

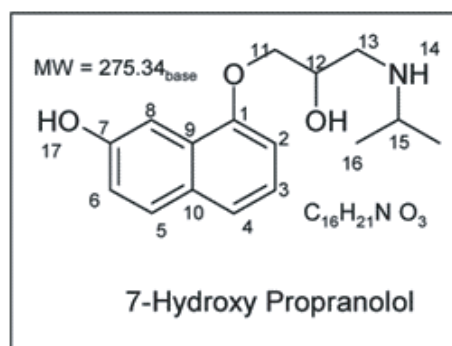
Residual Solvents

Appropriate selection of the solvent for the synthesis of drug substance may enhance yield or determine characteristics such as crystal form, purity, and solubility. Therefore, the solvent is often a critical parameter in the synthetic process. Since there is no therapeutic benefit from residual solvents, all residual solvents should be removed to the extent possible to meet product specifications, good manufacturing practices, or other quality-based requirements.

We have methods for screening these solvents, or we can modify, develop and/or validate methods for precise quantitation under cGMP guidelines.

Synthesis and Structure Elucidation

We develop novel small-scale small-molecule synthetic reagents, primary standards and chemical markers for pharmaceutical, biotechnology, clinical and contract research organizations (CROs). These compounds can be with or without isotopic labeling. Structural determination of existing and new chemical entities (NCEs) are performed and confirmed by using the four (4) principal spectroscopic techniques; Mass Spectrometry (MS), high field Nuclear Magnetic Resonance (NMR), Infrared (IR) and Ultraviolet/Visible (UV/VIS) spectroscopy.



"FOR CHEMICAL USE ONLY"

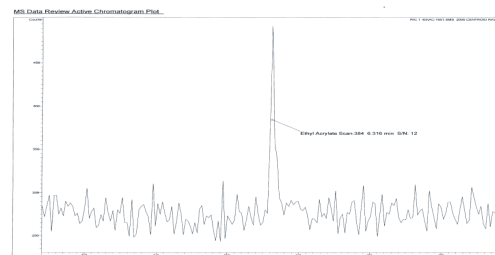
Alkylating Agents

Volatile impurities such as alkylating agents are an FDA concern due to their chemotherapeutic

and cytotoxic effects which are directly related to the alkylation of DNA. It is extremely important to have solid proof that all employed alkylating agents are removed prior to producing the API and DS.

The presence of residual alkylating agents in pharmaceuticals is currently attracting the interest of regulatory authorities both in Europe and in the United States. Although guidelines have not yet been established, concentrations are generally limited to values in the ppm range, and information in the low ppb range is highly desirable.

Residual alkylater, ethyl acrylate, showing an LOQ of 46 ppb and LOD of 12 ppb.



On-Site Liquid and Gas Phase Sampling

When applicable, liquid phase gas sampling has its advantages over vapor phase gas sampling since it is a more characteristic representation of what is inside your bulk storage tank or cylinder as opposed to the headspace, whereby with condensable gases stored as a liquid, a first distillation occurs during gas delivery.

Personal Commitment

Outsourced science has become indispensable for companies of every size. However, for outsourcing to be effective the expertise, commitment, efficiency and service must be impeccable, which is why the major gas and pharmaceutical companies work with **Atlantic Analytical Laboratory**.



Atlantic Analytical Laboratory Pharmaceutical Expertise



Audits & Approvals

- *US Food and Drug Administration (US-FDA)*
- *Defense Supply Center Columbus (DSCC)*
- *Coca-Cola™*
- *Pepsi™*

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Overview

Our extensive history in industrial gases and volatiles testing, going back over forty years, has led to the application of our technical expertise to the cGMP pharmaceutical world.

Our technical expertise is in Gas Mass Spectrometry (Gas-MS), Gas Chromatography (GC), Gas Chromatography Mass Spectrometry (GC-MS), Head Space (HS) sampling, Fourier Transform Infra Red (FTIR) spectroscopy; high purity gas analysis; cryogenic impurity determination for Liquid Nitrogen (LIN), Liquid Oxygen (LOX), Liquid Argon (LAR) and Liquid Carbon Dioxide; non-condensable gas analysis for total gas composition; multi-compendial analyses such as USP/NF, EP and JP grade testing; identification and quantitation of impurities such as residual alkylating agents, reactive sulfurs, mesylates and solvents via direct and HS pharmaceutical and biopharmaceutical testing on API, DS, medical devices and final finished products and container testing; development and validation of cGMP methods using the above techniques; and small scale de-novo synthesis with Certificate of Analysis.

We also offer both on-site liquid and gas vapor sampling, training and testing programs.

We have recently undergone an FDA inspection without a 483 being issued.



High Purity Gas Determination

Purities as high as 99.9999% can be determined by testing for total hydrocarbons (THC), total halocarbons, water, oxygen, nitrogen, argon, carbon monoxide, carbon dioxide, acetylene, etc., using MS, FTIR, GC, EH and GCMS techniques.

