



# Analytical Digest

WEST COAST ANALYTICAL SERVICE INC

The Quarterly Newsletter on Professional Analytical Chemistry

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Chemistry

Leachables

## Calendar

Nov 6-10

AAPS Biotechnology  
Conference  
and Exhibition  
Nashville, TN

## Quick Quotes

"Reason, Observation,  
and Experience -  
the Holy Trinity  
of Science."

- Robert G. Ingersoll

It is necessary  
to relax your muscles  
when you can.  
Relaxing your brain  
is fatal.

- Stirling Moss,  
Race car driver

## Wet Chemistry

In this issue we would like to present an overview of the Wet Chemistry Department at WCAS. Our regular readers have been introduced to several of our specific analyses and instruments in previous newsletters, and we continue to acquire new equipment and expand our instrumentation capabilities. As increasingly more areas of analysis are converted to automation; however, the area of general chemistry is often perceived as the last bastion of "real chemistry", and its importance is frequently overlooked.

The wet chemistry lab performs testing on a wide variety of matrices, with an emphasis on environmental, pharmaceutical, nutraceutical, and food samples. Approximately 25% of our work consists of analyses done on environmental samples such as oil, drinking water, wastewater, and soil. Analyses are conducted according to approved methods such as those found in Standard Methods for the examination of Water and Wastewater.

Most of our remaining work is testing of pharmaceutical drug products and excipients, and food components. Because these materials are regulated by the Food and Drug Administration (FDA), analyses must be conducted in strict accordance with current Good Manufacturing Practices (cGMP) and the appropriate published methods,

usually the USP/NF, EP, JP, or FCC. In contrast to the average pharmaceutical company that produces a limited product line and, therefore, uses and tests a limited quantity of raw materials, the wet chemistry lab has to date conducted partial or full testing of approximately 300 USP/NF monograph materials, 50 EP monograph materials, 40 from the FCC, and several from the JP, and has the capability of testing many more. We pride ourselves in performing some of the more-involved tests such as hydroxypropoxy groups, Xanthan Gum (alginates assay), and sulfur dioxide (maltodextrin). Because of the diversity in compendial test methods, it is often necessary for us to acquire specific reagents or reference standards in order to conduct a specific analysis. Despite the current trend toward harmonization, many monographs from multiple compendia require different reagents for the same test. It is particularly time-consuming to import reference standards specified in the foreign compendia. For this reason, we advise our clients to call our Client Services Department if possible before sending a new material for analysis. In this way we can determine if any materials are required for analysis beforehand, and provide a more accurate turnaround time. *see Wet Chemistry* ►



Autopol V polarimeter

## Lab Notebook

We have ordered our second LCMS! We should have another **Varian 1200L LC-MS/MS** delivered by the end of September. This will greatly increase our capacity, and also has a GC interface to enable us to perform GC-MS/MS analyses, along with chemical ionization GC-MS. We hope to have the system installed and qualified by the end of October.

**Sample size** is very important to the testing requirements normally found in the USP/NF/EP. We ask that you send at least twice the amount specified in the monograph so that we can perform Quality Control along with your samples.

Also as many of you already know, **sample containers** can contaminate your samples. If you are testing for organics you

may not want to use plastic, but if you are testing for inorganics you may not want to use glass. Always match the sample container with your testing needs, sample matrix, and shipping requirements. If you have any questions concerning the amount of sample to send or the type of samples containers to use, please feel free to call either Eric Lindsay (ext. 300) or Louis Albanese (ext. 303).

## Leachables

Leachables and extractables are receiving a great deal of attention in the pharmaceutical and supplement industries. Leachables are defined as substances that will leach out of a container/closure system when exposed to the drug product vehicle under typical storage conditions. These are compounds which could be expected to be present in formulations under "real-world" conditions. Extractables are substances that can be extracted out of containers under extreme conditions, such as extraction with organic solvent at elevated temperature. This is important in order to determine which compounds should be monitored in a leachables study.

Generally, compounds of interest include plasticizers, UV inhibitors, pigments, polymerization initiators, residual monomers, etc. One source of leachable that is not always considered is the adhesive from labels. These compounds can migrate through plastic containers into solutions, especially on prolonged storage.

One compound receiving a lot of attention is di(ethylhexyl)phthalate (DEHP), a commonly used plasticizer in flexible PVC products and suspected human carcinogen. DEHP is known to leach into fluids from PVC-based IV tubing, especially if the fluid contains high concentrations of organics, such as fat emulsions in TPN mixtures. Other, presumably less toxic plasticizers are being introduced to replace DEHP in these applications.

Generic testing of leachables is covered by USP Chapters <381> (elastomeric closures) and <661> (containers). However, more specific testing is sometimes required, involving determining extractable compounds, followed by monitoring for those compounds as leachables. If you have any questions about designing a leachable/extractable study, feel free to contact us. ■

## The Analytical Digest

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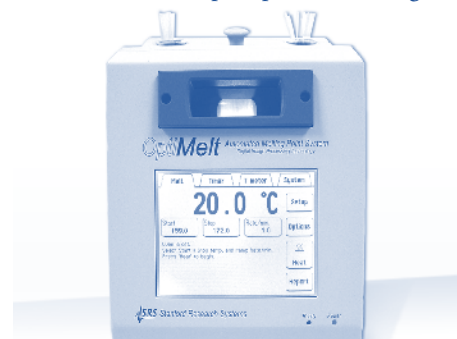
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## Wet Chemistry

► *continued*

Lest our readers think that wet chemistry is an archaic technique, our department is currently using several automated methods that help eliminate the potential analyst subjectivity inherent in many of our methods. Our potentiometric titrations are performed by autotitrator. We have recently acquired two new instruments that permit us to offer analyses done in accordance with compendial requirements as well as testing under various alternate conditions. The first of these is a Rudolph Autopol V polarimeter that uses a xenon lamp so that optical rotation measurements at multiple wavelengths can be performed. Temperature is closely controlled by heating or cooling the sample to a specified temperature using a peltier tray. The temperature set point can be specified allowing both the accurately controlled temperature required by regulated analysis, or less accurately controlled rapid analyses often preferred for preliminary R&D studies. Instrument performance can be verified as required with a NIST-traceable quartz cell or with other standard solutions. Our latest acquisition is a Stanford Research Systems MPA 100 automated melting point system. This instrument uses the heating block capillary method specified for most compen-

dial materials. Determinations can be done manually if desired by viewing the capillaries through a glass window and recording the onset and completion of a melt. Additionally, a digital camera records the sample throughout the melt, and by measurement of sample transmission and application of digital image processing, reports the onset, meniscus point, and liquefaction point. Temperature ramp rates from 0.1°C/min. to 20°C/min. in 0.1°C/min. increments can be programmed, permitting analysis under compendial requirements, as well as rapid temperature rise analysis such as might be required for samples of unknown melting point, samples that melt with decomposition, or those that decompose prior to melting. ■



MPA 100 melting point system