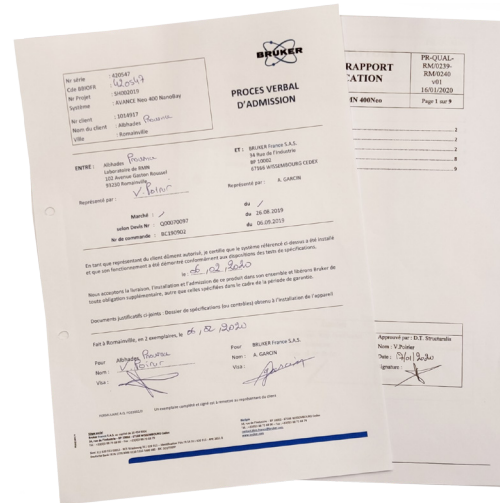


Successful commissioning of an NMR system for a GxP environment: details of a modern and efficient approach to achieving compliance.

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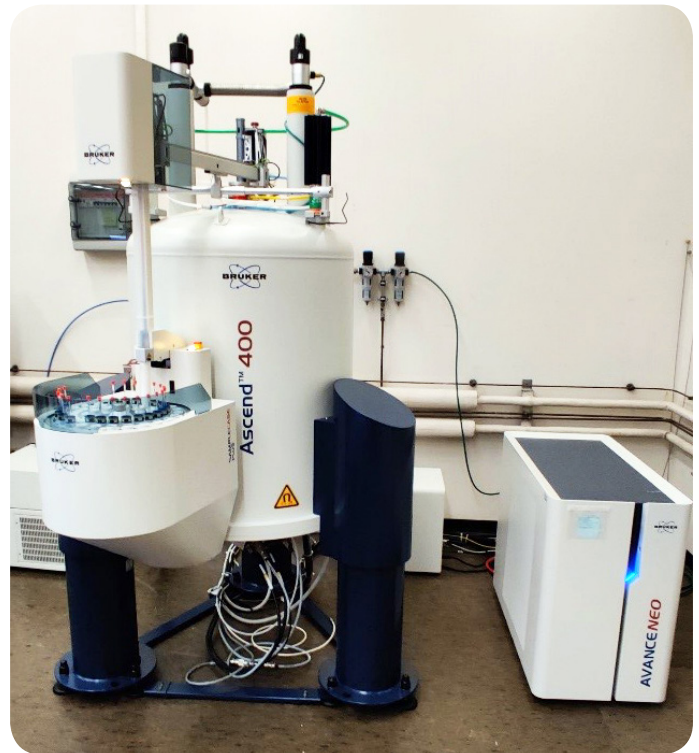
“Albhades has always chosen to comply with GxP, including for NMR techniques. Its Paris site, unique in France today, has chosen to invest in 2 new NMR spectrometers in less than 3 years to meet the requirements of the health products sector”.
Sylvie Farre, Sales Director, Albhades

“Bruker BioSpin continues to broaden and deepen the range of its products and services that are designed to assist customers operating in regulated environments. It is very pleasing to see the details of how we are able to help customers such as Albhades.”
Falko Busse, President, Bruker BioSpin

Summary

For companies working in the field of late-stage pharmaceutical development and manufacturing it is mandatory to maintain compliance with a multitude of regulations and standards. In this paper, we describe the process of successful qualification and commissioning of a new NMR system designed for use within a GxP environment: the system was accepted as complete and ready for use on the 6th February 2020.

*Albhades are a supplier of contract analysis services for the Health Products and Bruker BioSpin manufactures a range of products based on magnetic resonance – more details about both companies are given at the end of this white paper.



1Several white papers are available from Bruker BioSpin <https://www.bruker.com/nc/products/mr/mr-in-pharma/instrument-qualification.html> : T171911 (Data Integrity), T173714 (Qualification), T171911 (Change Control) and T174487 (Performance Qualification), T179520 (NMR under GxP in Drug Development and Manufacturing)

Introduction

Good manufacturing and laboratory Practices (GxP) covers many different facets of pharmaceutical development and manufacturing: this brief note describes two important parts of the current set of regulations that relate to analytical instruments i.e. qualification and compliance with Data Integrity (DI) regulations. Details of instrument qualification and the principles of DI are frequently cited in the technical literature and they typically describe various aspects of their practical implementation, although the analytical method most often cited is based upon separation science (HPLC and UPLC etc.). Additionally, it has also become accepted custom and practice to “outsource” instrument qualification and data integrity activities as much as possible to the vendors of the instrumentation since this approach represents both sound technical practice and good value for money:

- The vendors know their systems well and are clearly able to incorporate relevant and robust challenge tests into the qualification documents.
- It can represent a considerable time saving to the customer since their own specialist colleagues do not have to take the time to develop bespoke protocols.

