

# Outsourcing Solution Preparations

by Edwin Neas

According to Ref. 1, "Outsourcing lets companies save critical resources and spend more time on core competencies...they have used outsourcing to grow market value by billions while decreasing their book values. The key factors that lead companies to outsource work are the search for efficiencies, extending work capacity, consolidation of their resources, and consistency in their production.<sup>1</sup> This policy should apply to all departments within a company since all of the above-mentioned benefits lead to the final goal of a quality finished product. Quality control and other laboratories spend up to 30% of their day preparing solutions for subsequent analysis of their incoming product test samples. For those laboratories that are regulated, their test procedures (e.g., HPLC analysis) are required to perform system suitability.

The USP states: "System suitability tests are used to verify that tests are based upon the concept that the equipment, electronics, analytical operations, and samples to be analyzed constitute an integral system that can be evaluated as such."<sup>2</sup> The solutions used with these systems are part of the analytical operations of the system suitability. If a system suitability failure occurs as a result of a solution mispreparation, there will be work capacity losses beyond the initial preparation time to an entire lost day of sample testing. This loss of time is due to investigation of the failure and retesting system suitability, which is inherently inefficient. This not only increases the stress level of the analyst and his/her manager, but also adds costs associated with reagent disposal and new solution preparation. In addition, there is the subsequent cost of delaying the release of product to customers, thus reducing productivity within the corporation. These costs can become significant and are avoidable.

A review of the steps involved in the preparation of a mobile phase reveals the continuous opportunity for daily inconsistencies or mistakes. These include the following:

- Setup time (finding chemicals, glassware, records, and so on)
- Glassware rinse before mixing (e.g., methanol rinse)
- Balance calibration and weighing of salts
- Mixing time
- Calibrating pH meter and adjusting pH of buffer
- Filtering and degassing of reagents
- Replacing chemicals and general cleanup
- Documentation.

The preparation time required for an average mobile phase is about 90 min; when the cost of raw materials is included, this amounts to approx. \$133 per preparation. Other variables involved in the preparation of mobile phases may include contaminated reagents, pH probe contamination, contaminated filtration, and degassing equipment. Problems in these areas can lead to baseline noise and negative or unexpected peaks, which result in system suitability failure.<sup>3</sup> In addition, analyst variability in mobile phase preparation can result in considerable inconsistency in resolution and elution times. This is illustrated in *Figure 1*, which demonstrates the difference in elution time and chromatographic resolution when an adjustment of 0.5% is made in acetonitrile concentration to the USP mobile phase used for Penicillin G standard separation. *Figure 2* demonstrates the difference in elution time and chromatographic resolution when the pH of the mobile phase used for Penicillin G standard

separation is adjusted by more than 0.1 pH units.

Outsourcing of premixed testing solutions, e.g., mobile phases and tablet dissolution media, will allow QC and other laboratories to recover >20% of their day for their core analysis work. Outsourcing can eliminate reworks and nonconformance investigations due to solution mispreparation, avoid costly delays on shipment of finished product to market, diminish daily inconsistencies, and reduce costly waste disposal. However, prepackaging mobile phases and other solutions in large batches for use in the laboratory over long periods of time requires a packaging system that will maintain the solutions' integrity.

An example of such a system is the CHEM+NECT (Chata Biosystems, Fort Collins, CO), a virtually unbreakable and gas-impermeable packaging system that provides quick connect capabilities for attachment to a wide variety of instruments. The packaged chemistry is maintained in a closed system, eliminating exposure of the chemical mixture to outside contaminants and vapor losses. Once empty, the lightweight package is easily disposed of in the appropriate trash vessel. The mixed chemical solutions are prepared in compliance with GMP practices and dispensed into the packaging within a cleanroom environment. Each production batch is guided by a 13-page batch record with complete raw material traceabilities and double sign-offs on all critical steps. The batch record includes a formula sheet sign-off by the end user. A Certificate of Analysis is sent to the end user confirming a quality manufacturing environment, procedures, and the results of any QC testing ordered.

