



Measuring Pharmaceutical Products Using HunterLab Instruments

In the pharmaceuticals industry color is used as:

- an indicator of quality where there is a color difference between acceptable and unacceptable product
- a conformance criterion for FDA or company manufacturing standards
- an indicator of degradation and loss of potency over time
- to differentiate between medications
- to verify efficacy of dip test strips where a defined color is associated with the presence of an active ingredient
- part of a brand's identity.

HunterLab instruments can be used for color evaluation of pharmaceutical intermediates, final products, byproducts, and medical devices such as those listed below.

- Tablets and capsules
- Powders and granules
- Liquid solutions, syrups, and gels
- Ointments, creams, and lotions
- Dip strips
- Plastic parts.

(Instrument recommendations for specific applications are shown at the end of this *Applications Note*.)

Recognizing the importance of color for pharmaceuticals, the U.S. Pharmacopeia includes guidance on color and color measurement in its collection of standards. The relevant monographs (which may be purchased through www.usp.org) are discussed below.

U.S. Pharmacopeia Monograph 631

Monograph 631, titled “Color and Achromicity,” defines color and colorlessness (achromicity), the visual observing situation, and the three attributes of color (hue/value/chroma and the corresponding X, Y, Z), principles that apply to HunterLab’s instruments. The monograph also describes how color should be evaluated visually using “diffuse, uniform illumination under conditions that reduce shadows and nonspectral reflectance to a minimum.” When powders are evaluated, the surface viewed “should be smoothed with gentle pressure so that a planar surface free from irregularities is presented.” If the illumination affects evaluations, “those obtained in natural or artificial daylight are to be considered correct.” It stipulates that “a suitable instrumental measurement may be used” instead of visual evaluation and explains how color difference measurements can be made by comparison of samples to known standards of similar color, such as Munsell chips for reflectance measurements and the A-T USP fluid standards for transmittance measurements. Both of these types of standards are shown in the pictures below.



Munsell Color Standards



USP Fluid Standards

The Munsell and USP standards serve as guides for color selection and a standardized means for verbal color communication, but lack the precision of tristimulus instrumental measurements necessary to meet today's quality assurance requirements. A suitable compromise is to define the product color in nominal terms using the Munsell or USP standards, while using tristimulus color measurements to verify color consistency.

All of the requirements of Monograph 631 can be met using HunterLab instruments. The visual observing situation (including the diffuse, uniform illumination specified) is standardized using HunterLab spectrophotometers and colorimeters. A smooth, regular powder surface can be presented to a LabScan XE by pressing the powder into a plaque or pouring it into a glass sample cup and reading it through the glass bottom of the cup. Powders may also be measured in a glass sample cup using a ColorFlex, D25LT, or MiniScan XE Plus. Powders can be measured using a ColorQuest XE, UltraScan XE, UltraScan PRO, or UltraScan VIS by pouring them into a glass transmission cell and measuring them through one of the glass sides of the cell. As far as the illumination requirement, a number of standard illuminants, including several daylight illuminants, are available with all HunterLab spectrophotometers. In addition, the xenon flash lamps of the ColorQuest XE, LabScan XE, UltraScan XE, UltraScan PRO, and UltraScan VIS themselves provide a very good match to D65 daylight. All HunterLab instruments can provide color difference measurements by comparison of samples to standards.

U.S. Pharmacopeia Monograph 1061

Monograph 1061, titled "Color—Instrumental Measurement," first gives a synopsis of color measurement, explaining how a color measurement instrument simulates the three components of the visual observing situation: the spectral energy of the illumination (the light source or illuminant), the absorbing characteristics of the sample (the sample itself), and the visual sensitivity of the observer (the human observer or CIE standard observer). It also provides the equations for converting spectral reflectance or transmittance to CIE X, Y, Z tristimulus values, from which all other color values may be calculated. (The formulas for CIELAB values are provided at the end of the monograph.) Then it gets into the requirements, the crux of the monograph. These requirements are listed in the table below in order of appearance in the monograph, along with an evaluation of whether HunterLab's instruments comply with each. This monograph describes measurement of opaque solids and transparent liquids. It is not applicable to measurement of hazy liquids or translucent samples.

