LIFEFACTFUTURE

COMPUTERISED SYSTEMS AND GMP: REGULATION OF DIGITAL SOLUTIONS IN PHARMACEUTICAL MANUFACTURING

Report of LFF Regulation Event #1
05.02.2025

The first public webinar of the LifeFactFuture project addressed regulatory issues related to pharmaceutical manufacturing. Specifically, the webinar addressed the upcoming update of the Annex 11 of the GMP regulation which pertains to the use of computerized systems.

This report provides a short synthesis of the event.

The project LifeFactFuture is funded by Business Finland, 2024–26

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SUMMARY AND KEY POINTS

LifeFactFuture organized its **first public webinar February 5th 2025 addressing the regulation of digital solutions in pharmaceutical manufacturing**.

The webinar was very well attended with **more than 100 participants** online representing several universities, regulatory authorities, and **more than a dozen Finnish and international companies.** Although the primary focus of the event, as with the overall project, was Finland, the event even attracted international participants – for example, key representatives of international HQs of consortium partners and high-profile academics from non-Finnish universities.

For pharmaceutical manufacturing in Europe, digitalization is regulated by the Annex 11 of the Good Manufacturing Practice (GMP) guidelines for which the latest revision came into operation in 2011. A lot has happened to digital technologies since then, to put it mildly, and the need for revised guidelines has been widely recognized.

A drafting group under the European Medicines Agency (EMA) has been working to prepare a draft revision. The Drafting Group is chaired by **Ib Alstrup**, Danish Medicines Agency, with a representative of Finnish Medicines Agency (Fimea) among the other 13 group members. The revision process is time-consuming: The preparation of a draft concept paper began in October 2021 with a tentative timeline of final adoption in September 2026.

For the webinar keynote, Ib Alstrup presented the status of the revision. Since the revised draft has not yet been released for public consultation, some details are still tentative. However, the direction of the changes is very important for the pharmaceutical industry in Finland, and the presentation raised several important points. For example, it was clear that the new regulation provides clearer requirements for certain processes, highlights that the responsibility for compliance is always on the regulated user (i.e., it is not an acceptable excuse that third-party vendors such as cloud vendors are unwilling to provide certain legislation), and that the renewal of regulation is also putting barriers for traditional manual and paper-based documentation processes.

Widespread belief:
Regulation is limiting the possibilities of implementing new processes and procedures.

Reality:
Regulation is also limiting the possibilities of keeping old processes and procedures.

Implication:
What does this mean for your company's processes and procedures?

Elina Asikanius, Finnish Medical Agency, provided an insight into EMA and Fimea's reflections on the use of AI applications. She noted that the requirements are specific to the context of use, and that the use of AI does not change the requirements for the regulated user (e.g. the clinical trial sponsor, marketing authorization applicant/holder or manufacturer).

During both regulatory presentations there was a clear endorsement of using digital technologies, including AI technologies. Ultimately, it does not matter (much) to the regulator whether and how AI is used – the requirements stay the same. The use of Artificial Intelligence therefore needs to be conducted with a human-in-the-loop.

In addition to the important keynotes, the event featured brief introductions from LFF consortium leader **Toni Ahlqvist, Sara Gambier** (Bayer Oy), and **Pekka Mikkola** (DAIN Studios). The event also featured an interactive session in Miro (see highlights on p. 5), and a broad final discussion with panelists from Fimea, LFF university partners (UTU, HEL), and LFF companies.

HIGHLIGHTS FROM KEYNOTES

Below are some key points from the keynote presentations and the following Q&As:

Ib Alstrup (Danish Medicines Agency): "GMP Annex 11 Update (based on the Reflection Paper)

- A new annex on AI (Annex 22) will be created, separating this from the general regulation on computerized systems. The purpose is to future-proof the regulation through separating parts that require faster cycles of revision (AI) from more durable regulation.
- **IT security is considered, by inspectors, a critical and inherent part of GMP.**
- Without strong Access Management, Audit Trails and User Requirement Specifications (URS) a Validation Report is considered useless.
- There is an expectation that it should be possible to obtain data in an electronic format including the complete audit trail. An audit trail functionality which automatically logs all manual interactions on GMP critical systems, where uses, data or settings can be manually changes, should be regarded as mandatory.
- The audit trail should positively identify the user *who* made the change, give full account of *what* was changed, i.e. both the new and all old values should be clearly visible, it should include the full time and date of *when* the change was made, and the user should be prompted for a reason *why* the change was made. It should not be possible to edit audit trail data or deactivate audit trail functionality for normal or privileged users working on the system.
- The regulated user remains fully responsible when validation and/or operation is conducted by a vendor or a service provider. The user should ensure that documentation for provisions included in Annex 11 is available at their facility and can be explained during regulatory inspection. The user should have a contract with the vendor or service provider, including, but not limited to topics such as right to audit, agreed oversight (SLAs and KPIs), support during regulatory inspections, resolution of issues, and exit strategy.
- **If vendors, e.g., cloud providers, claim that these options are not possible, the result is that the user will not be compliant with GMP.** Users should therefore not accept this claim or enter into such contracts without certainty for GMP compliance. It is believed that the new regulations could help European pharma industry, now explicitly bound by regulation, vis-à-vis global cloud vendors.