The most obvious drawbacks to the use of heavy, hard-walled containers such as glass and metal is the high cost of shipping, handling, and recycling, along with the subsequent safe and efficient use and disposal of these types of containers. In addition, dispensing a solution from sealed, hard-walled containers is not possible without the introduction of a gas (typically air) to prevent vacuum from stopping flow. Therefore, dispensing from hard-walled containers requires air exposure to the solution inside the vessel. The introduction of unfiltered air can lead to microbial contamination of the chemistry solution. If the solution is filtered under vacuum to achieve sterility after dispensing, destabilization and/or evaporation of some of the components can occur, thereby altering the resultant chemical solution.

The CHEM+NECT system, combined with the quality production of custom mobile phases and other chemical solutions in a Class 10,000 cleanroom, provides long-term stability of these chemistries. This allows end users to purchase large batches of their custom chemistry for month-to-month and site-to-site consistency

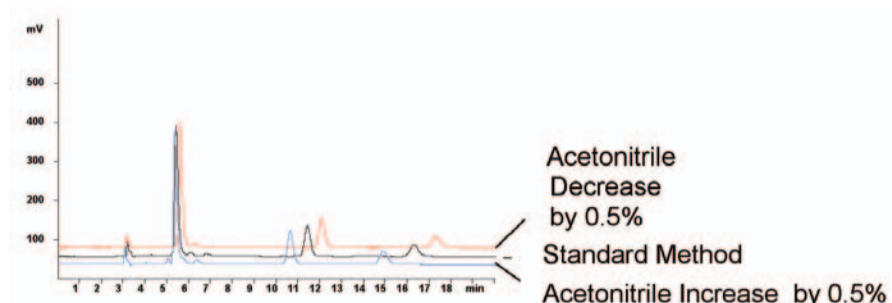


Figure 1 Effect of organic percentage on separations.

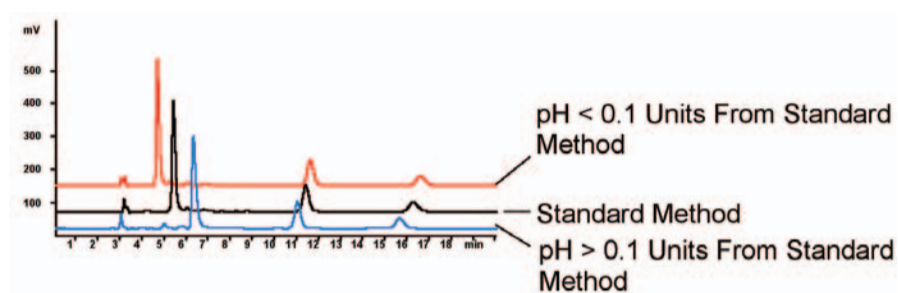


Figure 2 Effect of pH on separations.

and removal of system suitability errors due to mispreparation of the solution. The system enables daily consistency, which is imperative to achieving optimum assay performance and harmonization both within and between laboratories that share common reagents. This promotes method transfers and assays that run on multiple instruments. When investigations are being done on multiple instruments (or across laboratories/sites), it is easy to assess the reagent suitability by a quick comparison of chromatography across instruments, permitting users to focus investigation resources elsewhere.

Outsourcing laboratory reagents effectively increases analyst working time, eliminates errors due to reagent mispreparation, and provides at least one consistent variable on all instruments in use. Combined, these factors typically result in an average savings of \$30,000 annually per reagent. In addition, the reduction of down time in the laboratory leads to faster delivery of the company's product to market. The manufacturer of CHEM+NECT provides prepared mobile phases, dissolution media, heavy metal testing stations, and other chemicals to more than 70 pharmaceutical companies. By outsourcing, a major medical device manufacturer recently captured 70% of its market before its competition could launch a similar product. These results were achieved while simultaneously decreasing labor costs and increasing consistency. The company attributed its success to the CHEM+NECT system.

## References

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