Analytical Method

Related terms:

Peptide, High-performance liquid chromatography, Serum (blood), Gas chromatography-Mass spectrometry, Chromatography, Immunoassay, Liquid chromatography-mass spectrometry, Sample Preparation, Quality Control

Regulatory guidelines for the development of a biotechnology drug product

Mark J. Waskiewicz, in Therapeutic Protein Drug Products, 2012

7.4.4.2 Characterization and release assays

Analytical methods can loosely be categorized into two groups: release/stability and characterization. Drug product release assays are described in the drug product dossier. Analytical method descriptions should be presented in enough detail that a scientist skilled in the art should be able to execute the method using the description provided. If methods are used for stability testing only, those method descriptions should be presented in the stability section. The results of release testing for drug product manufactured historically are presented in a batch table. Characterization methods are presented in the drug substance portion of the dossier, and can be used on the drug substance, the drug product, or both.

Early phase assays and assays used for product and process characterization should be fit for their intended use; that is, the variability of the analytical methods should be controlled such that the analytical method will allow the detection of a meaningful change in a product quality attribute. For pivotal trials and commercial production, analytical methods should be validated.

Moving into the Clinic

Alan J. Russell, Timothy Bertram, in Principles of Tissue Engineering (Fourth Edition), 2014

Final combination product testing

Analytical methods for final product testing vary substantially, depending on the composition of the TERMP. In general, any product intended for customization to individual patients (e.g., autologous products) requires confirmation that release and potency standards are met via non-destructive test methods. Such test methods are typically novel and specific to each product type and are frequently based on a battery or 'matrix' of tests that evaluate cellular function and physical parameters of the scaffold. In contrast, lot-testing strategies, statistical sampling, and more routine analytical methods are available for scaffold-only products and cell-based products produced in large lots (e.g., allogeneic and xenogeneic cellular products). In the future we may see allogeneic therapies that are customized for patient-specific

and xenogeneic cellular products). In the future we may see allogeneic therapies that are customized for patient-specific needs. Naturally, such innovations will require a combination of analytic approaches.

Atomic Spectroscopy, Forestry and Wood Products Applications

Cathy Hayes, in Encyclopedia of Spectroscopy and Spectrometry (Third Edition), 2017

Introduction

Analytical methods of atomic spectroscopy have been used in forestry and wood product research since their earliest development. Nowadays, almost all of the spectroscopic techniques available are employed in the analysis of metals and trace elements in diverse samples of industrial and environmental origin. The techniques that find most regular application include flame atomic absorption spectroscopy (F-AAS), graphite furnace atomic absorption spectroscopy (GF-AAS), inductively coupled plasma atomic emission spectroscopy (ICP-AES) and, occasionally, also direct current plasma atomic emission spectroscopy (DCP-AES). In many applications F-AAS is a sufficiently sensitive and precise technique; however, in the analysis of some environmental samples for trace elements (forest soils, plant material and water) where concentrations may be very low (of the order of 100 ng ml^{-1}) the greater sensitivity of GF-AAS and ICP/DCP-AES is required. In considering the applications of atomic spectroscopy to forestry and wood products it is worthwhile remembering that the analytical method available for use is often determined by the volume and variety of analyses carried out in individual laboratories.

Forestry and Wood Products, Applications of Atomic Spectroscopy*

Cathy Hayes, in Encyclopedia of Spectroscopy and Spectrometry (Second Edition), 1999

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Handbook of Modern Pharmaceutical Analysis

Stephen Scypinski, Joel Young, in Separation Science and Technology, 2011

A Standard Operating Procedure

Analytical method transfers are generally governed by a standard operating procedure (SOP). The SOP describes the responsibilities of the expert laboratory, receiving laboratory, and associated quality organization(s). The SOP should provide requirements for materials used in the transfer (e.g., how many batches should be tested, how to select batches for testing), personnel training requirements, and documentation requirements. Documentation requirements may

include a master plan and transfer protocol(s). The SOP will describe the content of these documents as well as procedures for approval, storage, and change control of formal documents such as the transfer protocol and the transfer report.

Therapeutic Areas II: Cancer, Infectious Diseases, Inflammation & Immunology and Dermatology

H.A. Kirst, N.E. Allen, in Comprehensive Medicinal Chemistry II, 2007

7.21.9 Analytical and Bioanalytical Chemistry

Many analytical methods for aminoglycosides are available to screen samples, identify compounds, monitor separations, test quality or purity of bulk or formulated drugs, or assay concentrations, degradation products, metabolites, or residues from diverse material. To minimize patient toxicity with optimum efficacy, therapeutic drug monitoring was developed to guide dosing by correlating aminoglycoside concentrations with indicators of toxicity. Commonly used analytical methods include different microbiological, radiological, immunological, and chromatographic assays. Microbiological assays are still used for many applications since they are readily performed without expensive specialized equipment. Automated immunoassays are popular, but an assay for each test compound is required. Chromatographic methods must separate and quantify nonvolatile, polar, water-soluble, basic molecules lacking a natural ultraviolet or fluorescent chromophore, which require alternative detection systems. Development of new analytical methods for aminoglycosides should continue in order to meet needs for rapid, accurate analysis of large numbers of samples.

