Compounder's International
Analytical Laboratory
Better Quality Through Quality Testing

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Please note: Our email address is lab@compounderslab.com

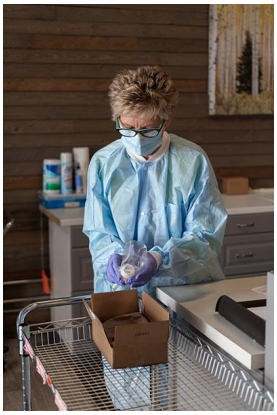
Ever Wonder What Happens When You Send Samples for Testing?

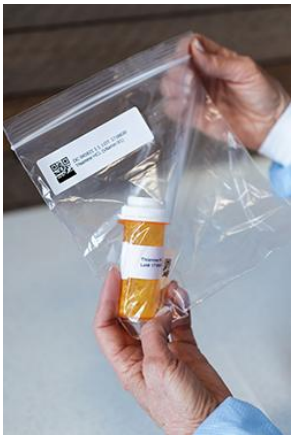
Compounding pharmacies often find it important to explain to their customers how their medications are made and the meticulous steps that are involved to ensure safety, accuracy, and quality. Sometimes we, as a testing laboratory, are asked similar questions. Have you ever wondered how we process your samples to ensure accurate test results in a timely fashion? What do we do to make sure samples are not mixed up with others that may look similar? How do we test for Potency, Sterility, Endotoxins, Stability, and more? These are good questions, glad you asked!!

Every day, multiple times each day, we receive samples through our front door from FedEx, UPS, and USPS. Sometimes even currier deliveries arrive! You may wonder how they are handled. Here's a quick overview of our step-by-step process. In future e-mailings we will focus, in more detail, on many of these tests and describe how they are performed, what test results mean, why they may be important to you and your patients, and the regulatory issues involved. We hope you will enjoy this brief tour!

Arrival

For security reasons, our doors are locked. No one enters our building without an employee personally letting someone in. The FDA wants it this way and so do we! We want to make sure nothing happens to your samples once they arrive at our lab. At the front desk, Mary receives all sample shipments. She dons necessary PPE in case something in a package has broken or spilled, and opens packages, removing your samples and sample submission form(s) along with your formulation sheet(s). If something needs to be refrigerated or frozen, those items are immediately placed into the receiving department refrigerator/freezer while the appropriate information is logged into our Laboratory Information Management System (LIMS).





Each sample is automatically assigned a Tracking I.D., and a QR Code label is generated. Each sample with QR code is placed into a new zip-locked bag to assure no cross-contamination or mix-up occurs. The description of each sample is entered into our LIMS system along with lot numbers, and everything is cross-checked between the paperwork and the sample container label. Also entered, is the information concerning what tests are being requested, as well as desired test dates if a stability study is being requested to determine BUD(s). If anything is not clear to us concerning what is being requested, or if a description or lot number does not match between the sample and the submission form, Mary is quickly in touch with you to clarify. ***Everything must be correct!***

Distribution

There are three lab departments at CIAL (Our Price List and Sample Submission forms are separated by lab department):

- Microbiology
- Potency/SIA
- Special Chemistry

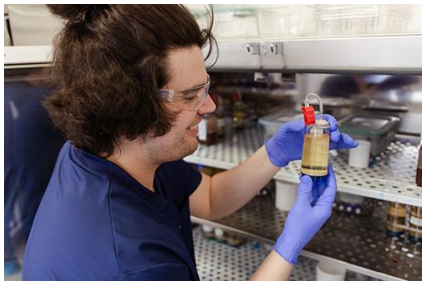
VIEW PRICE LIST **VIEW SAMPLE SUBMISSION FORMS**

According to the tests requested, your samples are distributed to the appropriate lab department. Again, those which need to be refrigerated or frozen are immediately placed into appropriate environments. (This equipment is continuously and accurately controlled and tracked by a computer which alarms if temperature drifts out of specification).

At this point, each sample with its associated tests is scheduled and assigned to an analyst / technician for testing. Decisions concerning this assignment are based upon analyst / technician specialty and specific instrumentation required for testing.

Testing Process-Microbiology Lab

To test sterility, endotoxin levels, antimicrobial effectiveness, etc. your sample(s) are brought into our ISO 5 environment by our technicians who are appropriately garbed so we can assure samples will not be contaminated. The appropriate processing parameters are calculated, samples pooled, dilutions made, correct media inoculated, calibrations checked, etc. all in accordance with USP <71>, <85>, <51> testing guidelines. These tests are almost always started on the same day, or the next day, following arrival. For sterility tests, samples contained in the appropriate media are placed into temperature monitored incubators and checked for growth daily. If contamination is identified, you are notified immediately and another test is begun using media from a different lot, in an effort to rule out the media as the possible contamination source. (Interestingly, in all of the tens of thousands of samples we have tested for sterility, to date only six have been found to actually have been contaminated! This speaks well of our compounding customers as well as our testing techniques and personnel). When all testing is complete, the data is entered into our LIMS system and your report is generated, then uploaded to your private web portal for viewing or printing.



