

Formerly known as



West Coast Analytical Service

Analytical Digest

THE NEWSLETTER ON PROFESSIONAL ANALYTICAL CHEMISTRY

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New NMR Installed!

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Calendar

Composites+Polycon

January 15-17

Tampa, FL

MD&M West

February 10-12

Anaheim, CA

PittCon

March 8-13

Chicago, IL

Quick Quotes

Most of the fundamental ideas of science are essentially simple, and may, as a rule, be expressed in a language comprehensible to everyone.

Albert Einstein

Life exists in the universe only because the carbon atom possesses certain exceptional properties.

James Jeans

Assay, Purity, and Impurities

While the word "assay" generally means to measure a property or the concentration of a component, in the context of pharmaceutical quality control the word more specifically refers to the concentration of an ingredient, one which needs to be measured with a high degree of accuracy and precision (e.g. 98-102% of label claim). The component may be a major ingredient (~100%) as in an active pharmaceutical ingredient (API) or a minor ingredient (0.1%) as part of a drug product. But the ingredient is expected to be present and the concentration should be controlled with tight specifications. This requires that the ingredient be assayed using a test procedure with minimal error. An assay may not be highly specific for a particular ingredient. For example, all amino acids are typically assayed using a perchloric acid titration and most chloride salts are assayed using an argentometric (silver) titration. Many monographs require a combination of an assay which is not particularly specific with a related impurities test.

In a pharmaceutical assay, one generally does not use a calibration curve over a wide range. Instead, a single calibration standard is analyzed at a high concentration near the upper working range of the instrument so that the noise level of the instrument is insignificant compared to the signal. The sample is analyzed at that same concentration. During validation, the linearity of the calibration is documented over a narrow range (e.g. 80-120%). This standard is analyzed multiple times and the relative standard deviation (RSD) of the results must be small (e.g. <2% over six replicates). Then the unknown sample is tested, which we typically perform by preparing and analyzing the sample in duplicate. There are a few other QC parameters involved, but that's the crux of the method.

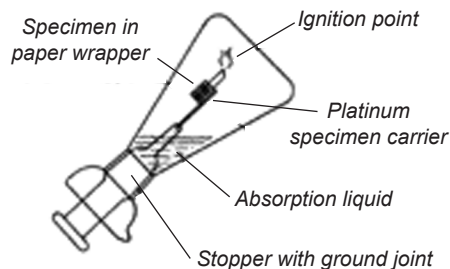
Purity, on the other hand, is defined as the absence of impurity in a substance. The unwanted impurities are measured in the presence of the desired material. There is a big difference between the two types of measurement, analytically speaking. Typically, trace

impurities are present at low concentrations, sensitive and specific tests are required, and errors can be rather large (3-20%) as compared to an assay (2%). Specifications for purity can be >99% or even >99.999%. This would mean that the total impurities that one could detect would be <1% or even <10 ppm.

Here is an example that may help to clarify this discussion. Let's say you have cesium chloride with a specification of >99%. You want to confirm the assay value of cesium chloride by testing for Cs by ICPMS and chloride by ion chromatography. The first problem is the specification. Neither of those methods is capable of attaining results with less than 1% error. A titration for chloride would be the best choice for an assay. However, the specification of >99% is probably a purity value, which means we should probably test the sample for impurities, with a specification of "not to exceed 1%". Give Jack Northington a call at ext. 103 if you have any questions.

An Update: Elemental Analysis After Combustion

We have updated our web article on the Pros and Cons of oxygen flask vs Parr bomb combustion. Chlorine, bromine, fluorine, sulfur, and phosphorus can all be tested for using



Combustion Flask

either of these prep methods. This technical article, as well as almost 200 others, can be found at www.wcas.com and then click on "Technical Articles" over to the left. Give Jack Northington a call at ext 103 with questions.