Analytical Techniques used in Therapeutic Drug Monitoring

Michael C. Milone, in Therapeutic Drug Monitoring, 2012

A General Classification of Analytical Methods

Analytical methods can be divided into three categories, based upon their precision and accuracy, using a schema original developed by the International Union of Pure and Applied Chemistry (IUPAC) [1]. Those analytical techniques with the highest precision and accuracy are generally referred to as definitive methods. A *definitive method* must have negligible systematic error relative to the application of the measurement. Due to the exacting nature of measurements required for definitive methods, few laboratories have the resources necessary to develop them and they are generally not amenable to routine application in TDM; however, they are typically employed by laboratories such as those of the National Institute of Standards and Technology (NIST, formerly known as the National Bureau of Standards), and are critical for the generation of standardized reference material (SRM) that can be used to aid in method harmonization (discussed further below). In contrast to definitive methods, *reference methods* are those methods possessing "small, estimated inaccuracies relative to the end use requirement". Reference methods are generally complex, but are more amenable to application in clinical laboratories. Methods using liquid chromatography combined with tandem mass spectrometry (LC-MS/MS), with proper validation, often meet the requirements for a reference method. Lastly, *routine methods*, usually immunoassays, generally represent those assays that may have greater uncertainty but have other advantages, such as ease of performance, high throughput and lower cost. Nevertheless, all methods applied in the clinical laboratory should have a degree of uncertainty that is appropriate for the clinical decision that will be based upon the result. Thus, it is important to have a thorough understanding of measurement uncertainty to interpret any test, especially TDM tests.

Handbook of Modern Pharmaceutical Analysis

Henrik T. Rasmussen, in Separation Science and Technology, 2001

IX. Summary

Analytical methods are required to characterize drug substance and drug product composition during all phases of pharmaceutical development. Early-phase methods must support changes in synthetic routes and dosage form and elucidate the structures and levels of impurities. In later phases, goals change to the development of rapid and robust methods for release and stability evaluation that can be transferred to quality units. Accordingly, method development should be viewed as an iterative process.

All phases of analytical development are ideally supported by chemical separation techniques such as HPLC, TLC, GC, SFC, and CE. HPLC continues to be the primary method of analysis throughout the pharmaceutical development process. Although HPLC is limited in its ability to separate more than 15–20 components in a single analysis, and variations in columns and instrumentation manufacturer to manufacturer complicate transfer of methods, HPLC can readily be implemented to meet ICH requirements for method performance. For early-phase methods, HPLC can be coupled dynamically to mass and nuclear magnetic resonance spectrometers to facilitate the identification of unknown impurities. In later phases, HPLC can be implemented in a fully automated format as a high-throughput method for release and stability testing.

Whereas the other separation methods have been demonstrated to also provide the requisite performance for release and stability testing for select drug substances and drug products, more typically the techniques are applied as supportive methods for HPLC during early-phase development and in niche areas during late-phase development. Because each separation method provides a different mechanism of separation to HPLC, utilization in early-phase development can be used to confirm specificity of HPLC methods. In later phases, both SFC and CE have shown applicability to chiral separations, and GC remains as the unique technique for the determination of residual solvents.

Despite the broad-based utility of separation methods, *a priori* prediction of operating conditions for the separation of a given API and its impurities has remained elusive. However, systematic approaches, or the use of generic conditions, can be exploited in method development. This chapter has endeavoured to summarize these approaches within the context of the goals that a method should achieve in the various stages of pharmaceutical development.

Assessment of proteins of the immune system

Henry A. Homburger, Ravinder Jit Singh, in Clinical Immunology (Third Edition), 2008

PROTEOMIC METHODS

Analytical methods now applied to the qualitative analysis and measurement of proteins include liquid chromatography (LC) techniques and mass spectrometry (MS). Test methods that employ these techniques are regarded as the methods of choice for several analytes routinely measured in clinical laboratories, including drugs, drug metabolites, and steroid and peptide hormones. However, for routine measurement of most proteins, including immunoglobulins, immunoassay techniques such as nephelometry and immunometric methods are preferred. The matrix of blood plasma is very complex and may cause artifacts in the measurement of proteins by chromatographic methods. A common problem is suppression of the analytical signal in chromatographic assays which results in low signal-to-noise ratios. Improved analytical sensitivity and specificity for clinically relevant protein analytes has been accomplished by immunoaffinity chromatography and by immunosubtraction techniques.

An application of advanced proteomic techniques that has gained acceptance in recent years is the analysis of therapeutic antibodies. Monoclonal antibodies are now widely used as therapeutic agents to treat several immune-mediated and autoimmune diseases. For example, antibodies to tumor necrosis factor (TNF) are used to treat rheumatoid arthritis and inflammatory bowel diseases (Chapters 52 and 74).

The pharmaceutical industry standard for therapeutic monoclonal antibodies is to have the purest immunoglobulin with no contamination with other variants. C-terminal modification of the heavy chains with variable numbers of lysines in these drugs is a common structural variation during the manufacturing process and demands careful analysis. Using capillary isoelectric focusing chromatography, these variants can be readily separated and analyzed, as shown in Figure

96.9A.

Carbohydrate modifications are also known to influence the function and thermodynamic stability of immunoglobulins. Carbohydrate moieties on immunoglobulins can be analyzed using a variety of techniques, such as capillary electrophoresis chromatography and MS spectrometry. An example of such an analysis is shown in Figure 96.9B.

Chromatography and mass spectrometry methods have been reported to have good precision, linearity, and accuracy. We anticipate that these methodologies will gain acceptance for the analysis of intact immunoglobulins. The methods are rapid, can be automated, and require minimal sample preparation. It is predicted that multidimensional liquid chromatography, e.g., LC-LC-LC-MS, will become a routine analytical tool in the manufacture and quality assessment of reagents. It is likely that improvements in separation technologies will make it possible to lower the manufacturing costs of antibody production and significantly improve the quality of the clinical assays in routine laboratories.

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