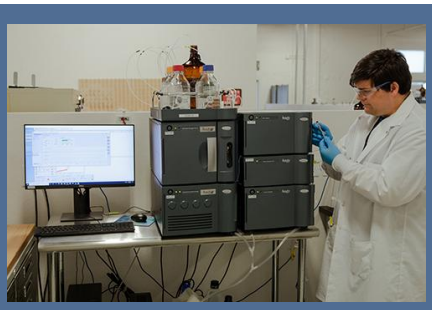
Tests we perform in this department:

- Sterility (USP <71> <795>)
- Sterility Method Suitability (USP <71> <795>)
- Endotoxin (USP <85> <797>)
- Fungi/Mold (USP <71> <795>)
- Antimicrobial Effectiveness (USP <51>)
- Water Activity (USP <1112>)
- Visible Particulates (USP <790>)
- Microscopic Examination of Unknown Substance (CIAL Method)
- Microbial Enumeration of Nonsterile Products (USP <61>)

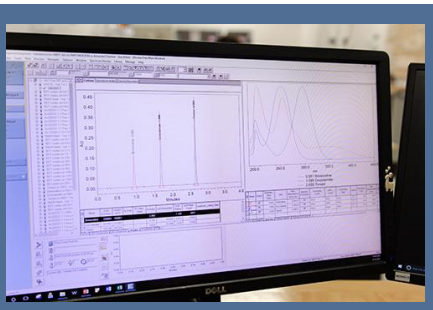
Testing Process-Potency Lab

Samples for which you request potency, stability, uniformity of dosage units, etc. are brought into our Potency Lab for analysis. Most of these will be analyzed on ultrahigh performance liquid chromatographs (UHPLC) per USP <621>. These very powerful state-of-the-art instruments analyze the amount of each substance present in a sample by first separating them from the

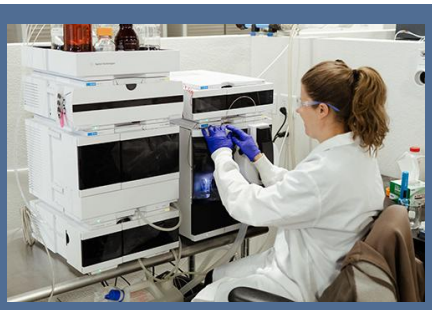
other ingredients, gathering them into “peaks”, then determine their amounts by the size / area of each peak. These instruments are also capable of displaying the UV spectrum of each peak which helps verify their identity and checking for interferences in the assay. Some are also equipped with mass spectrometers which are highly sensitive and able to identify/verify ingredients by their molecular weights.



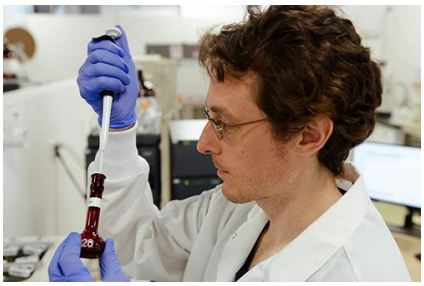
Acquity UHPLC



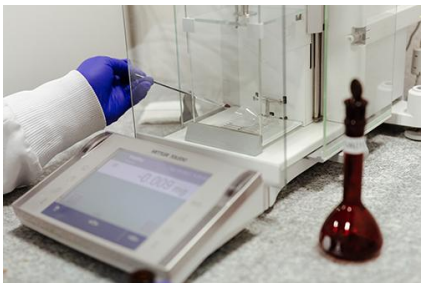
Chromatogram and Spectra



UHPLC / Mass Spec.



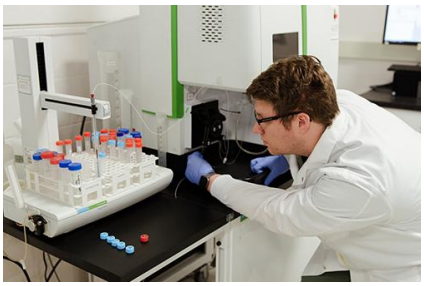
To perform potency assays, we must check all the active and inactive ingredients present on your formulation sheets to determine the best approach we should take in preparing each sample for analysis. This is why formulation sheets are so important. All samples must be placed in solution in an appropriate solvent and at the correct dilution, so a strategy must be worked out as to the best way to accomplish the goal. We have methods and guidelines to follow, but since there is such a great variety in the samples we receive, we frequently must experiment and customize our procedures. Also, we must calibrate our UHPLC instruments with high quality and very expensive reference standards for each ingredient being assayed. Standards and samples must be tested multiple times to verify accuracy and repeatability of the assay. Highly accurate balances, pipettes, and Class A volumetric glassware are used in the process. If a test result is questionable we follow our Out Of Specification (OOS) process, checking all aspects of the assay, frequently repeating the test to verify results.