Monograph 1061 Requirement	HunterLab Instrument Compliance
Spectrophotometers should have a band width of 10 nm or less.	All of HunterLab's current spectrophotometer products (ColorFlex, ColorQuest XE, ColorQuest XT, LabScan XE, MiniScan XE Plus, UltraScan XE, UltraScan PRO, and UltraScan VIS) meet or exceed this requirement.
For colorimeters, filters should be used to provide tristimulus values.	HunterLab's D25 product line meets this requirement.

Monograph 1061 Requirement	HunterLab Instrument Compliance
When spectral reflectance of opaque solids (such as powder plaques) is being measured, specular excluded (RSEX) mode should be used.	The geometry of the ColorFlex, LabScan XE, and MiniScan XE Plus excludes the specular such that measurements are made in this mode. The ColorQuest XE, UltraScan XE, UltraScan PRO, and UltraScan VIS may also be standardized to read in this mode.
When spectral transmittance of clear liquids is being measured, both the illumination and observation angles should be within 5 degrees of the normal to the sample surface.	When RTRAN measurements are made using the ColorQuest XE, ColorQuest XT, UltraScan XE, UltraScan PRO, or UltraScan VIS, the instrument geometry is diffuse/0° (the light source passes straight through the sample to the detector at 0°). ¹
When measuring spectral transmittance of clear liquids, the path length should be kept constant, and a 1 cm path length should be used “unless special considerations dictate otherwise.”	10 mm (1 cm) transmission cells are available for use with the ColorQuest XE, ColorQuest XT, UltraScan XE, UltraScan PRO, and UltraScan VIS, though longer path lengths are not prohibited by the monograph. HunterLab also has transmission cells available in 20-, 33-, and 50-mm path lengths.
For transmittance measurements, distilled water should have a transmittance of 100% at all wavelengths.	The ColorQuest XE, ColorQuest XT, UltraScan XE, UltraScan PRO, and UltraScan VIS may be standardized using distilled water in the transmission cell as a blank for setting the top of the scale. If the transmission cell of distilled water is then read back, they return 100% transmission at all wavelengths.
For transmittance measurements, the X, Y, and Z factors used for illuminant C should be 98.0, 100.0, and 118.1, respectively.	The X, Y, and Z factors optimized by HunterLab for the ColorQuest XE and ColorQuest XT using Universal Software are 98.0, 100.0, and 118.1. The X, Y, and Z factors optimized by HunterLab for the UltraScan XE using Universal Software and dictated in ASTM E308 are 98.1, 100.0, and 118.2. The ASTM E308 factors are used for all instruments in EasyMatch QC.

¹ For non-hazy samples, experiments have shown that measurements made in TTRAN mode do not differ from those made in RTRAN even though the geometries are slightly different.

Monograph 1061 Requirement	HunterLab Instrument Compliance
For reflectance measurements, opaque porcelain plaques should be used to set the top of scale versus the perfect diffuse reflector.	HunterLab is specifically mentioned in footnote 2 of the monograph as being a supplier of suitable standards. Porcelain on steel standard tiles are used to set the top of scale of the ColorFlex, ColorQuest XE, D25LT, LabScan XE, and MiniScan XE Plus versus the perfect diffuse reflector. Everwhite opal tiles are used to set the top of scale of the UltraScan XE, UltraScan PRO, and UltraScan VIS versus the perfect diffuse reflector.
After calibration, the instrument should be checked versus a reference material that is close in color to the sample for monitoring instrument performance.	A green tile is provided with the ColorFlex, ColorQuest XE, LabScan XE, UltraScan XE, UltraScan PRO, and UltraScan VIS as a middle wavelength check. This tile is also an option with the MiniScan XE Plus. The D25LT system includes a set of colored check tiles. Standards of other colors may be purchased from HunterLab and used for color checking.
For spectrophotometric measurements, reflectance or transmittance should be determined from 380 to 770 nm.	The UltraScan PRO has the capability of measuring reflectance and transmittance over the range of 350-1050 nm and meets this requirement. The UltraScan VIS measures over the range of 360-780nm and meets this requirement. The UltraScan XE measures over the range of 360-750 nm and the ColorFlex, ColorQuest XE, ColorQuest XT, LabScan XE, and MiniScan XE Plus measure over the 400-700 nm range.
For spectrophotometric measurements, reflectance or transmittance should be determined at intervals of 10 nm.	All of HunterLab's current spectrophotometer products (ColorFlex, ColorQuest XE, ColorQuest XT, LabScan XE, MiniScan XE Plus, UltraScan XE, UltraScan PRO, and UltraScan VIS) meet or exceed this requirement.
For colorimetric measurements, a filter colorimeter should be used.	HunterLab is specifically mentioned in footnote 5 of the monograph as being a supplier of suitable tristimulus colorimeters. HunterLab's D25 product line meets this requirement.

