# Enhancing Biotech & Pharmaceutical Drug Development and Manufacturing with Instrumental Color Measurement

## Introduction

Color measurement is a critical quality attribute in the entire pharmaceutical and biotech drug development process. Even slight color variations in drugs or biologics often signal underlying issues (impurity, degradation, process shifts). Historically, color was judged by human observers comparing liquid samples to pharmacopeial standards, but this is slow, subjective, and cannot be validated. Modern spectrophotometers and colorimeters provide objective, quantitative color data (e.g. CIELab values and pharmacopeial color indices) throughout R&D and production. This white paper explains why precise color control matters in biotech/pharma, the types of products and standards involved, and how HunterLab's spectrophotometers deliver compliant, validated solutions for color and turbidity QC.

## Overview of Biopharma and Biotech Markets

Biotechnology and traditional pharma overlap in healthcare products but differ in **product types, science and regulatory paths**. Biotech products use living organisms or biomolecules (e.g. monoclonal antibodies, recombinant proteins, cell or gene therapies) as the basis of the drug product, whereas pharmaceutical products are most often chemically synthesized small-molecule drugs. For example, **biologics** (large molecules like antibodies, vaccines, cell or gene therapy products) belong to the biologics/biopharma segment. **Small-molecule drugs** (tablets, capsules, OTC pills, generics) dominate traditional pharma. Market segments reflect this mix: branded drugs (patented small-molecules), generic drugs, large-molecule biologics (monoclonal antibodies, cell therapies, vaccines) and **biosimilars** (generic biologics).

## Overview of Regulatory

These differences in small/large molecule drugs extend to regulation. In the US, chemical drugs generally require a **New Drug Application (NDA)** for approval, whereas biological products require a **Biologics License Application (BLA)**. Note:  Biologics are governed under the Public Health Service Act, while other drugs fall under the Food Drug & Cosmetic Act. Once approved, products face different life-cycle management: small-molecules often rely on analytical chemistry (HPLC, UV) for QC, whereas biologics require chromatography purification, and biophysical assays. Despite these distinctions, both sectors use color QC: for example, small-molecule tablets are checked for uniform coating color, and protein solutions are monitored for yellowing or cloudiness.

Globally, similar pharmacopeial and regulatory authorities apply. In Europe the **European Pharmacopeia (EP)** sets standards; in Japan, the **Japanese Pharmacopeia (JP)**; in China the **Chinese Pharmacopeia (CP)**; and in the US the **United States Pharmacopeia (USP)**. These compendia publish official methods for color and turbidity in drugs and biologics. Companies in all regions must meet these guidelines and often additional ISO/ASTM/GMP quality systems for product consistency and safety. In practice, a “bio-pharma” company today may span both worlds – e.g. producing both a small-molecule drug and a biosimilar – and must adhere to NDA and/or BLA paths, distinct application techniques, and applicable color standards for each.

## Importance of Color Measurement in Bio-Pharma

Color is a **key quality attribute** at every stage – R&D, formulation, stability, release, scale-up and downstream processing QC/QA, plus documentation for new drug submissions. The color and appearance of a bio-pharma product provides a quick visual indication of product state: consumers and regulators expect uniform, consistent appearance. Any unexpected shift (e.g. a solution or vaccine becoming too yellow, or a tablet fading) can signal problems. For example, impurities or oxidation by-products often impart a color change; microbial growth or particulate contamination makes liquids cloudy or cloudy-white. Conversely, maintaining a target color ensures batch-to-batch consistency, correct API dosing in blends, and compliance with published specs.

During R&D and process development, precise color data help pharmaceutical scientists quickly compare prototypes and optimize formulations. During manufacturing scale-up, it helps verify that experimental or trail batches match color requirements from prior runs. In QC, color measurement can catch substandard material or other process issues early. For packaged dosage forms, color consistency also supports brand identity. In all cases, **instrumental color measurement provides quantitative, objective data** (L*, a*, b* values, ΔE* differences, or pharmacopeia indices) that **replace subjective visual checks**. The result is improved product quality, fewer recalls/reworks, and more efficient manufacturing – essential in high-stakes pharma/biotech production.