Tests we perform in this department:

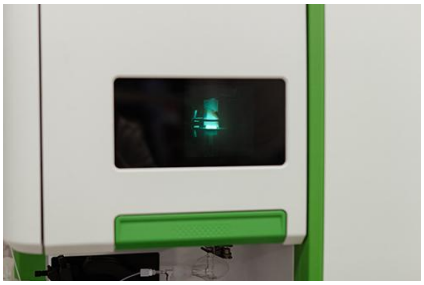
- Potency (USP <621> <736>)
- Potency Over Time Stability Studies (USP <621> <736> <795>)
- Stability Indicating Assay (SIA) Method Development/Validation (USP <1225>)
- Stability Indicating Assay BUD Determination (USP <621> <736> <795>)
- Minimum Fill Assay (USP <755>)
- Uniformity of Dosage Unit Test (USP <905>)
- Cleaning Validation for USP <800>
- Surface Recovery Validation
- Identity By Retention Time (USP <621> and individual monographs)

Testing Process-Special Chemistry Lab



Samples that are brought to our Special Chemistry Lab must go through a somewhat similar series of steps as those being processed for chromatographic potency. However, in this lab there are many different kinds of tests we perform, thus sample preparation, instrument calibration and result calculation is highly specific. For example, to test the viscosity (USP <912>) of an eye drop or cream, the sample and viscosity standard must be brought to a specific temperature and not varied more than 0.1°C during the test, due to the fact that viscosity will change with temperature. To test subvisible particulate matter in injectables or eye drops, (USP <788>, <789>) the outside of the sample container must be thoroughly rinsed off with particle-free water before opening, to avoid contamination. The

instrument is then calibrated with several particle size standards in the 10µm through 50µm range and above. The number of particles and the size of each individual particle is determined using a ribbon of light from a laser and the angle of scattered light is used to identify its size. Samples being tested for metals (USP <730>) must be dissolved and digested in strong acids and along with a carefully made series of standards, all must be drawn into a 10,000°C plasma (flame) of the ICP-OES instrument and their specific emission spectra measured for the intensity of light to determine metal concentrations.



In all tests, expensive and well-characterized standards must be used to calibrate these instruments. In addition, all processes must be validated and calculations made which will assure accurate results. To be certain of the accuracy of the determinations we report to you, it is common to test your samples and calculate results multiple times.

Tests we perform in this department:

- Subvisible Particulates (USP <788> and <789>)
- pH (USP <791>)
- Container Closure Integrity (USP <381>)
- Appearance/Odor/Color (CIAL Method)
- Karl-Fischer Water Determination (USP <921, 1a>)
- Loss on Drying (USP <731>)
- Identity by Infrared (USP <857>)
- Identity by UV-Vis (USP <197A>)
- Metals Analysis (USP <730>)
- Viscosity (USP <912>)
- Specific Gravity (USP <841>)
- Melting Point (USP <741>)
- Residue on Ignition (USP <281>)
- Chemical Identification (USP <191>)
- Absorbance/Absorptivity (USP <857>)
- Optical Rotation (USP <781S>)
- Crystallinity (USP <695>)

Bottom Line

Testing of compounded medications and their APIs requires a highly skilled and specialized lab with well-defined and carefully monitored/controlled systems and processes. Because of the enormous variety in the formulations which are made by compounding and outsourcing pharmacies, most “ordinary” testing labs find them to be overly challenging and will not engage in this arena. Indeed our lab is much more sophisticated than those QA/QC labs found in big pharma. Our instrumentation is fully state-of-the-art and our analysts more highly trained to deal with the complexity of testing approximately a thousand different APIs, in many combinations, and in a wide variety of dosage forms. Thus, there are over a million different combinations and permutations that are possible, and yet we test them on a daily basis. Every sample we receive and every test result is checked, double-checked, and even triple-checked to assure the results we send to you are as accurate as possible. Obviously, this is time-consuming but absolutely necessary. So if it appears that your sample testing results are not completed as quickly as anticipated, remember the many steps involved to assure the results you receive are as accurate as possible.

VIEW OUR PRICE LIST **SAMPLE SUBMISSION FORMS**

Give Us A Try

We think you will find working with us a refreshing experience! We are centrally located in the US (Colorado) so samples can easily be shipped to us overnight from where ever you are located.

We look forward to working with you!

Ronald Sutton, President

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