

Almac Voice

Analytical testing for clinical trials – why is it so important?



John Wood
Global Analytical Services Account Manager

Developing a drug is a costly and complex process where purity, safety and efficacy must be continually proven in order to meet strict regulatory requirements through clinical trials.



Before a drug can enter the trial phase, and more importantly a human, extensive analytical testing must be performed to ensure its safety and effectiveness, often in comparison to a standard treatment already offered.

It is very rare for a drug developer to have the analytical capabilities to conduct the extensive testing required in-house and consequently it is often outsourced. Analytical outsourcing is not uncommon, and the global pharmaceutical analytical testing outsourcing market is expected to increase to an estimated value of \$10.42 billion by 2026. This rise in market value can be attributed to constrained budgets and the need to reduce R&D expenses as well as manufacturing costs.¹

What should you know about analytical testing for clinical trial supplies and more importantly, why are these tests critical?

Clinical trials typically study the trial drug, comparator and placebo and it is critical to ensure these products look identical which is achieved by over encapsulation. Regulatory bodies regard over-encapsulation as a modification to the original product which means that supporting analytical data must be generated. This is typically comparative dissolution, to show that bioavailability is the same as the original product, and stability data to verify its shelf life.

Comparative dissolution testing follows the dissolution profile of both the un-modified product and blinded (over-encapsulated) product in order to confirm the blinding process (over-encapsulation) does not alter the properties of the commercial product.

The manufacture of over-encapsulated products are analytically supported in many ways including:

- **Method development** – development of new analytical methods if they do not currently exist. These can be derived from pharmacopeial methods where appropriate.
- **Method transfer** – formal transfer of validated methods from client or third-party sites.
- **Method validation** – validation of methods in line with ICH guidelines appropriate for the phase of clinical trial.
- **Release testing** – product release (both chemical and microbial testing) for innovator, comparator and placebo products.
- **Stability studies** – formal ICH stability studies under a range of conditions to inform and justify shelf life data.



In essence, methods must be developed to ensure they are fit for purpose especially when a product has been modified. This development activity can also improve aspects of methods, e.g. run time or sensitivity.

Once a method is well defined it must be validated according to GMP guidelines. The specific level of validation required for each method can vary in line with client requirements and phase of clinical development.

Methods which have been developed and validated at an alternative site will often undergo a formal transfer to allow GMP release testing to take place. This formal transfer, if conducted correctly, will remove the need for a second formal validation programme.

Release testing covers a variety of tests to address the purity, concentration, consistency, identity and safety of the product. Typical testing would comprise of appearance, assay and impurities, dissolution and microbial testing. It is essential that the methodology involved is robust to ensure the safety of the product and integrity within the clinical trial.

Since the over-encapsulation process is considered a modification to the comparator drug, stability studies are required to (re)set shelf life. These studies vary in length but are typically conducted over a 2 - 3-year period in real time. Time points are determined by regulatory requirements and earlier degradation studies are conducted whilst in development. The outsourcing provider will provide stability protocols and reports following each time point. Figure 1 showcases a typical stability study schedule:

Condition	Time Point (months)								
	0	1	3	6	9	12	18	24	36
25°C/60% RH	X	X	X	X	X	X	X	X	X
40°C /75% RH		X	X	X					

Figure 1 : Stability study schedule

Finally, in terms of material requirements, the number of original tablets will vary dependent upon pack size – the larger the pack the more will be required for each testing activity. Consideration must be given to the packaging type, for example, if bottles are the final packaging, the bottle count is important. Generally, the larger the bottle count the more over-encapsulated tablets will be required.

Analytical testing is a significant, critical, and sometimes unpredictable aspect of drug development. It not only has to be tailored to specific needs, but delivered on time, within spec enabling the successful launch of clinical trial. Analytical activities managed by CDMOs can save time and money as they generally operate from state-of-the art labs, have a wide variety of standard methods, and bring knowledge and experience from a wider variety of products.

Almac's approach to analytical testing of clinical trial supplies

Almac is unmatched in its ability to manufacture clinical trial supplies and provide analytical support from our global locations in the UK, Europe and the US. We are regarded as the high quality and low risk analytical service provider of choice for the release testing of clinical and commercial drug product supplies. Our proven expertise supports an extensive range of dosage forms and our services cover all typical drug product release tests.

In addition, with a license to hold controlled drugs, we can look after your whole range of products.

¹<https://thedailychronicle.in/news/2443116/pharmaceutical-analytical-testing-outsourcing-market-sees-a-faster-rebound-in-the-era-of-covid-19-leading-players-pharmaceutical-product-development-llc-exova-charles-river-boston-ana/#:~:text=Pharmaceutical%20analytical%20testing%20outsourcing%20is%20the%20constitution%20of,methods%20required%20for%20the%20development%20of%20these%20drugs.>

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Contact us:

UK

Almac Sciences
19 Seagoe Industrial Estate
Craigavon
BT63 5QD
United Kingdom

almacanalytical@almacgroup.com
+44 28 3833 2200