## What Color Reveals About Quality

The color of a pharmaceutical or biologic formulation is a proxy for its chemical integrity and formulation consistency. **Color changes or discrepancies often indicate quality issues**. Examples include:

- **Chemical Degradation:** Oxidation, or other degradative processes often increase yellowness. (e.g. an API slowly oxidizing in solution will shift from clear to slight yellow).
- **Impurities or Off-spec Raw Materials:** A stray impurity or poorly purified intermediate can tint a batch. (For instance, excess metal catalysts or side-products may give a brownish hue.)
- **Process Variations:** Unintended changes (pH shifts, heat) can modify color or appearance. For example, if a mixing vessel overheats, the product might deepen in color.
- **Microbial Contamination:** Cloudiness and off-color in injectables can signal bioburden. Turbidity rises rapidly with microbial growth, turning clear solutions cloudy.
- **Product Potency and Uniformity:** In solid dosage forms, uneven mixing of a chromatic API will cause visible color streaks. Color measurement can quantify such blending quality or coating thickness (e.g. measuring the L* of tablet coatings or powder blends).
- **Counterfeit Detection:** Deviations in color may reveal counterfeit or substandard products (a slight color mismatch can be a warning that ingredients or processes differ).

Instrumental measurement detects these issues earlier than visual inspection, often in real time, and certainly at measurement intervals. For instance, a spectrophotometer might report a $\Delta E^*>1$ from target color when a human eye still sees "slightly tinted" – enabling corrective action before release. In stability studies, tracking the b* (yellowness) value or CIE total color difference (Delta E or ΔE*) over time quantifies degradation rates, which correlates with shelf-life. By correlating specific color shifts with known failure modes, color monitoring becomes a powerful **quality assurance tool across the product lifecycle**.

Applications span prescription drugs, OTC medicines, biologics, vaccines, and supplements – practically any product where color or clarity is critical. The result is **consistent product appearance and compliance** for both FDA-regulated and consumer-facing products.

## Color Measurement Applications in Bio-Pharma

Color QC is applied across a wide range of pharmaceutical and biotech products, in both regulated and non-regulated categories:

- **Liquid Formulations:** Parenteral (injectables) and ophthalmic drug products require rigorous color and turbidity control. For example, intravenous solutions must be essentially colorless/clear: EP and USP define specific color limits (e.g. “Color Y1” as near-water clear) and opalescence grades (0–IV) for turbidity. Visually opaque liquids (e.g. cough syrups, biologic suspensions) use instrumental color (CIELab) and reference indices to ensure batch consistency. Color measurement also verifies that concentrated protein solutions or gene therapy vectors stay within color spec (a shift toward yellow can indicate degradation or process variation).
- **Solid Dosage Forms:** Tablets and capsules are measured using reflectance spectrophotometers. In tablet coating and blending, even slight color variations (in L*, a*, b*) are detected objectively. For instance, the HunterLab UltraScan PRO, UltraScan VIS, or Agera can monitor API powder blends by scanning a small sample of the mix: this ensures uniform color indicative of a homogenous blend. Color assays are used on powders, granules, and finished tablets alike. *Example:* During tablet coating, color spectrophotometers/colorimeters can automatically measure

each batch of tablets to verify the correct shade (based on a standard reference or target data).

- **Semi-solids and Packaged Products:** Creams, lotions and liquids in vials are also tested. Even OTC (Over-the-Counter) non-prescription topical creams and lotions may undergo color QC to differentiate strengths or batches. Dietary supplements (vitamins, nutraceuticals) – although though not FDA-regulated — often implement color measurement in QC for consistency and branding. Powder blends and intermediates in manufacturing lines are checked with a color spectrophotometer (especially if visually colorless).
- **Raw Materials and Excipients:** Incoming APIs and excipients (non-active dyes, fillers, buffers, etc.) are often subjected to color analysis. A raw material slightly off-color can indicate a purity issue (e.g. a darkening indicating oxidation). By establishing reference color limits (e.g. a pharmacopeial close to value in CIELab), materials are verified objectively.

Spectrophotometric analysis is versatile: it handles **transparent samples** (clear liquid solutions in cuvettes) and **opaque samples** (powders or solids in a sample cup or other vessel). HunterLab systems can switch modes (reflectance vs. transmission) and measure turbidity/opalescence in one device.

