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Good Laboratory Practice with a UV-Visible Spectroscopy System

Application Note

UV-Visible Spectroscopy

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The objective of good laboratory practice (GLP) is to obtain accurate and precise results. A prerequisite for achieving this objective is a properly-functioning measurement system that is well-documented. Validation of the system includes the analytical instrument (both hardware and microprocessor firmware), the computer (hardware and software), and a properly-validated test method. In day-to-day routine use it is necessary to ensure that the quality and the integrity of the generated data is maintained by following correctly the prescribed test methods. This note covers these four distinct areas, and describes the features of the Hewlett-Packard HP 8453 UV-Visible spectroscopy system that is designed to meet the requirements of both initial and recurrent validation.

Contents

System validation

Vendor's responsibility

A vendor's responsibility to the GLP-regulated laboratory is to supply instruments that have been developed and tested according to recognized standards and procedures. Hewlett-Packard's position is outlined in detail in *Good Laboratory Practice–A Primer*.[1]

The HP 8453 UV-Visible spectroscopy system is supplied with a *Declaration of Conformity* confirming that the spectrophotometer was within specifications when it left the factory. A *Declaration of Validation* summarizes the development and test procedures for the system software and lists the supporting documentation available for inspection by an auditor.

The following sections describe the onsite revalidation of the spectrophotometer, computer and software.

Spectrophotometer

The HP 8453 system is based on the HP 8453 UV-Visible spectrophotometer. Unlike conventional scanning spectrophotometers, diode-array spectrophotometers such as the HP 8453 have no optically-active moving parts and have proven to be extremely reproducible and stable both in the short (hours or days) and long term (months or years).[2]

With no moving parts there are no mechanical components to adjust or recalibrate. Thus reverification is primarily required to:

- check the instrument is within specifications, and
- check for significant changes in performance since the last verification.

Changes can affect the accuracy of quantitative analyses and can indicate potential problems. In most cases, changes in performance will usually be due to the intensity of the deuterium lamp deteriorating over time.

Verification. The HP 8453 system's excellent reliability, stability, and its built-in self-verification makes frequent, full verification unnecessary. In principle, the full verification procedure is necessary only after a repair or when the lamp is changed (the lamp should be changed when the noise reaches an unacceptable level).

However, based on common practices with conventional spectrophotometers, we suggest full verification at six-monthly intervals.

There is a significant difference between the United States Pharmacopoeia (USP) and the European Pharmacopoeia (EP) with regard to performance verification of UV-Visible spectrophotometers. The USP states *"the instrument performance should be verified as prescribed by the manufacturer."* In contrast the EP gives specific tests and performance requirements for wavelength accuracy, photometric accuracy, stray light, and resolution.

The HP 8453 system meets both sets of requirements by providing a range of tests, including all EP required tests, and allowing the user to select those tests which should be performed to provide full verification according to company or national regulatory needs. Table 1 lists the available tests.

Test	Description
Wavelength accuracy	The specifications are: 1. Within ±0.5 nm, and is tested at 241.13, 249.87, 278.10, 287.18, 333.44, 345.47, 361.31, 385.66, 416.28, 451.30, 467.83, 485.29, 536.64 and 640.52 nm using holmium oxide in perchlorate solution (NIST[3] 2034)❖. The instrument is blanked on air and the transmittance spectrum of the standard is measured. The wavelengths of the peak minima found are then compared to the specified wavelengths for the standard (EP method).
Photometric accuracy	The specifications are: 1. Within ± 0.005 AU at 440.0, 465.0, 546.1, 590.0, and 635.0 nm, at approxi,ately 1 AU using the NIST[3] 930e, 10% transmittance, absorbing glass standard. The instrument is blanked on air and the absorbance values at the specified wavelengths of the standard is measured. These values are then compared to the specified value for the standard. 2. ± 0.01 AU 235, 257, 313, 350 nm using a 6 % w/v potassium dichromate (solid available as NIST[3] 935a) solution in 0.01 N sulfuric acid†. The instrument is blanked on 0.01 N sulfuric acid and the absorbance values at the specified wavelengths of the standard is measured. These values are then compared to the specified value for the standard (EP method).
Stray light	The specifications are: 1. Less than 0.05 % at 340 nm measured with 50 g/l $NaNO_2$ solution. 2. Less than 0.07 % at 220 nm measured with 10 g/l NaI solution. 3. Less than 1 % at 200 nm measured with 1.2 % KCl solution (EP method)❖. In transmittance mode the instrument is blanked on air. The transmittance value at appropriate wavelength is measured with the appropriate solution in place.
Resolution	The specification is: The ratio of the absorbances at 269 and 266 nm of a 0.02 % v/v solution toluene in hexane is greater than 1.5◆. The instrument is blanked on air and the absorbance values at the specified wavelengths of the standard is measured. The ratio is calculated compared to the specified value (EP method).
Noise	The specification is: Less than 0.0002 AU rms (root mean square) at 500 nm and 0 AU. No filters or standards are required. With sample area empty, 60 consecutive absorbance measurements of 0.5-second integration time are made at the user specified wavelength(s). Noise is calculated from the measured data using the equation: *Noise (rms) = SQRT ((SUM(X-x)^2)/n)* where x are the measured values, X is a 11-point moving average and n is the number of points.
Baseline flatness	The specification is: Less than 0.001 AU rms at 0 AU. No filters or standards are required. With nothing in the sample area a blank is measured and then a *sample* absorbance spectrum is measured using 0.5-second integration time. The baseline rms value is calculated using the same equation as above but with a normal average.
Stability	The specification is: Less than 0.001 AU at 340 nm at 0 AU, measured over 1 hour. No filters or standards are required. With the sample area empty measurements are made at the user specified wavelength(s) every 1 minute using 5 seconds integration time over 1 hour. The difference between the maximum and minimum values measured is taken and compared to the specification. The instrument should be allowed to warm up for at least 60 minutes before performing the test and room temperature should remain constant during the test.

