Healthcare AI Quality

A pharma industry perspective

Dominik Schneider, Domain Architect Data & Analytics
Sebastian Fischer, Sr. Manager, Global Regulatory & Scientific Policy

AI Quality Summit - 2nd of November 2022
Agenda

1. Introduction
2. Current Approach for AI Quality in Healthcare Business
3. AI Act from a Pharma Perspective
introduction
Science is at the heart of everything we do.

From advancing genome editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – Merck is everywhere.
60,000 Employees worldwide

66 Countries

key figures

19.7 Sales (€ billion) in 2021

1668 Founded

2.4 R&D (€ billion)

Healthcare AI Quality
current approach for AI quality in healthcare business
There are several laws and regulations for the development and production of pharmaceutical goods and foods, summarized as „GxP“ (Good Practices) rules – in place to protect the customer.

- **GLP** - Good Laboratory Practices
- **GCP** - Good Clinical Practices
- **GMP** - Good Manufacturing Practices
- **Companion Diagnostics, MedTech** (e.g. devices for administration and tracking)
- **Pharmacovigilance**

**Primary guiding regulation and publications:**

- **FDA Title 21 CFR Part 11**: Electronic Records; Electronic Signatures - Scope and Application
- **EU GMP Annex 11**: Computerised Systems
- **ISPE GAMP 5**: A Risk-Based Approach to Compliant GxP Computerized Systems
An IT system needs to be GxP validated if:

- It can influence **product quality** or **customer/patient safety**
- It records/processes/stores data that is subject to regulations
- It can influence internal quality requirements

We distinguish in:

- **Qualification** of the Infrastructure Layer (Network, Server, IT is responsible)
- **Validation** of the Application Layer & Processes (Business is responsible)

→ **Focus here:**

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<th>GAMP category</th>
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<td>self-developed (AI) applications</td>
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<tr>
<td>configured commercial-off-the-shelf (AI) applications</td>
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For self-developed data & analytics (incl. AI) applications – GAMP category 5

Split into design & development, verification & validation and operations phase

Full traceability: user req. → functional req. → design / config. → test (functional and UAT)

Three environments: DEV, VAL, PROD
Techniques Applied for Quality Assurance

- Use cross validation techniques
- Know your use-case well, to assure dedicated selection of loss function (MSE, MAE, …) and dataset split (stratified k-fold, time series split, random)
- Feature importance for explainable AI
- Use simplest model to get the job done → explore a variety of algorithms during a PoC.
- Generally, rather be too conservative than positive.

Case: Analysis of scans from tissue samples through ML model → Immune status of patient, PD-L1 scoring.
Risk: Image or tissue artefacts, not sufficient no. of cells/tissues on image, text on image, …

QA approach (excerpt):
- Training of separate ML segmentation model that recognizes data quality issues in images
- Manual labelling of blurred image parts, training with DICE loss, performance evaluation based on hold-out set
- Data quality check using that model is applied ahead of actual image analysis
AI ACT FROM A PHARMA PERSPECTIVE
April 2021 – Proposal for a Regulation laying down Harmonised Rules on Artificial Intelligence and Amending Certain Union Legislative Acts:  Drafts AI Act

Horizontal Legislation

Risk-based Approach

Low

Medium

High

Healthcare AI Quality
EU Draft AI Act: Rules for MedTech

- **Essentially all AI-applications in MedTech are high risk**
  - Medical Device & *In vitro* diagnostic (IVD) Regulations (Annex II)

- **Very broad definition of AI: List of techniques (Annex I)**
  - AI Act applicable for large portion of “Software as Medical Device” (SaMD)

- **Involvement of Notified Bodies (NB) for certification**
  - Learnings from MDR/IVDR: Availability of NBs after AI Act coming into force?
EU Draft AI Act: Potential Impact on Pharma Development

- Pharmaceutical Industry uses a lot of Medical Devices and IVDs in development or uses them post-marketing.

- What about non-device AI applications in pharmaceutical development?
EU Draft AI Act: 
Non-Medical-Device AI in Pharma = AI in Medicines

Explicitly mentioned as high-risk applications (acc. to Article 6)?  
→ No.

Is it the intention of the legislator to regulate “AI in medicines” as high-risk?  
→ Probably(?)  
→ Why: Safety of patients is a key concern of the legislator (→ MedTech)!

AI in medicines could be added at any time to the high-risk scope - even after enactment of an AI Regulation:  
Authorization of EC to amend Annex II via Delegated Act (Art. 7)

What to expect from an European AI act in Pharma?
Thank You

Dominik Schneider
Domain Architect Data & Analytics
dominik.a.schneider@merckgroup.com

Sebastian Fischer
Sr. Manager, Global Regulatory & Scientific Policy
sebastian.fischer@merckgroup.com