the default means of assessing appearance, it is inherently subjective and prone to human error as well as visual environment inconsistencies. Instrumental color measurement offers an objective, quantifiable, and reproducible method aligned with international CIE (Commission Internationale de l'Éclairage) and pharmacopeial standards. By implementing full visible-range spectrophotometry with HunterLab's **UltraScan VIS** and **Agera L2**, manufacturers can achieve precise, traceable color control across all dosage forms – ensuring product uniformity, regulatory compliance, and consumer confidence.

## Overview: The Role of Color in Solid Oral Dosage Manufacturing

Tablets, pills, capsules, and caplets represent the largest segment of global pharmaceutical production. Each form is carefully engineered for dosage accuracy, dissolution rate, absorption/digestion, and visual appeal. Color uniformity



communicates product identity, differentiates strengths, and reinforces brand integrity. Even slight hue variations can prompt regulatory concern or consumer rejection. In film-coated tablets, uneven color may indicate improper coating distribution, inadequate mixing of pigments, or inconsistencies in drying. For capsules, color uniformity between suppliers (raw materials suppliers, CDMOs, as well as at global manufacturing sites) is essential for ensuring batch interchangeability. With increasing globalization and multi-site production, consistent color evaluation is crucial. Spectrophotometric color measurement provides a standardized framework that bridges formulation development, process validation, and production, enabling quantifiable comparison across materials, equipment, and facilities. Color measurement has also been utilized to identify counterfeit products.

## Importance of Color Measurement by Application

Color measurement plays a pivotal role at multiple points within small molecule, solid-dosage manufacturing. For the API/drug substance, color and appearance is critical for purity, stability, and degradation analysis plus for ultimate consumer acceptance. During formulation development, instrumental color analysis helps determine optimal pigment concentrations and coating compositions. In tablet and caplet production, it verifies the uniformity (thickness, coverage/opacity, consistency) of the applied coatings to surfaces. For capsules, color QC ensures that gelatin or plant-based shells maintain the correct visual identity and consistency across different suppliers and production runs. Pills and uncoated tablets also benefit from instrumental color measurement, as compression, surface texture, and polishing can influence reflectance and perceived appearance. Quantifying color with  $L^*$ ,  $a^*$ ,  $b^*$  coordinates and data outputs provides the accuracy and precision needed to control these variations, maintain brand consistency, and satisfy both internal, consumer and regulatory quality expectations.



## What Color Reveals About Product Quality

Color provides valuable analytical information about the quality and stability of solid oral dosage forms. Deviations from established standards can indicate various process upsets including coating or formulation issues such as moisture absorption, excessive drying, pigment segregation, or degradation. For instance, darker tablets may signal overheating or caramelization of the coating, while shifts in hue can reveal pigment oxidation or polymorphic transformation in the API/active ingredient. Capsules exhibiting slight differences in gloss or hue may reflect inconsistent shell plasticizer content or storage conditions. By continuously tracking  $L^*$ ,  $a^*$ ,  $b^*$ , and  $\Delta E^*$  values, manufacturers can detect early changes that are imperceptible to the human eye, ensuring rapid corrective action and preserving long-term batch consistency.

## Color Measurement Applications Across the Manufacturing Lifecycle

Spectrophotometric color measurement can be applied throughout the product lifecycle—from R&D through commercial production. The API/drug substance is qualified at any point. During raw-material qualification, pigments, dyes, and excipients are verified for consistent color and appearance before entering production. In granulation and blending, reflectance color data can indicate uniformity of pigment. During tablet compression and coating, color trending provides a real-time indicator of endpoint readiness, ensuring that coating processes are consistently applied between batches. For capsules, instrumental color control confirms uniform appearance among co-manufacturers and suppliers across global production sites. Finally, at packaging and release, objective color verification supports both brand presentation, as visual deviations can indicate mislabeling or contamination. Color measurements have even been used to detect counterfeit pill and tablet products. Further, integrating these measurements into digital quality systems enhances traceability and supports GMP and data-integrity compliance.



## Challenges in Applying Color Measurement: Visual vs. Instrumental

Visual assessment remains common but is inherently subjective and inconsistent. Differences in lighting conditions, observer experience, and sample orientation lead to unreliable results, especially when comparing high-gloss or curved samples like capsules and film-coated tablets. Instrumental color measurement eliminates this variability by using calibrated optics, standardized illumination, and defined geometry. Both UltraScan VIS and Agera L2 are equipped with **specialized sample holders** and accessories designed for pills, capsules, and tablets, ensuring secure and repeatable positioning during measurement - even with exceedingly small quantities of API. These fixtures maintain proper alignment for curved and reflective surfaces, preventing shifts that can distort color readings. As a result, color measurement becomes repeatable, auditable, and statistically meaningful, transforming appearance control from a subjective observation into a quantifiable process metric.

## Global Color Methods and Standards

Objective color measurement aligns with global regulatory frameworks, including those defined by the CIE, United States Pharmacopeia (USP), and European Pharmacopoeia (EP). The CIE L\*a\*b\* system provides the universal color language used to quantify appearance across industries. The USP (<1061>, <631>) and EP both recognize instrumental colorimetry as an accepted analytical method for assessing the appearance of solid (and liquid) dosage forms. Compliance with 21 CFR Part 11 and EU GMP Annex 11 requires electronic recordkeeping, secure audit trails, and validated instrumentation which are integral features of HunterLab systems. By adhering to these standards, manufacturers ensure that color data are accurate, traceable, and comparable, reducing regulatory risk and enabling harmonized operations across facilities.