❖ EP test method and/or specification
◆ EP/BP test method, BP specification

Table 1
Components of spectrophotometer performance verification

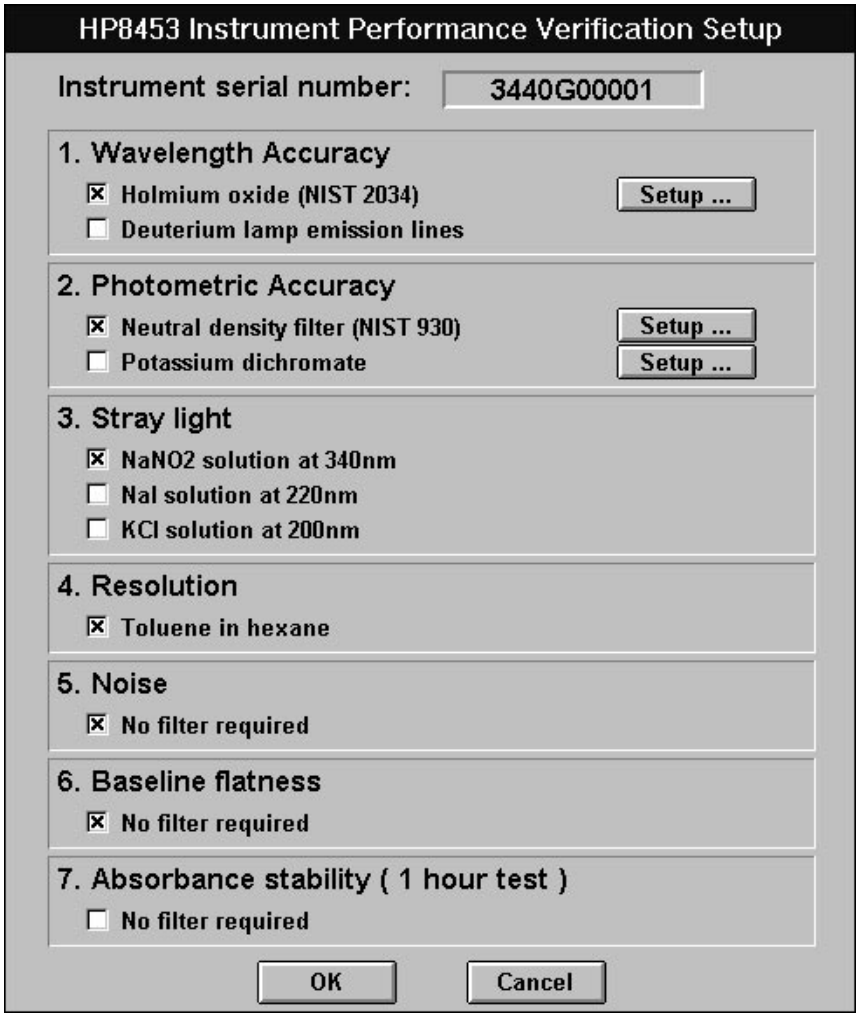

Figure 1
Verification report printed automatically by the HP 8453 system

The HP 8453 verification procedure allows the user to select those tests that are appropriate to national or international guidelines, as shown in figure 1.