## Challenges in Color Quality Control of Bio-Pharma Drug Products

Despite its significant importance, color QC in pharma/biotech is challenging when done by traditional ***visual*** methods:

- **Subjective Visual Matching:** Pharmacopeial color standards (EP/USP liquid scales, color discs or comparators) rely on the analyst's eye. Human perception varies widely with lighting and observer, leading to poor repeatability. One person's “light yellow” may be another’s “slightly tinted,” and background colors and other factors skew judgments.

- **Coarse Scale Steps:** Pharmacopeial scales consist of a small number of discrete reference solutions or chips. For example, USP Color has 20 steps (A–T), and EP has 37 color standards grouped in families. Adjacent steps can differ by a large color increment, making borderline samples very difficult to classify. A sample might fall between two standards, yet an analyst must pick one “closest” by eye, introducing ambiguity and subjectivity.
- **Difficulty with Light or Near-Clear Samples:** Very pale or nearly water-white samples are especially problematic. A liquid may show almost no visible color and be near-clear to water, thus a technician cannot reliably match it to any standard. Pharmacopeia accommodates this by labelling a product colorless or “water-white” but slight hues escape detection visually. Meanwhile turbidity (cloudiness) at low levels is also difficult to assess visually. Analyst subjectivity is a significant challenge.
- **Sample Volume and Preparation:** Using visual standards requires preparing and handling many reference solutions. Larger sample volumes are needed (e.g. 10 mL each) and may not be available, especially in early product development work. A small sample (as low as 500 micro liter) can be measured with a color spectrophotometer. Generating stable standards also consumes reagents and glassware. Inconsistency in how standards are made (slight concentration errors in the HCl solutions for EP standards, for instance) further adds error. Liquid standards also can degrade over time and change color.
- **Lack of Data Capture and Traceability:** Visual tests cannot be electronically recorded. If disputes arise (“who said this batch was Y2?”), there is no instrument readout to review. In modern GMP environments requiring data integrity (21 CFR Part 11), visual methods fail to provide audit trails or security.

These limitations underscore why many bio-pharma developers and manufacturers have moved away from these subjective, visual methods to analytical instrumental methods. A spectrophotometer delivers a fully objective result: continuous tristimulus data with CIE computation of color (plus industry standards) and is reproducible across laboratories and manufacturing sites globally. Color spectrophotometry also allows small sample sizes (when only small volumes are available) as well as automated reporting of data and systems that are established and validated. Overcoming the gap between visual and instrumental methods, however, requires validated methods to ensure regulatory acceptance.

## Global Standards and Methods for Color & Turbidity

Global pharmacopeias and industry standards define how to measure color and turbidity in pharmaceuticals. Key references include:

### European Pharmacopeia (EP) 2.2.2: Degree of Coloration of Liquids

This method defines a **visual color scale** of 37 liquid standards in five (5) families (Brown, Brown-Yellow, Yellow, Greenish-Yellow, Red). Each standard is a diluted solution (e.g. cobalt, ferric, copper salts) in hydrochloric acid. EP specifies the procedure for matching a sample to the nearest standard visually. An analyst visually matches the sample to the closest EP reference solution.

EP 2.2.2, Part III, also permits instrumental measurement using CIE colorimetry including: a color spectrophotometer (380–720nm suggested, 400-700nm acceptable with validation in a 10 nm interval). CIE Illuminant C or D65 is used with 2- or 10-degree CIE Observer to compute L*a*b* values and ΔE*. The instrument also can report an EP value (ex. “EP B1”, or Brown 1, indicating the closest match. The CIE color values as well as the EP ‘closest to’ can be reported individually or simultaneously. *(See Figure below for an example of EP liquid color reference vials.)*

