Audit report ABX

Distribution list	:	Jelena Ehmke (ABX); Henrik Silber; Marianne Patt; Cecile Bourdeau; Almut Walte; Rainer Suchi
Audited Company	:	ABX Radeberg
Reason for audit	:	Initial qualification as supplier of APIs, reagents, and hardware kits
Date	:	11./12. December 2019
Auditor(s)	:	Dr. Rainer Suchi (Lead Auditor) Dr. Cecile Bourdeau (Subject Matter Expert) Prof. Marianne Patt (Subject Matter Expert) Dr. Almut Walte (Subject Matter Expert)
Approval: **(Signature of chair of SASAI board)**		_____
Date of approval: **(DD. MMM YYYY)**		_____

Content

1 Introduction

1.1 Description of the company

ABX was founded in 1997 at Dresden. Already in 1998, the first laboratory was opened at Radeberg with 5 employees. The production of reagent kits for the manufacture of PET radiopharmaceuticals started in 2001. Since 2006, ABX belongs to Cambridge Isotope Laboratories, a subsidiary of Otsuka Pharmaceuticals (Japan). In 2015, an own cyclotron became operational. This is used for R&D purposes. Since 2017 ABX also produces [^{177}Lu]Lu-PSMA-617, a radiopharmaceutical for use in clinical trials.
Currently, ABX has about 280 employees, amongst them more than 30 with a Ph.D.
The product portfolio comprises: production and development of PET and SPECT precursors and reference standards; manufacturing of reagents kits and cassettes; custom syntheses and manufacturing according to GMP for APIs; design, custom synthesis and production of peptides; preparation of ASMFs, US-DMFs and technical documents for reagent kits, cassettes, PET and SPECT precursors and the performance of stability studies. With this product/service portfolio ABX had sales of about 30 million Euro (2018), more than 80 % generated outside Germany.
ABX holds a Good Manufacturing Practices (GMP) certificate for active pharmaceutical ingredients (API) from the local competent authority (Landesdirektion Sachsen) and an ISO 13485 certification. It is also regularly inspected by the United States Food and Drug Administration (US-FDA).

1.2 Scope of the audit

The European Association of Nuclear Medicine (EANM) started the Shared Audit and Supplier Assessment Initiative (SASAI). The idea of SASAI is to perform quality audits of starting material suppliers by a small team of independent, qualified auditors and to share the audit report afterwards with interested parties. Main reason for this initiative is to help local PET centres in their duty to perform on-site audits for their suppliers.
The scope of the audit of ABX was the initial qualification as supplier of APIs, reagents and hardware kits. It should also serve as a proof of concept audit, and by successful completion demonstrate the general feasibility of the SASAI project.

1.3 Auditors

Lead auditor:

- Dr. Rainer Suchi
  Qualification: > 30 years' experience as quality assurance and quality control manager of a radiopharmaceutical company; qualified person; certified auditor; > 50 audits (GMP; GDP; Medical devices) as lead auditor

Subject matter experts:

- Dr. Cecile Bourdeau
  Qualification: 11 years' experience as radiopharmacist in production, quality control, quality assurance and regulatory affairs of radiopharmaceutical companies; qualified person; daily work with products from ABX (DOTA, precursors, reagent kits)
- Prof. Marianne Patt
  Qualification: 27 years' experience as research scientist, head of a university PET center; qualified person; daily work with products from ABX (DOTA, PSMA, reagent kits)
- Dr. Almut Walte
  Qualification: 13 years' experience as radiopharmacist, in research, quality assurance and quality control manager of a university radiopharmaceutical department; qualified person; daily work with products from ABX (DOTA, PSMA, reagent kits)

1.4 Persons met during the audit

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1.5 Regulations & Guidelines used as basis

- EU GMP VOL IV part II (API)
- ICH Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients
- Verordnung über die Anwendung der Guten Herstellungspraxis bei der Herstellung von Arzneimitteln und Wirkstoffen und über die Anwendung der guten fachlichen Praxis bei der Herstellung von Produkten menschlicher Herkunft (AMWHV)

1.6 Acknowledgement

The auditors wish to thank all involved persons for their open and cooperative attitude during the performance of the audit.

2 Observations and deviations

2.1 Facility Tour

- Goods receipt area
- Production
- Quality Control (QC)
- Warehouse for finished goods
- Packaging and Dispatch

2.2 Audited quality systems

- Company structure/org chart
- Review of relevant licences
- Date and result of last regulatory inspection
- Document control
- Training
- Deviation handling
- Corrective And Preventive Action (CAPA) process
- Change control process
- Complaint management process
- Recalls handling
- Release process
- Self-inspection program
- Validation and qualification program
- Maintenance/calibration program
- Pest control
- Environmental monitoring program
- Product Quality Review
- Data integrity policy
- Supplier management and contracted services
- Contract

2.3 Audited products

- Mannose Triflate bulk
- Hardware kit for F-PSMA
- Reagent/Hardware kit for Ga-PSMA-11
- PSMA 11
- Sterile closed glass vials
- Precursor for FET
- Salt solution

2.4 Deviations

2.4.1 Classification of detected deviations

Critical: The observed condition will seriously affect the quality of the product, violate essential GMP requirements and Quality Assurance practices or effect regulatory compliance. These observations require immediate action, e.g. stop production, product quarantine etc.

Major: The condition may affect the quality of the product. The observation documents a clear non-compliance with the GMP requirements and quality assurance practices. An action to be taken with a high priority is recommended.

Minor: This may not necessarily affect the quality of the product, but the condition violates GMP requirements. Actions should be taken within a reasonable timeframe.

Recommendation: These issues are not GMP violations and should be regarded as supportive for further improvements. They are recommendations made by the auditor for improvements to a process/ system.

2.4.2 Critical

2.4.3 Major

2.4.4 Minor

2.4.5 Recommendations

3 Summary

Lead auditor: Date:

Dr. Rainer Suchi

SME: Date:

Dr. Cecile Bourdeau

SME: Date:

Prof. Dr. Marianne Patt

SME: Date:

Dr. Almut Walte