The system's verification procedure prompts the operator to insert standards and make the appropriate measurements. It performs calculations and generates a validation report. In addition, the results are archived in a binary file for reporting or reviewing.

Self-test. A full performance verification as described above takes time and is not practicable on a daily basis. It is common practice to do a full performance verification on a monthly to six-monthly basis. However, if it is not done frequently there should be some way to monitor performance between verification.

The HP 8453 spectrophotometer has a built-in self-test procedure that the user can initiate at any time. This self-test comprises:

- electronic tests (that are also performed automatically when the spectrophotometer is switched on), and
- optical performance tests.

These tests are summarized in Table 2. The self-test detectets any changes in performance between full performance verifications. The results of the self-test are stored in an electronic logbook and can be printed and reviewed as required.

The self-test should be performed at weekly or even daily intervals.

Test	Description
Electronic	Tests are performed to ensure proper operation of microprocessors, RAM, communications interface, analog-to-digital converter and shutter.
Optics	Dark current, intensity profile, wavelength accuracy and resolution at the 486.1 and 656.3 nm emission lines of the deuterium lamp are checked.

Table 2
The most important components of the spectrophotometer self-test

Computer and software

The operating software for HP ChemStations undergoes extensive validation during development, as documented by the *Declaration of Validation* shipped with each instrument. The equipment itself also contains additional software routines for revalidation of particular parts of the electronic data processing. Data acquisition is implicitly tested by the automated validation routine for the HP 8453 spectrophotometer as described above.

Data analysis and the reporting components of the software can be verified using the *software validation kit* shipped with every copy of the ChemStation software. This kit includes:

- spectra for single component calibration and evaluation,
- spectra for multicomponent calibration and analysis,
- methods designed to exercise spectral processing and quantification,
- an automation file that performs the validation process automatically, and
- documentation of expected results.

A test is performed by loading and running the appropriate automation file. The software automatically steps through a series of method loading, data loading, data analysis and reporting processes to produce printed reports that are then compared with the expected results. The user can adapt the validation process to meet specific needs.

Detailed descriptions of the transformations used by the HP 8453 system are given in the *Understanding Your ChemStation* manual. This enables the user, if required by an auditor, to reproduce manually all the calculations performed by the software.

Method validation

Method validation is the process of establishing that the performance characteristics of the analytical method are suitable for the intended application. The United States Pharmacopoeia (USP) position on method validation is well documented.[5,6] The analytical variables considered in the validation of methods should typically include precision, accuracy, limit of detection, limit of quantification, selectivity, linearity and ruggedness.

Advanced software for HP 8453 systems includes tools that simplify the validation of an analytical method. An important basis for evaluating many of these variables are proper statistical tools. The advanced software includes full statistical evaluation of all results. The statistics include the ability to enter the standard deviation for the preparation of standards and the statistics obtained by the HP 8453 spectrophotometer on the measurement of each sample. Such measurement statistics are usually only available with a diode-array spectrophotometer. When *maximum likelihood* is selected these measurement statistics are used in the calibration routine to improve the fit.

Accuracy is the closeness of an individual test result to the true value.[5,6]

A measure of the accuracy of a method can be obtained using the Optimize Wavelength function of the advanced software. A typical sample is measured and quantified at all wavelengths over the measured wavelength range. The wavelength giving the most accurate results can be easily determined.

Precision is the degree of agreement among individual test results obtained by repeatedly applying the analytical method to multiple samplings of a homogeneous sample.[5,6]

The advanced software includes a test method that calculates the standard deviation of the results of a series of sample analyses. This is a direct measure of the precision of the method.

Sensitivity refers to the response obtained for a given amount of analyte.

Sensitivity is often denoted by two analytical factors called the *limit of detection* and the *limit of quantification*.[5,6]

Limit of detection is the lowest concentration of analyte that is detectable at the most sensitive instrument settings.

The detection limit is usually considered to be reached when the signal from the analyte is equal to three times the noise in the measurement. The advanced ChemStation software gives quantitative results with standard deviations that are based on the noise in the measurement. The detection limit is approximately three times the standard deviation.

Limit of quantification is the lowest concentration of analyte that can be determined with acceptable precision and accuracy.

Here it is necessary to define the acceptable limits of precision and accuracy, and this will depend on the objectives for the analysis. With the required precision and accuracy defined the tools described above can be used to determine the acceptable limits.

Linearity is the ability of the method to produce test results that are proportional, either directly or by a well-defined mathematical transformation, to the concentration of analyte in samples within a given range.[5,6]

For UV-Visible measurements the usual linear relationship is Beer's law. The advanced ChemStation software gives both graphical and statistical evaluation of the linearity of the calibration curve, see figure 2. The graphical display shows the calibration curve with 95 % confidence intervals. Statistical values include the percent error of each standard from the calculated relationship and the correlation coefficient and standard error of regression of the fit.