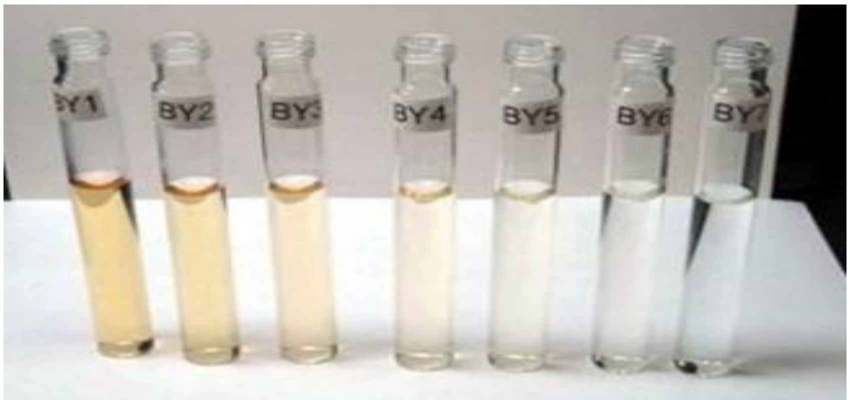


*Figure: Example of EP reference pharmacopeial liquid color standards (BY or Brown Yellow hue series) in tubes with controlled illumination and background. These and other visual standards (per EP 2.2.2) span families of brown, yellow and red visual colors.*

**United States Pharmacopeia (USP): Methods <1061> Chromaticity and <631> Color and Achromicity of Liquid Preparations:**

USP provides similar standards. It defines 15 fixed color indices (A–T) for clear solution color assessment. The USP <1061> method specifically addresses instrumental color measurement (recommending use of color spectrophotometers across 380–720 nm). USP <1061> recommends the CIE color measurement illuminant/observer combination. Further, USP advises using tristimulus or spectral measurements to replace the older visual <631> method, recommending that instruments be calibrated with purified water and suitable references (e.g. certified color solution standards).

*Figure: Example of USP pharmacopeial liquid color standards (15 standards designated A-T) in vials with controlled illumination and background.*

**Japanese (JP) and Chinese Pharmacopeias (CP):** These largely harmonize with EP/USP methods. For example, JP often references similar color chapters (Chapters 2.2.2 etc.) and includes its own color reference tables. CP likewise aligns with EP colors and clarifies solution color for Chinese regulatory submissions. (In practice, global companies use harmonized EP/USP methods and simply note JP/CP compliance).

**ASTM Standards:** ASTM also defines several metrics related to liquid color and haze. **ASTM D7315** covers the use of nephelometric turbidimeters and defines reporting in NTU (Nephelometric Turbidity Units). **ASTM D1003** defines transmission haze (generally for plastics) but is analogous to solution turbidity, reporting in haze units. In bio-pharmaceuticals products, EP 2.2.1 adopts these principles: it classifies parenteral turbidity (opalescence) into Categories 0–IV, corresponding to formazin turbidity standards of 0, 3, 6, 18, and 30 NTU. An EP/OP output will classify the turbidly in these Categories or "Out of Range".

**Turbidity and Opalescence:** EP 2.2.1 "Clarity and Degree of Opalescence of Liquids" and USP <643> set limits on allowable turbidity (cloudiness) of injectables. These use nephelometric measurements. For example, an intravenous solution that reads above 5 NTU (per a formazin-based scale) might fail EP Category I (clear to slightly opalescent). More generally, any unexpected increase in NTU during stability (e.g. from 0 to 10 NTU) triggers investigation.

**Internal Specifications and Broader Scales:** Beyond pharmacopeias, some companies use other industrial color scales (Gardner, APHA/Hazen for yellow) for internal QC. These are not pharmacopeial but often preloaded in instruments for cross-checks.

In summary, **global guidelines allow instrumental color and turbidity measurements** (e.g. USP <1061>, EP 2.2.2 Method I/II/III). A spectrophotometer with adequate range (typically 350–780 nm or more) and software can implement all relevant methods (EP, USP, ASTM) in one system. Compliance requires following the protocols: e.g. using the correct cell pathlength (10 mm for EP), illuminant and observer settings (D65/10° or C/2°), and report formats (report nearest color standard, or ΔE values). Critically, an instrumental method **should be fully validated** (with calibration records, SOPs and performance checks) to replace the old visual test and satisfy regulators.

## HunterLab Instrument Solutions for Biopharma Color QC

HunterLab offers a family of spectrophotometers tailored for pharmaceutical/biotech QC, each built for compliance and versatility:

- **UltraScan® PRO:** A research-grade dual-beam spectrophotometer (350–1050 nm range, 5 nm intervals). It covers UV to near-IR, enabling advanced applications (e.g. UV filtering materials or broad-range color analysis). The UltraScan PRO *conforms to USP <1061> and the EP 2.2 color method*, allowing direct implementation of pharmacopeial tests. It can measure reflectance, transmission and turbidity within one sample. Thus, the same instrument can analyze color of powders (reflectance mode), liquids in cuvettes (transmittance mode) and cloudiness (EP/OP or nephelometric turbidity) up to ~150 NTU. The UltraScan PRO supports 10 mm cells and is available with HunterLab's EZMQC/ER validation software (including design qualifiers (DQNB) for IQ/OQ/PQ), making compliance straightforward.