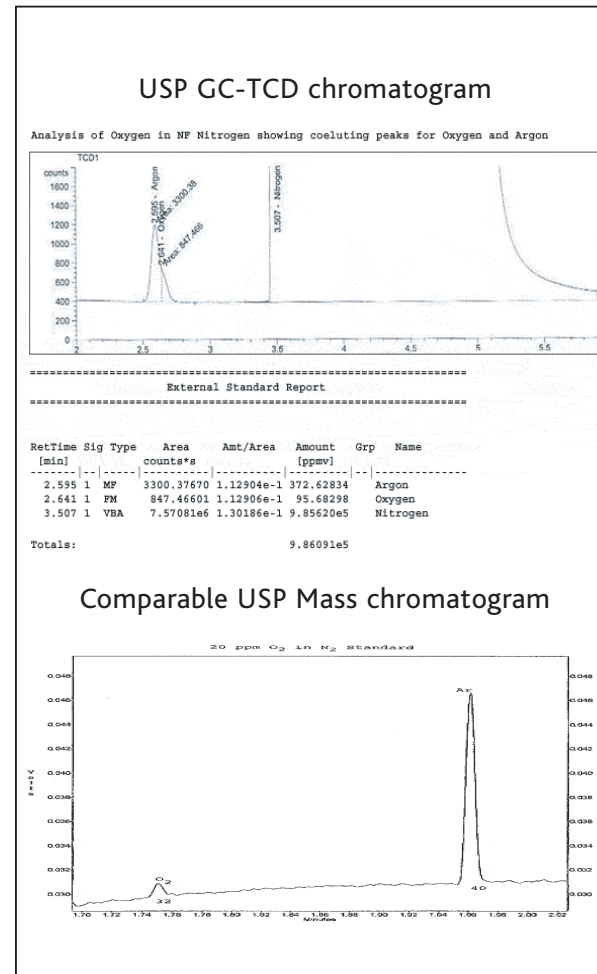
Gas Mass Spectrometry

Gas-MS can identify and quantitate multiple gases simultaneously from very small sample volumes. Gases such as hydrogen, helium, nitrogen, oxygen, neon, argon, krypton, xenon, carbon monoxide, carbon dioxide and methane are routinely analyzed from the high percent to low ppm range.

Multi-Compendial Gas Testing

We have methods in place for current USP/NF, EP and JP nitrogen, oxygen, carbon dioxide and medical/medicinal air testing; ending with generation of a full Certificate of Analysis when all tests are completed.

With respect to USP/NF Nitrogen, you now have a testing option. The current monograph method uses GC-TCD which does not provide a valid quantitation limit for oxygen since the oxygen and argon chromatographic peaks overlap. It provides a method for the determination of the limit of oxygen as less than 1.0% and a corresponding assay of Nitrogen to greater than 99.0%. Our superior yet comparable method using Gas – MS is designed to produce accurate oxygen quantitation down to 10 ppm in Nitrogen thus providing pharmaceutical industries with tighter manufacturing control capability.



When ultimate oxygen sensitivity is required at the ppb level, our fully validated Delta F systems are factory calibrated to NIST standards and have been proven to reliably determine these oxygen levels.

Determination of Impurities

With the current amount of testing required by the FDA on the actual drug substance, drug product and the packaging it is contained in, little testing, if any, is being performed on the volume of gas between the product and the container. This is where our expertise in "headspace" assays is

outstanding, and may be used to understand side reactions for stability studies.

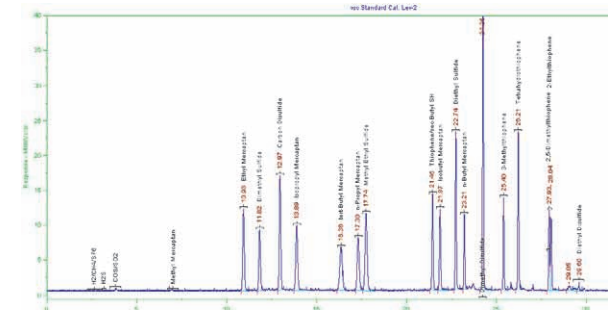
The current FDA guidelines are not specific on the need for this testing; however, in our opinion we feel that it is just a matter of time before this scientific concern is addressed officially. Those companies choosing to integrate this testing into their general practice now will have a competitive advantage in the future.

HS sampling combined with Gas-MS testing can be used with pharmaceutical products, devices, packaging and delivery systems to verify that the interior atmosphere is properly blanketing the drug substance.

HS sampling combined with GC/MS can identify and quantitate which volatile impurities may be present, often in the low ppb range.

Reactive Sulfurs and Mesylates

Pictured below is one level of standards that has been analyzed on one of our gas chromatographs dedicated for Sulfur Speciation using a Sulfur Chemiluminescence Detector (SCD). Not only can we determine total sulfur content, but we can also determine which specific sulfur compounds are present and at what concentration down to a Limit of Quantitation (LOQ) of 20 ppb.



Mesylates are salts or an ester of methanesulfonic acid which are often formed to increase solubility and bioavailability. We are well positioned to identify and quantitate mesylates and other reactive volatile sulfurs.