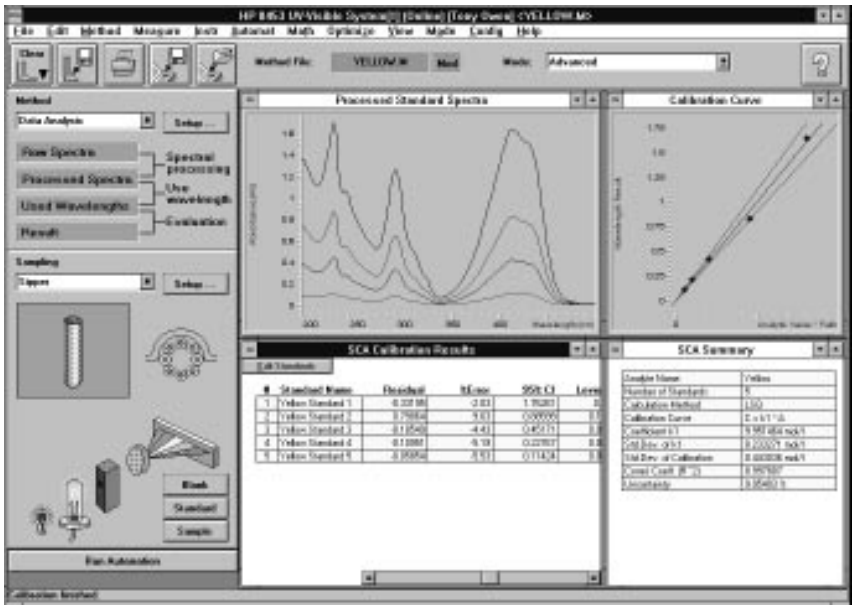

Figure 2
Calibration results

The Evaluate Standards function of the advanced software can be used to optimize linearity. This feature performs calibrations using the specified calibration parameters at all wavelengths available using all standards.

The quality of the calibration curve at each wavelength is indicated by the correlation coefficient, standard deviation of regression or *uncertainty* which, to give a quick overview, are plotted against wavelength. The best calibration is the one at the wavelengths where the chosen statistic gives the best value, see figure 3.

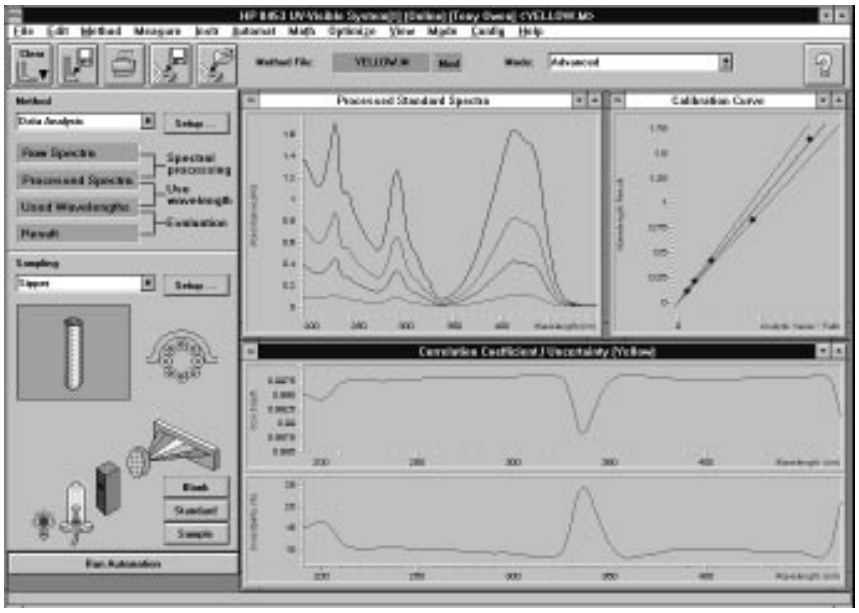

Figure 3
Results of the Evaluate Standards function of the advanced software

Range is the interval between the upper and lower levels of analyte (including these levels) that have been demonstrated to be determined with the required precision, accuracy and linearity.[5,6]

The range may be determined by analyzing samples containing varying concentrations of the analyte and using the tools described above to test whether the required levels of precision, accuracy and linearity are achieved.

Selectivity is the ability of a method to quantify accurately and specifically the analytes in the presence of other compounds.[5,6]

Other compounds could be synthesis precursors, known impurities, excipients, and degradation products, that may be expected to be present in the sample matrix and that also have a UV-Visible absorbance.