Nuclear Magnetic Resonance (NMR) is frequently employed during late stage development as well as manufacturing: a fact that is not very widely appreciated outside of a small and close-knit group of technique specialists. Bruker BioSpin is aligned with the trend for instrument customers to outsource GxP activities as much as possible by offering a “GxP assistance kit” and therefore ensures that the NMR technique is “mainstream” in terms of compliance. This has been achieved by:

- Offering technique-specific IQ/OQ/PQ/CSV protocols*
- Providing a range of supportive documents including various certificates as well as certified calibration standards.
- Extending an already widely accepted PQ supportive software
- Incorporating multiple DI supporting features into the most recent versions of the TopSpin software package.
- Delivering a series of “white papers” that describe the context and show how the tools from Bruker BioSpin can help customers achieve compliance.

Here, we report on the successful deployment of the GxP assistance kit from Bruker BioSpin to an installation at the Albhades site in Paris, France. This kit was supplied with a brand new state-of-the-art NMR spectrometer a 400MHz AVANCE NEO spectrometer equipped with an iProbe and a 60 position auto-sample. Of particular note was the close collaboration between the teams in Albhades and Bruker BioSpin throughout the process of system specification, ordering and commissioning.

Discussion

Albhades offer a variety of contract services to the pharmaceutical industry, including NMR, and a decision was taken to invest in a new system so that they could continue to expand by providing multiple NMR methods under GxP conditions. Through discussions with Bruker BioSpin the configuration of the system was defined in detail and a decision was subsequently taken to install a new 400 MHz NMR spectrometer: all the components of this system are modern high performance units that have been proven multiple times in a variety of installations worldwide.

After the system was ordered, the dialogue between the two companies continued although contact became more frequent as the installation and commissioning phase approached. Documents to support compliance were supplied by both parties – this is exactly how it must be for all installations since the BBIO documentation (i.e. qualification protocols, certificates and system manuals etc.) must fit into Albhades’ frameworks of SOPs and associated documents as well as their IT infrastructure. As part of a general review initiated by Albhades’ QA, a few months before commissioning started, versions of the qualification protocols were supplied to Albhades for general review.

Once the system was delivered to site, it was commissioned quickly: it took only 3 weeks from start to finish i.e. unpacking, assembly, magnet cool down and energisation, and also full system testing. The GxP aspects that are the subject of this note (i.e. IQ, OQ, PQ and CSV*), were also completed within this short time period.

After commissioning and formal sign off of the system, PQ is continually being applied by Albhades’ personnel, for example:

- Weekly general performance tests using certified references (e.g.: lineshape $^1\text{H}/^{13}\text{C}/^{31}\text{P}/^{19}\text{F}$ sensitivity, water suppression, temperature check...)
- Specific system suitability tests and method suitability tests from each validated method that is run.

Additionally, maintenance is also an essential part of maintaining compliance with GxP regulations, and in the case of this instrument, it consists of:

- Routine preventive maintenance
- Annual full preventive maintenance and qualification from Bruker (based on Albhades’ requirements)

*(Installation Qualification - IQ, Operational Qualification - OQ, Performance Qualification - PQ and Computer System Validation - CSV)

Conclusions

Operating NMR under GxP is considered “mainstream” and the example described here shows how GxP capability can be achieved with speed and efficiency. The system was commissioned quickly and close collaboration between vendor and customer was an essential feature.

The NMR system within Albhades described in this note has full GMP capability and it is offered as part of a contract services business that includes for example PE, USP, JP monographs and development and method validation according to ICHQ2 and pharmacopeia. The range of applications include batch release, identification, assay by qNMR, quantification of impurities, structure determination and identification of unknowns.

Bruker BioSpin continues to work with many customers around the world to help deliver GxP capability for NMR systems (both new systems and also those that are currently in use). In addition, Bruker BioSpin are extending and strengthening their GxP offerings across the portfolio.

About Albhades:

Albhades supports the pharmaceutical, medical device, cosmetics and OTC industries in their analytical needs in quality control, analytical development and process validation. Thanks to a mature, well-proven quality system (GMP, ISO 9001, ISO 13485, Cofrac...) and state-of-the-art technical platforms, Albhades provide analytical services on a very large scope: Organic, Mineral, Microbiological, Cell Biology, Mechanical tests, Stability studies etc.

For organic analyses, its NMR platform is constituted of 3 GMP-compliant spectrometers and a team of experts, able to provide unique services, from R&D tests to batch release analyses.

Albhades accompanies customers on a daily basis in their needs for analysis while ensuring an irreproachable quality assurance and a professional service with human contact.

About Bruker Corporation:

Bruker is enabling scientists to make breakthrough discoveries and develop new applications that improve the quality of human life. Bruker’s high-performance scientific instruments and high-value analytical and diagnostic solutions enable scientists to explore life and materials at molecular, cellular and microscopic levels. In close cooperation with our customers, Bruker is enabling innovation, improved productivity and customer success in life science molecular research, in applied and pharma applications, in microscopy and nanoanalysis, and in industrial applications, as well as in cell biology, preclinical imaging, clinical phenomics and proteomics research and clinical microbiology.