- **UltraScan® VIS:** A high-performance visible spectrophotometer (360–780 nm, 10 nm intervals), the UltraScan VIS is optimized for color measurements of liquid bio-pharma solutions as well as powders/tablets. It meets USP <1061> and EP 2.2.2 (Method III) requirements. Like the PRO, it measures reflectance, transmission and turbidity in one unit, with accuracy and precision. The UltraScan VIS also includes all key bio-pharma color scales and indices in its software libraries (EP colors, USP colors, Gardner, etc.), so any colored sample can be reported in the appropriate system.
- **Vista™:** A versatile, compact benchtop spectrophotometer (400–700 nm, 10 nm intervals) transmission-only color spectrophotometer. Vista is fully validated for **EP 2.2.2 Method III**. It is designed for ease of use in a QC lab. Vista is a stand-alone color spectrophotometer and includes Essentials software with all EP/USP/JP/CP indices or EZMQC for full CFR 21 Part 11 compliance. Key features across all HunterLab systems include low stray light, high wavelength accuracy, and detector stabilization for reproducibility.

These HunterLab systems offer **unique advantages** over generic spectrophotometers:

- **Combined Modes:** HunterLab instruments measure **reflection, transmission and turbidity/opalescence in a single device**. This is critical for biopharma because a laboratory often needs all these measurements. (In contrast, many competitor spectrophotometers only do transmission, and turbidimeters only do turbidity.

- **Pharmacopeia Compliance Built-In:** Each HunterLab instrument is preloaded with EP/USP/JP/CP color and turbidity methods. For example, UltraScan PRO/VIS automatically computes ΔE* vs all 37 EP color standards and reports the nearest EP standard. They conform to USP <1061>/<631> and EP 2.2.2 protocols, so method parameters (wavelength interval, illuminant D65, observer, cell path) follow official requirements. This turns a complex pharmacopeial test into a "push-button" routine.
- **Validation and Data Integrity:** HunterLab provides extensive validation documentation and software to meet QA needs. Their EZMQC/ER systems assist users in creating IQ/OQ/PQ protocols and automatically check instrument performance. All instruments support 21 CFR Part 11 features: user access controls, encrypted audit trails, data archiving, and prevention of data deletion. Raw spectral data are locked in, and any measurement can be traced, fulfilling regulatory expectations for electronic records.
- **High Sensitivity and Sample Efficiency:** HunterLab spectrophotometers are built to measure very small spectral differences accurately. They require only minimal sample (e.g. a few mL or microliters of liquid or a small tablet surface) and are nondestructive. Because they are engineered for small samples, they reduce waste of expensive biologics or APIs during testing. Sampling accessories are optimized.
- **Software and Reporting:** HunterLab's software (EZMQC, Essentials) delivers custom reporting. Users can define templates to output pass/fail, ΔE*, color indices, or full spectral data. The software automatically applies validation rules: for example, tolerance checks on L*, a*, b* or NTU, and flags any out-of-spec result in real time.

Together, these features make HunterLab instruments **best-in-class** for color QC in pharma/biotech. They address the exact challenges and requirements of drug manufacturing, converting subjective color checks into automated, reliable assays.

**HunterLab Product Solutions: Specs and Benefits**

HunterLab's recommended systems for biopharma are summarized below. Each system is available as a stand-alone bench-top unit, complete with **Essentials or EZMQC software** for 21 CFR Part 11 compliance, and a full validation package (IQ/OQ/PQ documentation).