The advanced ChemStation software includes an Optimize Wavelength feature that is used to find the wavelengths giving the best sensitivity for the target analyte.

To use this feature the calibration standards are first measured and the proposed analytical parameters entered. Then the spectrum of a typical sample is measured and the Optimize Wavelength function of the advanced software quantifies the sample using calculated calibration coefficients at all available wavelengths and plots the results against wavelength, see figure 4.

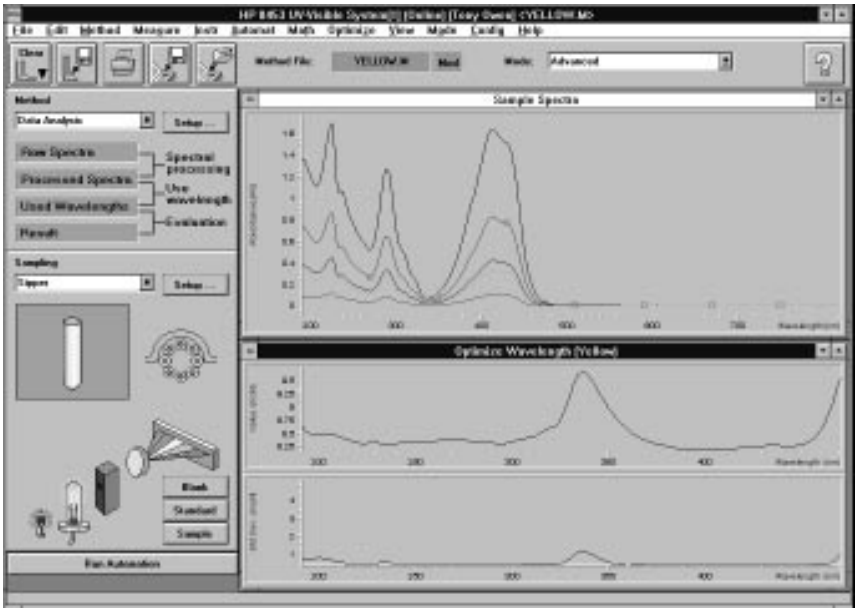

Figure 4
Results of the optimize wavelength function of the advanced software

When the concentration of the analyte in the sample has been determined by an alternative technique, the wavelength giving the best selectivity is the one with the result closest to the known value. When the concentration of the analyte is unknown, the wavelength giving the lowest concentration is usually the one that gives best selectivity (impurities always add absorbance causing erroneously high results).

Ruggedness is the degree of reproducibility of test results obtained by the analysis of the same samples under a variety of normal test conditions.[5,6]

The method should not be prone to interdiem or interlocum variations. The reproducibility of the method should be established under varied conditions, for example, different reagents batches or different assay temperatures. Testing for ruggedness involves interinstrument and interlaboratory measurements that are beyond the scope of a single instrument.

Documentation

A vital part of any validation process is proper documentation. Table 3 shows an example of the method documentation that is generated by the system. The report gives a complete overview of all parameters, data acquisition, data analysis and report for a specific method. Additional documentation is available if the method uses a calibration (see below).

Table 3
Method report

```
--------------------------------------------------------------------------------
                        *** Method Report ***

   Method file (modified)
      YELLOW.M
      Last update                 Date 02/03/95  Time 15:18:09
      Operator                    Tony Owen
      Product                     UV-Visible ChemStation, SI 17
      Number of Standards         5
--------------------------------------------------------------------------------
   Method Information:
      Default Method

   Method Checklist:

      Pre measure macro:          none
      Post measure macro:         none
      Store Spectra to File:      none
      Auto Analyze:               off
      Single Analysis

   Sampling System:               Sipper

      Pump Direction:             Clockwise
      Pump Time (sec):            20
       Wash Time (sec):           0
      Wait Time (sec):            3
      Sample Return (%):          0
      Air Segment (sec):          0

   Data Analysis:

      No Spectral Processing
      Use Wavelength(s):
         Single (nm):             414
      Evaluation:                 SCA
         Calibrated at:           Date 02/03/95  Time 15:18:07
         Operator:                Tony Owen
         Weighting Method:        Least squares
         Calibration Curve:       C = k1 * A

         Analyte Name             Unit
         Yellow                   mol/l

   Method Report Parameter:

      Information                 on
      Checklist                   on
      Instruments/Acquisition     on
      Data Analysis               on
      Report                      on
      Include Calibration Report  off

   Calibration Report Parameter:

      Standard Spectra            on
      Processed Standard Spectra  on
      Path Length Table           on
      Data Analysis Parameters    on
      Coefficients                on
      Used Wavelength Results     on
      Calibration Table(s) of Analytes on
      Curve                       on
      Residual Spectra            on
      Diagnostics                 on

   Result Report Parameter:

      Sample Information          off
      Sample Spectra              off
      Processed Sample Spectra    off
      Used Wavelength Results     off
      Evaluation Results          off
      Statistical Information     off
      Residual Spectra            off
      Confirmation Results        off
      Include Method Report       off
      All Sample Spectra overlaid on
      Summary                     on
      Evaluation Result Statistics on

--------------------------------------------------------------------------------
                        *** End Method Report ***
--------------------------------------------------------------------------------
```

