3rd Quarter, 2001 • Vol. 9, No. 3 • Circulation: 6,432 • Editor: Eric W. Lindsay

The WCAS Analytical Digest

WEST COAST ANALYTICAL SERVICE, INC.

wcas.com

Assay Versus ID

Generally when one is testing raw materials, there are tests for both identification (ID) and assay. The two tests are usually quite different, and usually you need both. Most raw materials have specifications and test methods.

A raw material used in pharmaceuticals must meet the specifications given in the USP/NF (US Pharmacopeia/National Formulary) using the test methods specified in the monograph for that raw material, so that the material can be sold as USP grade. Other industries have specifications and test methods such as ACS (American Chemical Society) for general chemicals, Food Chemical Codex (FCC) for the food grade chemicals, etc.. For materials not listed in any such collection of specifications (compendia), suppliers may have their own specifications and test methods.

An ID test can be something elaborate such as matching chromatographic retention times of a standard or matching a infrared spectrum. It can also be very simple such as a flame test. The results from the ID test generally say nothing about the concentration of chemical, especially for the more simple tests. For example, to identify sodium acetate, one confirms the presence of sodium through a flame test (the flame burns yellow) and a couple of positive and negative precipitate tests. The test does not indicate the presence or absence of other chemicals or the concentration of sodium.

An assay method, on the other hand is intended to measure the concentration of the chemical, assuming the major ingredient has been identified. Assay specifications are usually very tight such as 99.0-101.0%. This usually requires a very accurate and precise analytical method such as a titration, a colorimetric or gravimetric assay. Chromatographic

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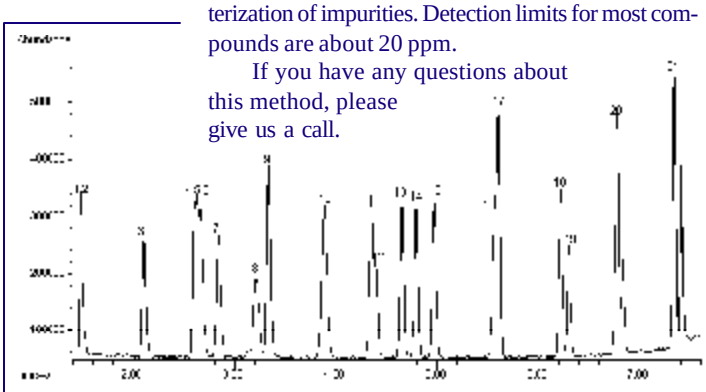
Residual Solvents Method by GCMS

For established pharmaceuticals and raw materials, residual solvents are usually determined using USP <467>, Organic Volatile Impurities. This determines four solvents: methylene chloride, chloroform, trichloroethylene and 1,4-dioxane. However, during the drug development process, many other potential solvents may be used in the synthesis and purification of drug substances.

Measuring these other solvents can be accomplished using GCMS. GCMS has advantages over other GC techniques, in that solvents may be positively identified, and complete chromatographic resolution usually isn't necessary for identification or quantitation.

WCAS has developed a method that routinely determines 19 different solvents. Other compounds may be added, but the usual 19 cover most commonly used solvents, including the four required by <467>. The analysis can also screen for unknown volatiles. This method, although based on <467> Method I, does not replace it. It is intended to be used in the drug development process for characterization of impurities. Detection limits for most compounds are about 20 ppm.

If you have any questions about this method, please give us a call.



Peak Assignments for the above

1. Methanol-d3 (IS)
2. Methanol
3. Ethanol
4. Acetonitrile
5. Acetone
6. Isopropanol
7. Ethyl ether
8. Freon-113
9. Methylene chloride
10. Methyl tert-butyl ether
11. Methyl ethyl ketone
12. Hexane
13. Ethyl acetate
14. Chloroform
15. Tetrahydrofuran
16. Benzene-d6 (IS)
17. Benzene
18. Trichloroethylene
19. 1,4-Dioxane
20. Methyl isobutyl ketone
21. Toluene

Quick Quotes

The best way to have a good idea is to have a lot of ideas.

Linus Pauling

Anyone can look for fashion in a boutique or history in a museum. The creative person looks for history in a hardware store and fashion in an airport.

Robert Wieder

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Published Quarterly by Professional Analytical Chemists

Projected move date is October 13, 2001

The WCAS Analytical Digest
WEST COAST ANALYTICAL SERVICE, INC.
9240 Santa Fe Springs Road
Santa Fe Springs, CA
90670
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WCAS Laboratory Tidbits

We will be exhibiting at the following shows in the coming months:

AAPS - October 21-25 in Denver, CO. This is the American Association of Pharmaceutical Scientists Annual Meeting and Exposition. Our booth number is 941 and Craig and Eric will be at the booth. Eric will also be participating in a Roundtable Discussion titled "Effective Partnering with Contract Laboratories" on Thursday, 9:00 to 11:00 a.m. We hope to see you there!

SupplySide West - November 28-30 in Las Vegas, NV. This conference and trade show is for the supplement industry. Our booth number is 1245B. Craig and Eric will also be at this booth.

Nutritionals 2002 - February 5-7 in Anaheim, CA. This is billed as "The full spectrum of solutions for the nutritionals and functional foods manufacturer!" Looks like your stuck with Craig and Eric again!

Visit us at one of these shows for a chance to win something wonderful!

Assay versus ID

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assays usually have larger errors. Titrations and other wet chemical assays are usually not very specific, and their use assumes the material has been correctly identified. For example the assay methods for both sodium and potassium chloride involves measuring the chloride ion concentration using a silver nitrate titration. This method does not identify the sodium or potassium.

Drugs in the Environment

In the last 20 years, scientists have realized that some Pharmaceuticals and Personal Care Products (PPCPs) are produced and used in such large quantities that they have an impact on the environment. Many drugs are either partially metabolized in the body and/or their metabolites retain pharmacological activity. So most drugs make it into the environment through human wastes. Even though they may degrade in the environment to relatively harmless substances, they are constantly being replenished. Therefore some drugs can be detected at very low levels in water. Their impact on the ecosystem is under study.

A review was written by C.G. Daughton and T.A. Ternes and published in Environmental Health Perspectives, 107, page 907, (1999). This and other articles are available online at

http://www.epa.gov/esd/chemistry/pharma/index.htm

Our interest in this area is to develop a screening test for determining pharmaceutical drugs in the environment, primarily drinking water supplies. The test would be based on GCMS similar to EPA 8270. However many drugs are not amenable to GC. Currently we are experimenting with extraction and derivatization techniques with model compounds to determine the best experimental approach. This approach should be useful for determining analgesics (ibuprofen, acetaminophen), anti-convulsants (diazepam, dilantin), steroids, antidepressants (Prozac, amitriptyline), and cardiovascular drugs. Antibiotics and lipid lowering drugs are generally not amenable to GC even with derivatization.