| Instrument | Spectral Range / Geometry | Measurement Modes | Key Compliance | Notable Features & Benefits |
|---|---|---|---|---|
| **UltraScan PRO** | 350–1050 nm (5 nm data interval, D65/10°) Dual-beam optical design | Reflectance, Transmission, Turbidity/EPOP (4° sphere) | USP <1061>, EP 2.2.2 (Method I), ASTM E313 etc. | • Extended UV range captures near-UV/IR effects<br>• Research-grade accuracy, high stray-light rejection<br>• Multi-mode: one instrument for powders, solutions, haze<br>• Validated for EP 2.2.2 (10 mm) and USP 1061; supports EZMQC/ER for IQ/OQ/PQ<br>• CFR Part 11 software, audit trails (EZMQC). |
| **UltraScan VIS** | 360–780 nm (10 nm intervals, D65/10°) | Reflectance, Transmission, Turbidity/EPOP (4° sphere) | USP <1061>, EP 2.2.2 (Method I) | • High-performance visible spectrophotometer<br>• Meets USP color guidelines and original EP 2.2 protocols<br>• ±45°/0° geometry optimized for solids<br>• Preloaded with all pharmacopeial color/turbidity scales (EP, USP, Gardner, NTU)<br>• Compact bench-top |

HunterLab

| | | | | |
|---|---|---|---|---|
| | | | | design with standalone or network software |
| **Vista™** | 400–700 nm (10 nm intervals, D65/10°) | Transmission, Turbidity/EPOP (2°/diffuse) | EP 2.2.2 (Method III) verified, USP <1061> kit available | • Bench-top, filter-wheel-based spectrophotometer<br>• Factory-validated for EP 2.2.2 (Method III)<br>• Fast measurements (~1 sec), ideal for QC lab throughput<br>• Standalone mode (built-in touchscreen + Essentials software) or PC-connected<br>• Part 11-compliant software; meets pharmacopeial and ISO standards |

*Key HunterLab instrument solutions for color and turbidity measurement in pharmaceutical applications. All systems measure both transmitted and reflected light, can detect haziness (EPOP/turbidity) up to ~150 NTU, and come with full validation software (EZMQC, Essentials) for regulatory compliance.*

## Competitive Comparison

In the competitive landscape, few vendors address pharma color QC as comprehensively as HunterLab. Below are key differentiators:

- **Hach/Lovibond:** These brands are known for water-quality instruments (turbidimeters, simple spectrophotometers, comparators) but lack pharma-specific features. Their colorimeters (e.g. Lovibond tintometers) are visual or single-beam devices not preloaded with EP/USP color indices. They also typically measure only transmittance or turbidity. In contrast, HunterLab's spectrophotometers measure reflection **and** transmission with high precision, and include built-in pharmacopeial libraries.
- **Shimadzu, Perkin-Elmer, Agilent (UV-Vis Spectrophotometers):** These brands offer broad-spectrum UV-Vis instruments that meet the wavelength requirements of pharmacopeial color methods (e.g. 380–720 nm). However, they are general-purpose spectrophotometers, not turnkey color QC systems. They typically lack dedicated pharmacopeial color matching software or fixed protocol support (EP/USP indices). Implementing EP/USP methods on a generic UV-Vis requires custom calibration and interpretation. HunterLab's systems come *ready* with pharmacopeia methods and validation tools. Moreover, HunterLab instruments are optimized for color accuracy (stray-light suppressed, dual-beam for stability), whereas some general UV-Vis models prioritize flexibility over colorimetric precision.
- **Other Colorimeters (e.g. Konica-Minolta, X-Rite):** Some colorimeters can measure liquid color, but often only at a fixed pathlength (10 mm or 20 mm) and without turbidity capability. They may not support large liquid samples or solid powders natively. By contrast, HunterLab instruments allow variable pathlengths and measure tablets or powders under controlled geometry. Additionally,

HunterLab

HunterLab software can instantly report *the closest EP/USP color plus ΔE*, a feature often missing in generic colorimeters.

## Comparison of Color Spectrophotometer vs UV-Vis Spectrophotometer

UV-Visible spectrophotometry and color spectrophotometry are often competitive - two light-based analytical instrumentation techniques.

***UV-Visible spectrophotometry*** measures light absorption across the ultraviolet and visible spectrum to determine analyte presence, concentration and molecular structure prioritizing wavelength resolution and individual wavelength analysis.

***Color spectrophotometry,*** conversely, measures light reflectance or transmission in the visible spectrum to quantify color and ensure consistency of a multitude of products, emphasizing speed and comparison of samples and standards.

