

## Biopharmaceuticals: Process Related Impurity Analysis



A well-characterised biopharmaceutical product is defined during its development by identification and quantification of both process-related and product-related impurities. Process and product related impurity testing can be used to show purity, batch to batch consistency and where certain impurities are removed during process development or as part of process validation. The ICH Q6B Guidelines state that levels of process related impurities should be determined and acceptance criteria established. These residuals are typically present in trace levels in sample matrices which can be challenging.

Highly specific and sensitive techniques are required for robust quantification to address these challenging method development and validation projects. Residuals from cell-culture media include antibiotics (example kanamycin). Surfactants (example Triton-X) are added to aid in separating the protein, peptide and nucleic acids from the process stream. Inducers such as IPTG are used to induce gene expression and to aid the refold process. Glutathione and dithiothreitol (DTT) are used during reduction and refolding of proteins and others related to downstream processing include DCA and heavy metals.

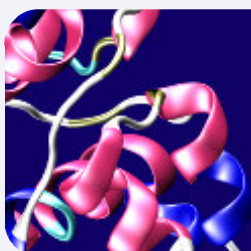
Intertek apply a range of in-house analytical techniques and instrumentation including GC-MS, HPLC with UV detection, LC-MS or LC-MS/MS, NMR, ICP-MS and UV assay. Residuals from cell-culture media such as antibiotics are particularly challenging. Intertek ASG has been very successful at applying LC-MS/MS to an increasing number of these species such as kanamycin providing a highly sensitive method even to ppb levels and also at developing combined methods where multiple residuals can be determined at the same time (e.g. kanamycin and IPTG) and so achieve superb cost effective solutions for our clients. Some of the common process residuals that Intertek provides services for include:

- Kanamycin
- Tobramycin
- Gentamycin
- Amoxicillin
- Chloramphenicol
- Glutathione
- Dithiothreitol (DTT)
- IPTG
- Triton-X
- Antifoaming agents
- Tween / Polysorbate
- DCA

Intertek ASG is a GLP/cGMP facility which is highly experienced in the development and validation of methods for process related impurity analysis, in accordance with ICH Guidelines Sections Q2(R1) and Q6B.

### Intertek Analytical Services

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### Did you know?

The laboratory has been inspected by the UK Medicines and Healthcare Products Regulatory Agency (MHRA) for GLP and GMP compliance and by the US Food and Drug Administration (FDA) for cGMP compliance in relation to customer's pharmaceutical manufacturing license.