

# Almac Voice

## Quality Control Release Testing – more than a tick box exercise



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**Quality Control (QC) testing is critical to finished products and any key raw materials and excipients used in commercial manufacture. While QC release testing is often regarded as a straightforward process, there are many factors to consider when outsourcing this work.**



When considering analytical testing, emphasis typically falls on method development and validation. However, it is important to remember that these steps are merely a means to an end—the overall goal is the release of commercial drugs to the market. When developing **novel analytical methods**, it is beneficial to remember this goal and select methods that require **standard equipment** to ensure multiple labs can perform the testing. Since release testing is required for each manufactured batch before it can reach the market, having multiple labs qualified to run the release testing ensures continuity of supply.

For a product to be approved, analytical release specifications must be in place to test each individual product to ensure that they adhere to the stringent quality requirements demanded by regulatory authorities. These list the criteria and the acceptable limits for the product and detail the correct methods to use to quantify these characteristics.

For direction, Pharmacopeias exist to protect public health by setting and maintaining the standards pharmaceutical products must adhere to. There are three main bodies to comply with:

- EP (European Pharmacopeia)
- JP (Japanese Pharmacopeia)
- US (United States Pharmacopeia).

Each product brought to market has unique chemical and physical properties, thus the analytical testing methods required also differ. Almac has contributed to 61% of all FDA approved NME's from 2017-2019 and 57% of all EMA approved NME's from during the same period. We therefore have significant experience in supporting clients and providing a consultative service when **setting release specifications**.

Release specifications that are generally accepted already exist in pharmacopeias for a range of products, and these demonstrate the quality they must meet to be acceptable for use in the designated application. The pharmacopeias publish monographs for products which contain specifications and compendial testing methods to aid with the release of these products onto the market.

Where **compendial methods** exist, they can be accessed and applied to a variety of products. However, there are key factors to consider with their application to test articles. Although the methods published have been demonstrated to be fit-for-purpose at their original lab, additional testing is often required to prove their effectiveness in alternative labs.



There are various ways to implement these methods (which in itself is a topic for further discussion), and as with any analytical testing regime, interpretation and set up of methods can be streamlined by using outsourcing teams with experience in interpreting pharmacopeias thereby providing added value to this stage of the products' development.

What is clear is that no matter the test article (raw materials, active ingredients, finished products) and method type (novel or compendial) there is a need to perform **robust** and **repeatable** analysis of each manufactured batch prior to use.

For raw materials and excipients, a delay in release can hold up an entire manufacturing schedule. For commercial batch release, an experienced lab will release products onto the market more quickly, and when selecting a vendor for this work **turnaround times** play an important part.

Quality of data is also an important factor to consider. It is not uncommon during testing to obtain results that are outside specification windows. If a batch fails to meet its specification for whatever reason, it will be put into quarantine until further data can be obtained to support the release. Deviations could be caused by many factors including:

- Degradation of the product
- Influx of foreign matter
- Biological contamination
- Change in polymorphic form

Each of these issues can require different analytical techniques to interrogate and it is not always clear which of these items has given rise to the issue. A lab operating a number of varied techniques can investigate a wider range of issues more efficiently and be able to close deviations and get the product released more quickly. During investigations batches are placed in quarantine which can be costly, it is therefore imperative that support is available to investigate any deviations in the data and determine the root cause. Initial checks are made to ensure the initial results were not affected by equipment or analyst errors (e.g. issues with system suitability or calibrations).

If this is not the case, then further analysis through root cause investigations are performed. This may result in repeating the original testing/partial testing in a controlled manner and in consultation with the Quality Assurance team and the client. Only when this investigation is closed can the material be released onto the market.

For all releases, the principles of GMP must be strictly adhered to, and the importance of this final testing means that any outsourcing partner should display an exemplary track record of compliance.



In conclusion, although QC release testing may appear to be straightforward there are a number of supporting factors to consider, and as the final step of getting products to market, the risks are high and QC testing failure can be costly both in terms of time and money. Factors for consideration include:

- Analytical methods and equipment availability
- Specification limits
- Troubleshooting capability
- Footprint of the lab, including GMP audit history and responsiveness

At Almac, we routinely perform QC release testing on API, finished products, excipients and raw materials using both novel and compendial methods. Our team of >530 analysts work on a myriad of different methods each year, across all therapeutic areas and phases of development. To find out more email:

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