System suitability

System suitability should not be confused with method validation. System suitability is designed to evaluate the components of the analytical system to show that the performance of the system meets the standards required by the method.[5,6]

Method validation is performed once at the end of method development, whereas system suitability tests are performed on a given system periodically to determine its adequacy or effectiveness. System suitability requirements for chromatography systems have been well defined,[6] but no similar definition exists yet for UV-Visible spectroscopy systems.

However, in practice, users have developed their own strategies for performing system suitability. For example:

A. Measure and calibrate using one standard with a concentration equal to 100 % of the expected component concentration. Then measure and quantify the standard and the standard diluted by a factor of 2. The results of both samples should be within a specified percentage of the known concentration. Remeasuring the standard demonstrates the quality of the initial measurement. This can be implemented automatically in the HP 8453 system by using the Automation function with a single standard and two control samples (standard and 50 % standard) and entering the acceptable error for the control samples. If a result for a control is outside the specified range it is automatically flagged in the results report.

B. Measure the standard and then a series of dilutions of the standard and calculate the extinction coefficient (absorbance/concentration) for each concentration. The values of the extinction coefficients should not vary by greater than a specified percentage. This can be implemented automatically in the HP 8453 system by using the Automation function with up to three standards. On calibrating the results of the calibration include the percent deviation of each standard from the calibration curve. This percent age error is identical to the deviation in the extinction coefficient of each standard.

Data quality

A properly-validated system and analytical method does not guarantee that valid results will always be generated in routine use. To achieve this the prescribed procedures must be followed exactly by the operator. The HP 8453 system provides features that help ensure this is done.

Global method file

A so-called *global method* defines the complete analysis. It is stored on disk as a single file. Loading the method from disk sets *all* parameters for data acquisition, data evaluation and calibration without operator interaction and thus eliminates the chance of error. For security, the software also includes two operation levels that are separated by a password. At the manager level, accessible only by the password, methods are developed, edited and stored. At the operator level, for routine testing, methods can be loaded and run. The parameters can be changed but any reports or any results generated by this method will include a *modified* flag. At the operator level methods cannot be saved so there is no chance of an operator changing a method and then resaving it under its original name. In addition, if any aspect of the current system is not compatible with the defined method, the system will block any attempt to make a measurement.

Maintenance	Replacing the Lamps Cleaning the Source Lens
Installation	Installing the HP 8453 UV-Visible System
Validation	Validating the HP 8453 Spectrophotometer Validating the General Purpose UV-Visible ChemStation Software Validating the Advanced ChemStation Software Validating the Biochemical Analysis Software
Operation	Measuring Sample Spectra Using Standard Cuvettes (manual mode) Measuring Sample Spectra Using the Sipper System

Table 4
HP 8453 system SOP templates supplied by Hewlett-Packard

Standard operating procedures

For those procedures and actions that cannot be controlled by the system, standard operating procedures (SOPs) should be provided. SOPs are documented instructions that should be followed by the operator for a process to be considered valid. SOP templates are provided in electronic format with the documentation are shipped with the HP 8453 system. They can be modified according to the users specific needs and the printed. They can be divided into three types (as shown in table 4):

- for maintenance of the HP 8453 spectrophotometer,
- for validation of the HP 8453 system, and
- for proper operation.

Error checks

Despite the above, errors can still occur, so wherever possible, it is advantageous to build in the system checks on the quality of the results as they are being generated. Such tests can flag values that may be erroneous for any of the following reasons:

- the wrong sample may have been measured,
- the sample may have been contaminated, or
- measurements that may have been made outside the linear range of the instrument.

An important part of the HP 8453 system are those features that are inherent to the system or which may be added to the method to ensure the quality of data obtained.

No measurement without blank—The HP 8453 spectrophotometer will not make a sample measurement if a blank measurement has not been made previously. Whereas this should be obvious, some spectrophotometers from other vendors will permit such meaningless measurements.

