

Software for the Gravimetric Calibration Testing of Pipettes

The accuracy and precision of pipettes used in production and research laboratories are key components in validating results and following quality control procedures.

Information on how automatic pipettes, diluters and manual action pipettes dispense both reproducible and accurate sample sizes is often required for review purposes by regulatory agencies such as the FDA, and also internal quality control standards. In-house performance monitoring programs have become very popular as an alternative to the costly practice of sending pipettes out for regular testing.

Computers have become a popular alternative to tracking and validating pipette performance manually. In this paper, popular computer solutions are explored focusing on Pipette Tracker, an off-the-shelf software product.

Manual Pipette Calibration Testing

Performance monitoring programs for pipettes require proper test protocol standards be put in place by a program administrator to meet the particular requirements of that facility or laboratory. Systems are required to file calibration test results for future reference. In addition, a system for maintaining an effective scheduling

program for testing pipettes at a regular time interval is necessary.

Manual gravimetric pipette calibration testing generally involves having each pipette transfer between 4 and 30 samples of distilled water to a balance. Sample weights are recorded on paper, and the balance is then tared for the next sample. This process continues until all sample weights have been recorded. Afterward, the operator manually converts the sample weights to volumes and then calculates the mean, standard deviation, co-efficient of variation and inaccuracy for these volumes. Finally, the operator determines if the pipette has passed or failed the test by comparing the statistical criteria determined by the facility protocol standards, and a calibration test report is prepared and filed. Calibration test reports include the date, time, operator and test result for the pipette.

Computer Solutions

Computers offer a unique opportunity to significantly automate pipette validation procedures. Until recently, the most common computer solution was the spreadsheet-based system in which individually saved spreadsheet files represent individual pipet test results. Gravimetric data from calibration tests are entered into the spreadsheet template, which

automatically calculates statistical results and quickly generates calibration test results.

Unfortunately, spreadsheets tend to offer poor pipette test scheduling capabilities and are often difficult to work with when retrieving information on a particular pipette or group of pipettes. Spreadsheets offer little in terms of organizing the information for a large number of pipettes, and reporting capabilities tend to be inflexible.

Another solution to automating pipette validation testing and tracking is the custom database system. Database architecture offers significant organizational advantages over spreadsheet solutions. Database systems offer users a system, which associates each individual pipette to a single electronic record, creating a robust historical archiving system for individual pipette test data. This usually eliminates the requirement for paper records to be stored or filed. Database systems can also offer more flexible reporting capabilities than spreadsheets, depending on the level of sophistication built into the database application.

Unfortunately, custom database solutions are almost always far more costly to produce and set up than

spreadsheet alternatives. Database systems tend to be less flexible than spreadsheet platforms with respect to the automation of calculations, and database interfaces are generally far more cumbersome to work with than spreadsheet interfaces. Unless custom database interfaces are programmed, ease of use may be a significant consideration. Well-constructed database systems with user-friendly interfaces generally require professional programmers experienced in database programming. Depending on the sophistication of the validation tracking system required, the time and expense to construct an in-house, custom-programmed database solution may be prohibitive.

Until recently, there were no turn-key, off-the-shelf solutions that took advantage of both the spreadsheet's ability to perform calculations and the robust organizational reporting capabilities of the database environment.

A Database Solution

Pipette Tracker software offers users an off-the-shelf, custom-built database interface that is designed for use in the Microsoft® Windows® operating system. It is specifically designed for the gravimetric validation testing and tracking of pipettes. With flexibility in configuration a major design consideration, the software can be installed, customized, and working in just a few hours.

During program set up, each individual pipette is entered into the database. Information including the serial number, manufacturer, pipette type and pipette location is

permanently recorded at this time. Pipettes are recorded as multiple-channel or single-channel devices with variable- or fixed- volume capability. Information about the pipette's acceptable error and reproducibility parameters as well as test frequency intervals for pipette test scheduling is also recorded.

The software also tracks how each pipette is to be evaluated during validation testing by prompting the user to supply the appropriate test protocol method during database entry. This protocol method could be one supplied with the software or one custom-designed by the user, allowing users to configure standardized testing procedures directly into the software. The database supplies the software's calibration run screen (Figure 1) with this information at the time of testing, saving users from having to determine

the appropriate testing protocol required for individual pipettes during testing.