### Color Spectrophotometer

- **Faster Measurement Speed**: Color spectrophotometers operate at **faster speeds**, often taking measurements in milliseconds or **a few seconds**. This is because they typically measure reflectance or transmittance across the entire visible spectrum (CIE range 360nm-780nm; 400–700nm also common and acceptable). Because color spectra span many wavelengths, there is not the critical need to scan and report absorbance or transmission data of individual wavelengths.
- Color Spectrophotometry **matches how the human eye see color**. There is no information about illuminant and observer in a UV-VIS spectrophtometer, which are essential to accurately assess color and color matches.
- Color spectrophotometers have **optimized sampling flexibility** and sample accessories built for the application (liquids or powders).

### UV-Visible Spectrophotometry

- UV-Visible Spectrophotometers offer high wavelength resolution but generally have slower measurement speeds due to scanning of the UV and visible spectra.

- UV-Visible spectrophotometry is ideal for analyzing the concentration of solutions, chemical reactions, and molecular structures, particularly when the sample absorbs light in the UV or visible range.

Each technology serves different purposes but can sometimes be used complementarily, especially when assessing color in solutions or materials that may also require concentration or quality measurements.

## Instrumental Protocols for Color QC

For routine QC, HunterLab instruments enable fully documented, validated protocols that replace old visual tests. It's critical to configure your color-measurement instrument exactly as prescribed by the specific industry method or standard you're following. Proper setup ensures your results are accurate, reproducible, and directly comparable to those from other labs or published specifications. Typical steps include:

- **Select the measurement mode**
  Use **transmission** for clear or colored liquids and solutions) and **reflectance** for opaque solids or powders (e.g. powders, pastes, granules, tablets, capsules).
- **Apply the specified illuminant and observer**
  Every compendium or test method (USP, EP, ASTM, ISO, etc.) will call out a CIE standard illuminant (such as D65 or C) and a standard observer angle (2° or 10°). Always use the combination mandated by your method.
- **Set the wavelength interval**
  Follow the standard's requirement for spectral resolution (often 10 nm for pharmacopeial methods like EP 2.2.2 or USP < 1061>), so that your scan precisely matches the defined procedure.
- **Sample Preparation:** Use standardized high-quality cuvettes (10 mm path for liquids per EP/USP). When very small volumes are measured (less than 1000uL/1 mL), micro-cuvettes may be necessary. Solutions should be as clear as possible or

considerations for opalescence/turbidity. For powders/tablets, present an appropriate surface. For tablets and capsules either measure individually or measure multiple samples in a larger container and average measurements.

- **Color Measurement:** Measure the sample liquid solution or powder/tablet. The software reports the CIELab values. For **pharmacopeial color tests**, the software will automatically compare the result to all EP (or USP/JP/CP) standard values and report: the nearest color index (e.g. “EP Y2”). The total color difference, the ΔE (Delta E) may also be reported as well as other color or whiteness indices.
- **Turbidity Measurement:** If testing turbidity with the EP Opalescence Method (EP 2.2.1) is required, select and report that metric. Compare to nephelometric mode (NTU) if needed. Use clean cuvettes and compare the sample’s NTU reading against a formazin-calibrated standard. HunterLab systems automatically report NTU and EP 2.2.1 opalescence/turbidity category (I-IV).
- **Documentation:** All data can be collected, archived, and analyzed. With HunterLab’s Electronic Recordkeeping software (21 CFR Part 11 compliant), the instrument’s software auto-logs all data. Output reports include date/time, operator ID (via login), instrument ID, method (EP/USP chapter), raw spectrum, computed values, and pass/fail verdict. This digital record (with audit trail) replaces written color observation notes.

Adhering strictly to these settings—mode, illuminant/observer, interval, and reference—guarantees color data meet the acceptance criteria of the chosen industry standard. By following these instrumental protocols, a lab eliminates the subjectivity of visual methods.

## Conclusion

Color, appearance, and turbidity are essential quality attributes in pharmaceutical and biotechnology discovery, product development, and manufacturing. These attributes are critical for product consistency, purity and identity, stability plus potency that must be controlled from development through production. Traditional visual color tests are limited by subjectivity, lack of sample, and coarse grading; modern spectrophotometers overcome these issues with objective, high-resolution measurement with maximized sample handling. By using validated HunterLab solutions (UltraScan PRO, UltraScan VIS, Vista), manufacturers can meet global pharmacopeial color standards (USP, EP, JP, CP) as well as global color parameters (CIELab), plus compliance with 21 CFR 11. In short, investing in instrumental color measurement yields better quality, reduced risk of rework/recalls, and efficient operations – a clear win for pharma and biotech operations.