Voiding of erroneous data—The HP 8453 spectrophotometer can measure a spectrum in 0.1 second but typically longer *integration times* of 0.5 or 1 second are used. This period is used to average several spectral measurements to improve the signal-to-noise ratio. In addition the standard deviations of the measurements are calculated. If there has been a problem which caused the measurement to vary during the integration time the standard deviation will be high, for example, a bubble passes through the light beam as the measurement was made. Valid samples should have no significant variation of absorbance during the integration time. The HP 8453 spectrophotometer records as null-and-void any measurement that shows a high standard deviation, automatically eliminating erroneous measurements at source.

Statistics—The HP 8453 system has extensive statistical evaluation tools built in all stages of data processing from acquisition, through calibration to evaluation. These statistical values are important quality tools, indicating the precision of the measurements being made, and are shown in Table 5.

General Purpose UV-Visible ChemStation	Advanced UV-Visible ChemStation
	Standard deviation of each measurement. Specification of calibration standards' standard deviation, as required for a proper statistical evaluation of the calibration (may be estimated from, for example, the precision of the balance used for weighing and the precision of the volumetric flasks used for dissolution of the standard).
Single component calibration: standard deviation of calibration, correlation coefficient, percent error of each standard from calibration curve.	Single component calibration: standard deviation of calibration, correlation coefficient, uncertainty, percent error of each standard from calibration curve, leverage, Cook's Distance. Single component quantification results, with 95 % prediction interval. Multicomponent analysis results, with 95 % prediction interval relative fit error (describes the quality of the fit of the standards to the measurement spectrum, and indicates incorrect sample identity or sample contamination.

Table 5
Quality statistics featured in HP 8453 systems

Confirmation analysis—The HP 8453 system can evaluate a sample with up to four independent data analysis processes simultaneously. An important application of this capability is confirmation analysis. This technique uses additional wavelengths to *cross-check* the result at the analytical wavelength.

Confirmation analysis can detect for correct identity of the sample, contamination of the sample, decomposition of the sample, and measurement outside the linear dynamic range of the spectrophotometer. Samples not satisfying the requirements of the confirmation analysis are automatically *flagged* as shown in figure 5.

Instrument logbook

The HP 8453 spectrophotometer has an internal logbook. This contains the results of all self-tests and any errors reported by the instrument. There is also access by the user to the logbook to allow noting of instrument verification and of any repairs performed on the instrument.

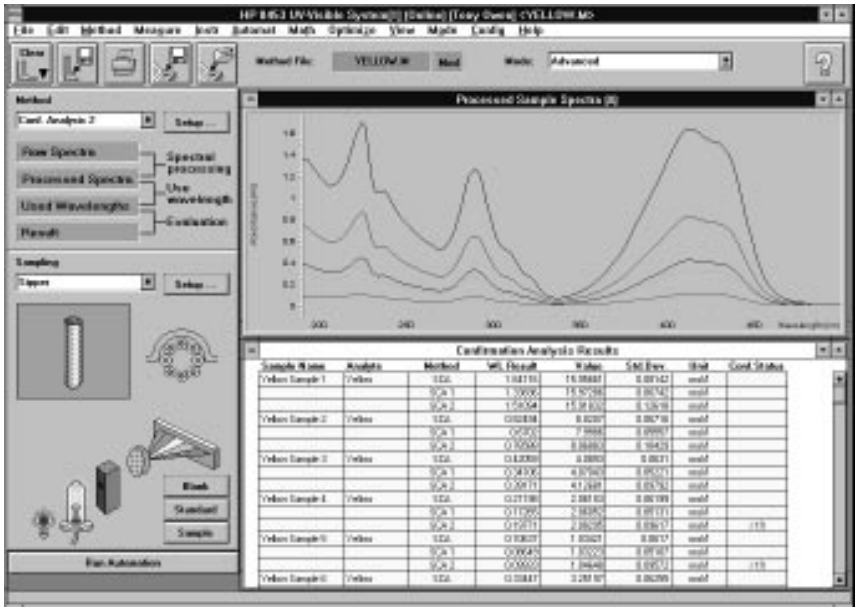

Figure 5
Confirmation analysis results (with a limit of 1 %)

Data integrity

System security

Access to the HP 8453 system is controlled at a number of levels:

- at network level,
- at computer level, and
- at software level.

When the HP 8453 system is connected to other laboratory equipment using one of HPs Unified Lab networking products, security systems ensure that unauthorized users do not have access. The HP Vectra family of PCs and the PCs shipped as ChemStation hardware with the HP 8453 systems have password capability. The operator can set a password in permanent read-only memory that will be requested at boot-up every time the PC is switched on, preventing unauthorized access by people with a flexible disk based operating system.