Once the pipettes are entered into the database, keeping paper records or spreadsheet printouts of results is no longer necessary because all of the information about the pipettes can be accessed electronically at any time. Results from a particular performance test can be referred to at any time from the database and the results viewed or printed. The database files, kept separately from the main program, can be regularly backed up to ensure system integrity, and filing cabinets can be replaced with a few computer diskettes.

Another advantage of the software's database interface is its worklist screen (Figure 2), which serves to automatically schedule validation

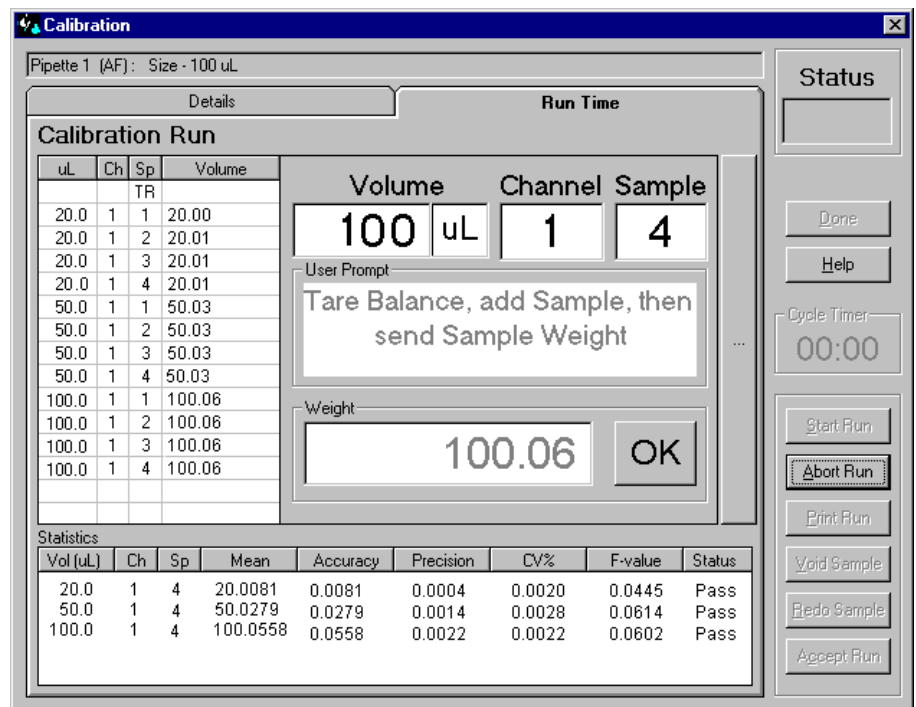


Figure 1: Pipette Tracker's Calibration Run screen, indicating a successful calibration test.

Due Date	Pipette ID	Description	Status	Location	Contact	Method
01/01/01	ABC-100	100 uL Adjustable	Due	Laboratory 101	Technician 3	METHOD 06
01/01/01	ABC-5 ML	5 mL Adjustable	Due	Laboratory 101	Technician 3	METHOD 04
01/01/01	ABC-5 ML	5 mL Adjustable	Due	Laboratory 101	Technician 3	METHOD 05
01/01/01	ABC-5 ML	5 mL Adjustable	Due	Laboratory 101	Technician 3	METHOD 06
01/01/01	QA-50	50 uL Adjustable	Due	Laboratory 101	Technician 3	METHOD 04
01/01/01	QA-50	50 uL Adjustable	Due	Laboratory 101	Technician 3	METHOD 05
01/01/01	QA-50	50 uL Adjustable	Due	Laboratory 101	Technician 3	METHOD 06
01/01/01	QA-10	10 uL Fixed	Due	Laboratory 101	Technician 3	METHOD 02
01/01/01	QA-10	10 uL Fixed	Due	Laboratory 101	Technician 3	METHOD 03

Figure 2: Pipette Tracker's Worklist screen, indicating pipettes due for calibration.

testing for all pipettes in the database. No longer do users have to keep track of the last time pipettes or groups of pipettes were tested. As mentioned earlier, the software requests a frequency interval as new pipettes are added to the database. This interval is then used by the worklist system to check each pipette record against the current date and determine if testing is due. If a pipette is due to be tested, it appears on the worklist screen for easy reference. In addition, the software can be preset to display pipette on the worklist screen days ahead of the scheduled test date so a user can arrange to have the pipette available for validation testing at the appropriate time.