Instrument Recommendations

Pharmaceutical products and appropriate instruments for their measurement are given in the table below. A web address is shown where an illustrated method for the product's measurement is available. Methods are always being added, so visit <http://www.hunterlab.com> and search under the Solutions menu if an address is not provided for your application. A method could be added at any time.

Product	Instrument	Method Address
Creams and Lotions	ColorFlex	http://www.hunterlab.com/measurementmethods/semis2.html
	ColorQuest XE	http://www.hunterlab.com/measurementmethods/semis4.html
	LabScan XE	http://www.hunterlab.com/measurementmethods/semis.html
	MiniScan XE Plus	http://www.hunterlab.com/measurementmethods/semis3.html
	UltraScan XE	http://www.hunterlab.com/measurementmethods/semis4.html
	UltraScan PRO	http://www.hunterlab.com/measurementmethods/semis4.html
	UltraScan VIS	http://www.hunterlab.com/measurementmethods/semis4.html
Dip Strips	ColorQuest XE	http://www.hunterlab.com/measurementmethods/area2.html
	LabScan XE	http://www.hunterlab.com/measurementmethods/area.html
	MiniScan XE Plus	http://www.hunterlab.com/measurementmethods/area3.html
	UltraScan XE	http://www.hunterlab.com/measurementmethods/area2.html
	UltraScan PRO	http://www.hunterlab.com/measurementmethods/area2.html
	UltraScan VIS	http://www.hunterlab.com/measurementmethods/area2.html

Product	Instrument	Method Address
Plastic Parts	ColorFlex	http://www.hunterlab.com/measurementmethods/partd.html
	ColorQuest XE	http://www.hunterlab.com/measurementmethods/parta.html
	LabScan XE	http://www.hunterlab.com/measurementmethods/partb.html
	MiniScan XE Plus	http://www.hunterlab.com/measurementmethods/partc.html
	UltraScan XE	http://www.hunterlab.com/measurementmethods/parta.html
	UltraScan PRO	http://www.hunterlab.com/measurementmethods/parta.html
	UltraScan VIS	http://www.hunterlab.com/measurementmethods/parta.html
Powders (often checked for whiteness)	ColorFlex	http://www.hunterlab.com/measurementmethods/powder2.html
	ColorQuest XE	http://www.hunterlab.com/measurementmethods/powder4.html
	LabScan XE	http://www.hunterlab.com/measurementmethods/powder.html and http://www.hunterlab.com/measurementmethods/plaques.html
	MiniScan XE Plus	http://www.hunterlab.com/measurementmethods/powder3.html
	UltraScan XE	http://www.hunterlab.com/measurementmethods/powder4.html
	UltraScan PRO	http://www.hunterlab.com/measurementmethods/powder4.html
	UltraScan VIS	http://www.hunterlab.com/measurementmethods/powder4.html
Tablets and Capsules	ColorFlex	http://www.hunterlab.com/measurementmethods/partd.html
	ColorQuest XE	http://www.hunterlab.com/measurementmethods/parta.html
	LabScan XE	http://www.hunterlab.com/measurementmethods/partb.html

Product	Instrument	Method Address
Tablets and Capsules (continued)	MiniScan XE Plus	http://www.hunterlab.com/measurementmethods/partc.html
	UltraScan XE	http://www.hunterlab.com/measurementmethods/parta.html
	UltraScan PRO	http://www.hunterlab.com/measurementmethods/parta.html
	UltraScan VIS	http://www.hunterlab.com/measurementmethods/parta.html
Transparent Liquids (often checked for yellowness and APHA)	ColorQuest XE	http://www.hunterlab.com/measurementmethods/trans.html
	ColorQuest XT	http://www.hunterlab.com/measurementmethods/trans.html
	UltraScan XE	http://www.hunterlab.com/measurementmethods/trans.html
	UltraScan PRO	http://www.hunterlab.com/measurementmethods/trans.html
	UltraScan VIS	http://www.hunterlab.com/measurementmethods/trans.html

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