## Recommended HunterLab Solutions and Why

The **HunterLab UltraScan VIS** is the premier solution for measuring the color of tablets, pills, capsules, and caplets. Covering the complete visible range from 360 to 780 nm, it meets all CIE requirements for precision colorimetry. Its diffuse/8° integrating-sphere geometry provides accurate measurement for curved, textured, and glossy surfaces common to coated tablets and capsules. The instrument's specialized sample holders and accessories secure individual dosage units for repeatable measurements, eliminating variability caused by positioning errors. These holders are designed specifically for pharmaceutical applications and can accommodate different shapes, sizes, and quantities of dosage forms.

The **Agera L2** serves as a laboratory and/or production-floor solution, combining a compact design with rapid reflectance color evaluation. Its 0°/45° circumferential geometry simulates human visual perception. Agera L2 delivers fast, reliable data ideal for in-process and quality-assurance testing. Its intuitive touchscreen interface, onboard software, and network connectivity allow immediate pass/fail decisions with the necessary data outputs. Like the UltraScan VIS, the Agera L2 includes optimized sample handling accessories like a sample cup for loose powders plus optional pill and capsule holders for secure sample positioning. Together, these instruments provide a seamless, end-to-end color control solutions, ensuring that every dosage form meets visual and regulatory specifications. More information can be found at [www.hunterlab.com](http://www.hunterlab.com).

## Features, Advantages, and Benefits of HunterLab Solutions

The **UltraScan VIS** combines high optical precision with robust stability, enabling reproducible measurement across all dosage forms. Its integrating-sphere geometry evenly distributes light over curved or glossy tablet and capsule surfaces, while its



wide spectral range ensures accurate color differentiation under any illuminant. The specialized tablet and capsule holders enhance sampling flexibility and precision, delivering consistent results across operators and shifts. The **Agera L2**, utilizing a compact 0°/45° circumferential geometry for color and appearance assessments, complements the UltraScan VIS with rapid throughput and user-friendly operation. Both instruments integrate with LIMS and electronic record systems, supporting 21 CFR Part 11 compliant data integrity. These combined capabilities deliver tangible benefits: faster release testing, fewer visual disputes, improved global consistency, and reduced rework due to color deviations across the drug development process.

## Hypothetical Case Studies

### Case 1 - Tablet Coating Uniformity

A pharmaceutical company manufacturing enteric-coated tablets experienced slight hue variations between coating lots, leading to consumer complaints about inconsistent appearance. Using the **UltraScan VIS** with its tablet holder, the laboratory quantified coating color with CIELAB coordinates and established  $\Delta E^*$  acceptance criteria. Process data revealed that small fluctuations in coating solution temperature and spray rate caused the deviations. After optimizing these parameters, the company achieved uniform coating color within  $\pm 0.3 \Delta E^*$ , eliminating rejections and improving batch reproducibility.

### Case 2 - Capsule Color Matching Across Suppliers

A global manufacturer sourcing hard-gelatin capsules from multiple suppliers found visible differences in shell color after filling, creating packaging alignment issues. Implementation of the **Agera L2** spectrophotometer at incoming inspection enabled precise color matching to the master reference. Capsules measured within a  $\Delta E^*$  tolerance of  $\leq 0.5$  were approved, while outliers were rejected before use. The



capsule-specific holder ensured consistent alignment of each capsule during testing. Standardizing color control across suppliers improved global consistency and reduced packaging rework.

### Case 3 – Pill Coating and Color Uniformity

A contract manufacturer/CDMO producing pills and tablets noted inconsistent coating and the need to coat multiple layers to achieve color and opacity objectives. The **UltraScan VIS** and **Agera L2** were both implemented, and both were equipped with a tablet holder. Analysis of color values and spectral reflectance curves demonstrated that instead of multiple coating applications, only two sprays needed to be applied across the capsule to achieve color and appearance specifications. Color uniformity was maintained within  $\pm 0.2 \Delta E^*$ . Cost savings using less coating saved 60 percent.

## Conclusion

Instrumental color measurement has become essential to quality control for tablets, pills, capsules, and caplets in bio-pharmaceutical manufacturing. By transitioning from subjective visual inspection to full-visible-range spectrophotometry, manufacturers gain precise, reproducible color data that reveal subtle process variations and support regulatory compliance. The HunterLab UltraScan VIS provides laboratory-grade spectral accuracy with dedicated sample-holding fixtures for every dosage form, while the Agera L2 offers rapid, verification using the same validated principles. Together, they form a unified solution that enhances product appearance, streamlines release testing, and strengthens global brand consistency. Through objective color control, pharmaceutical manufacturers and CDMOs can ensure that every dosage unit reflects not only the correct strength—but also the highest standard of quality.



## References

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7. [www.hunterlab.com](http://www.hunterlab.com) - Additional resources, product details, and pharmaceutical application support.