This package also offers a robust reporting system to generate hard-copy reports, allowing users to quickly retrieve information about pipettes or other database information. In addition to the obvious calibration test reports,

several other reports are also available. These include worklist reports and pipette historical data reports, outlining summaries of all the calibration test results for an individual pipette. Complete pipette inventory reports as well as calibration protocol reports are also available. All these reports can be easily queried from the database whenever required.

The software also includes a filter feature, allowing users to customize their report for a specific group of pipettes that may be of interest. This can be helpful if pipette information from a particular location or customer needs to be gathered separately from the rest of the records in the database. In this way, databases containing large numbers of pipettes can be organized and subdivided for reporting in anyway that is convenient for the user. Complicated filing systems are no longer necessary.

Automating Pipette Calibration Testing

The manual validation testing of large numbers of pipettes can be a very time-consuming and tedious task. With computer automation, significant time can be saved and results can be generated more quickly and more accurately. The software has several built-in features designed to automate pipette validation testing.

To automate the manual recording of sample weights from the balance, the software supports an RS232-compatible balance interface, allowing balance results to be sent directly to the program's calibration run screen (Figure 1) during validation testing. Balance results no longer need to be written down and entered into the computer at another time. Transcription errors can be eliminated. For users who do not have RS232-compatible balances, the software also supports a direct keyboard entry system. When an RS232 balance becomes available, the user can quickly switch to the automated balance interface without having to alter the existing database in any way.

During validation testing, the software automatically takes into account environmental variables that are often responsible for adversely effecting gravimetric test results. This is particularly true when validation testing is performed in uncontrolled environmental conditions, especially with smaller-volume pipettes. Environmental factors including temperature, barometric pressure, and relative humidity are immediately factored into mass-to-volume calculations from the calibration run

screen of the software. These calculations take place as each sample result arrives at the computer from the balance, allowing the user to receive continuous feedback during the calibration run about the performance of both the pipette and the sample transfer technique.

After each validation run is completed, the software automatically calculates all statistical results for the pipette. The associated mean, standard deviation, co-efficient of variation (CV%) and the inaccuracy are calculated for the pipette and displayed for the user on the monitor. These results become permanently recorded in the database once they are accepted by the user. In addition, pipette results are immediately evaluated and issued a pass or fail tag. This pass or fail tag is determined by comparing the pipette's CV% and inaccuracy results to the accepted range recorded in the pipette's database record for these values. Statistical results outside those of the recorded acceptable range generate a fail tag and those within the acceptable range generate a pass tag for the pipette validation test run. Users have the option of setting any range desired for these parameters during device setup, including those supplied by the manufacturer of the pipette.

The software offers users the opportunity to quickly determine whether a pipette is performing within acceptable parameters or needs to be

sent out for cleaning and repair. The resulting time savings and increased testing throughput make the software a viable alternative to manual testing procedures.

Software Validation Issues

As mentioned earlier, the software has been developed to assist users in meeting ISO 9000 and GLP requirements, as well as complying with internal standard operating procedures (SOPs). The calibration protocol methods included with the software were designed to follow the procedures recognized by the National Committee for Clinical Laboratory Standards (NCCLS) in its document, Proposed Guidelines for Determining Performance of Volumetric Equipment. If custom validation testing protocols are required, protocols appropriate to the users internal SOPs can be configured and saved as an individual protocol file. This offers users the flexibility to immediately conform to any SOPs.

The software also supports security and audit trail features to protect valuable database records and internal software settings from tampering. The program can be configured so that a system administrator controls all access to the software, assigning passwords and appropriate access levels to users for the various areas of the program. If, for example, calibration testers should not edit testing protocols or add new devices to the database, their access level can

be adjusted appropriately. When something is changed in the software, the program's audit feature logs this change, including the user who made the change as well as the time and date the change was made to the system. For users who are involved in ISO 9000 accreditation, a software validation tool kit document is available to assist users in their internal software verification of the software. The software can be seen as a strong tool for those who require a reliable and intuitive quality assurance system for pipette performance monitoring.

Summary

Pipette Tracker software offers a complete off-the-self database solution for the tedious and time-consuming task of pipette performance monitoring. The custom database interface offered by the software deals well with concerns and difficulties often associated with database solutions, offering easy installation and system setup as well as a powerful platform to automate pipette testing and associated calculations.

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References
1. NCCLS proposed guideline. Determining Performance of Volumetric Equipment. Vol 4(6). Order code 18-p ISSN 0273-3099. Figure 1: PipetteTracker's calibration run screen, indicating a successful calibration test. Figure 2: Pipette Tracker's worklist screen, indicating pipets due for calibration.