## Appendix I: *Definitions*

- **API (Active Pharmaceutical Ingredient):** The ***active*** component of a medication that produces the intended therapeutic effect. APIs can be small-molecule synthetics or large biomolecules. Maintaining consistent API color is crucial for ensuring potency, purity, and stability.
- **Excipient:** Any ***inactive*** substance formulated alongside the API in a drug product. Excipients (binders, fillers, etc.) aid in drug delivery, stability, metabolism, and absorption but have no therapeutic effect themselves. These inactive ingredients can include binders, disintegrants (assist the tablet or capsule break down for absorption), fillers (to increase the bulk of the product) and coatings (to protect the API or control its release). Excipients can contribute to a product's final color and appearance.
- **USP (United States Pharmacopeia):** A public standards-setting authority whose compendium (the USP–NF) specifies official quality standards for drugs marketed in the US. USP includes chapters on analytical methods and color limits. Most important: Method <1061> on colorimetry and <631> on solution color.

- **EP (European Pharmacopeia):** The official pharmacopeia of Europe (published by the EDQM). EP chapter 2.2.2 defines the **Degree of Coloration of Liquids** method using 37 reference solutions; EP 2.2.1 covers clarity/opalescence of injections. Compliance with EP color and clarity tests is required for products sold in Europe.
- **JP (Japanese Pharmacopoeia) / CP (Chinese Pharmacopoeia):** The national pharmacopeias of Japan and China, respectively. They contain chapters analogous to EP/USP for color and clarity. For global products, demonstrating EP/USP compliance is generally accepted by JP and CP.
- **OTC (Over the Counter):** Drugs that can be sold directly to consumers without a prescription. Many OTC products (pain relievers, vitamins, cough syrups, supplements) still use color QC to ensure consistency and consumer appeal.
- **Biosimilar:** A biologic product that is highly similar to an already approved biologic (reference product), with no clinically meaningful differences. Color measurement is important to confirm that a biosimilar matches its reference in appearance, reinforcing structural similarity.
- **21 CFR Part 11:** A section of FDA regulations governing electronic records and signatures. Color measurement software that is "Part 11 compliant" supports secure logins, audit trails, and non-editable data storage, which are required for FDA-regulated QC data (as noted for HunterLab EZMQC/Essentials).
- **Drug Substance:** A drug substance, also known as an ***active pharmaceutical ingredient (API)*** is the pure, active component of a medicine that provides its pharmacological effect. It's the substance that acts on the body to produce the desired therapeutic outcome.
- **Drug product:** The finished dosage form of a drug that is ready for use by patients. This includes: the **finished dosage** form (e.g. include tablets, capsules, injections, creams, etc.), the **drug substance** (an active pharmaceutical ingredient (API) and likely contains **inactive ingredients** (*excipients*). Essentially, a drug product is the

complete package that delivers the therapeutic benefit of a drug substance to a patient in a safe, effective, and convenient form.

## Appendix II: HunterLab First in Bio-Pharma Color and Appearance Measurement

HunterLab is the pioneer in color measurement of bio-pharma products including:

- **Large-molecule** clear liquid solutions including the API/drug substance, excipients.
- **Small-molecule** opaque powders, tablets and capsules, and dry excipients.

HunterLab has innovated over 20 years of supplying the global industry with analytical color spectrophotometer plus optimized sample handling accessories. HunterLab has several 'firsts' in supporting color measurement in the bio-pharma industry including:

1. The first analytical color spectrophotometer system to replace visual systems.
2. The first to report exact EP and USP values conforming to the respective pharmacopeial methods.
3. The first to report EP/JP/CP/USP with CIELab data plus turbidity/opalescence data.
4. The first to offer JP and CP color data look-ups and outputs.
5. The first software for 21CFR Part 11 compliance with color data.
6. The first software to report 0.1 resolution of EP color reporting value.
7. The first to offer an option to pick the specific EP hue family (ex. BY series).
8. The first to offer option near-clear reporting value per EP Methods 2.2.1 Opalescence.
9. The first to be listed in USP Method <1061>.
10. The first in number of global installations and the most cited in literature.