The HP 8453 system also carries a password which allows access to the software features at two levels, manager and operator.

Documentation

The process of generating raw data is fully documented both electronically on disk and on paper. Each HP 8453 spectrophotometer has a serial number and firmware revision number in firmware. This data is automatically read by the software each time the system is started and positively identifies the instrument with which measurements were made. Key information such as operator name, time, date, spectrophotometer serial number, and any other available information (for example, temperature if a Peltier temperature controller is connected) is automatically appended to each measured spectrum and to results files. This information can be displayed on the screen but cannot be edited.

As part of the method you can specify that all data should be automatically stored as it is acquired to ensure traceability of the results. Raw data is stored with all the annotation information described above. In addition, even if only one wavelength is used for the analysis, full spectral acquisition and storage can be specified so that all sample information is available for review.

Laboratory records can be supplemented with hard copy listings of methods, calibration and results, or a combination depending on specific requirements. These reports include all GLP-relevant data such as operator name, time, date, and spectrophotometer serial number. Reports are clearly labeled with page number and total number of pages, and a date and time stamp to prove completeness and integrity–particularly important when reports are to be submitted as raw data.

Data storage

With the correct encoding and archiving practices, measurement data can be stored safely and for long periods of time. All of the HP 8453 system data and method files are stored in binary format. These files cannot be edited using spreadsheet or word processing packages. WORM (Write Once Read Many) optical disk drives are available for the PCs from third parties for highest data integrity, because the data cannot be overwritten.

Glossary

HP 8453 system	A UV-Visible spectroscopy system comprising an HP 8453 spectrophotometer, HP UV-Visible ChemStation software, an HP Vectra PC with MS-DOS and Microsoft Windows or Windows for Workgroups operating system, and an HP printer.
ANSI/IEEE	American National Standards Institute/Institute of Electrical and Electronic Engineers.
application software	A program adapted or tailored to the specific requirements of the user for the purpose of data manipulation, data archiving, or process control.
audit tracking	A procedural formality built into operation of a system that ensures all interactions with the system are first authorized, before being carried out, and then recorded permanently in an operations log.
cGMP	Current good manufacturing practice.
change control	A procedural formality required for validation, defining how and when changes may be made, and in which situations revalidation is required.
correlation coefficient	A dimensionless value measuring the degree of association between two variables. A value of -1 indicates a perfect negative linear relationship, +1 indicates a perfect positive relationship.
ChemStation	A Hewlett-Packard name for an analytical workstation comprising a computer and software.
declaration of system validation	A Hewlett-Packard certificate testifying that the UV-Visible ChemStation software has been validated during its development and according to the Hewlett-Packard Analytical Products Life Cycle.
EPA	Environmental Protection Agency of the United States Government.
FDA	Food and Drug Administration of the United States Government.
GMP	Good manufacturing practice.
OECD	Organization for Economic Cooperation and Development.
PMA	United States Pharmaceutical Manufacturers Association, an organization whose members are employees of some of America's largest pharmaceutical companies.
quality assurance	A set of activities, often performed by employees in a similarly named department, that check the characteristics or qualities of a product actually exist at the time the product is sold.
revalidation	The repetition of validation necessary after the process has been changed significantly, for example, when a manual system is upgrade to an automated system.
ruggedness	An indication of how resistant the process is to typical variations in operation, such as those to be expected when using different analysts, different instruments, and different lots of reagents. Required under GLP guidelines.
standard error of regression	A measure of the fit of the data to the calibration curve. A value of 0 indicates a perfect fit.
standard operating procedures	Documented instructions that should be followed when operating a process for it to be considered valid. Required under GLP guidelines.
system suitability testing	The process of checking the performance of a system for a particular analysis.

uncertainty	An indication of the fit of the standard with the highest value to the line of best fit. Expressed in percent deviation.
USP	United States Pharmacopoeia. A non-governmental, non-profit, organization comprising volunteer scientists. It publishes the U.S. Pharmacopoeia and the National Formulary (USP-NF) containing the official, legally-recognized standards for pharmaceutical manufacture.
validation	A procedural formality requiring an operator of a process to: (a) define what is to be done, (b) to test that what has been defined can indeed be done, (c) to perform the operation as defined, and (d) keep records of everything as it actually happened, (e) for as long as the operator uses the defined process. Required under GLP guidelines.
verification	A step in a validation process where tests check that the performance specifications can be met, either of a sub-part of the process or the whole.

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Printed in Germany 02/95 on paper stock bleached without chlorine.

Publication Number 12-5963-5615E