Elina Asikanius (Fimea): "Use of AI in Medicine product lifecycle – Regulatory perspective"

The presentation provided the key highlights of the 2024 EMA Reflection paper on AI: *Link to paper.*

- Requirements for AI applications are specific to the context of use. A risk-based approach is encouraged with key focus on "high-patient risk" (for systems affecting patient safety) and "high regulatory impact" (for cases where impact on regulatory decision-making is substantial).
- Regulators assess the applicability and correctness of AI applications for a specific context of use. Sponsors are invited to follow the principles in AI RP and communicate proactively. Sponsors are encouraged to seek Scientific Advice early.
- Use of AI does not change the responsibility of the sponsor (clinical trial sponsor, marketing authorization applicant/holder, or manufacturer).

Exploring the Future of AI in Pharmaceutical Manufacturing

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The LifeFactFuture webinar underscored the transformative potential of AI in pharmaceutical manufacturing. It also highlighted the need for a balanced approach that fosters innovation while ensuring patient safety and regulatory compliance. The discussions emphasized the importance of collaboration between industry and regulators to navigate the complexities of AI implementation effectively.

The LifeFactFuture Webinar held on 5 February, "Computerised Systems and GMP – Regulation of Digital Solutions in Pharmaceutical Manufacturing", invited experts from the pharmaceutical and technology industries and regulatory agencies to discuss the evolving landscape of artificial intelligence (AI) in pharmaceutical manufacturing. The event featured insightful presentations and a dynamic panel discussion, shedding light on the opportunities and challenges that AI presents in this highly regulated industry. The event attracted almost a hundred participants, highlighting the significant interest in the evolving landscape of AI in pharmaceutical manufacturing.

Setting the Stage

The webinar commenced with a presentation by the Principal Investigator, Research Director **Toni Ahlqvist**, who introduced the LifeFactFuture (LFF) project. This Business Finland – funded initiative aims to accelerate the digital transformation of Finnish pharmaceutical and life sciences manufacturing by integrating world-class manufacturing with cutting-edge scientific knowledge and strategic foresight. Toni emphasized the project's objective of positioning Finland as a leader in data-driven capabilities within the life sciences and manufacturing sectors.

Sara Gambier, Product Supply IT Manager at Bayer Pharmaceuticals, followed with a presentation on the challenges and opportunities of integrating AI and digital solutions in pharmaceutical manufacturing. She highlighted the industry's struggle with adopting Industry 4.0 standards while other sectors are already progressing towards Industry 5.0. Sara underscored the importance of agility and rapid adaptation to these changes, emphasizing the need for regulatory frameworks to support this transformation.

Pekka Mikkola, Director, Industrial Data & Artificial Intelligence at DAIN Studios, provided a thought-provoking presentation on the current state of computerized systems and AI in the pharmaceutical industry. He discussed the rapid advancements in AI and robotics, emphasizing the necessity for companies to adapt to these changes. Pekka highlighted the importance of having a clear vision and strategy for AI implementation, focusing on people and processes rather than just technology. He also raised questions about the new opportunities and potential regulatory challenges that AI brings to the industry. *> Presentation slides*

Ib Alstrup, IT Medicines Inspector at Danish Medicines Agency and an expert at the scientific committee of the European Medicines Agency, provided an in-depth analysis of the upcoming changes to the EU GMP Annex 11, focusing on AI and computerized systems. He discussed the importance of robust access management, audit trails, and the validation of AI models, particularly in high-risk applications. Ib's presentation underscored the need for regulatory frameworks to evolve alongside technological advancements to ensure patient safety and product quality.

Elina Asikanius, Biostatistician at Finnish Medicines Agency Fimea, presented a reflection paper on the use of AI in the medicinal product life cycle. She emphasized that the requirements for AI applications are specific to their context of use, with a focus on high patient risk and high regulatory impact. Elina highlighted that the use of AI does not change the responsibilities of clinical trial sponsors, marketing authorization holders, or manufacturers. She also stressed the importance of having access to documentation and proactively communicating with regulators to ensure compliance. *> Presentation slides*

Panel Discussion: Opportunities and Challenges

The panel discussion featured **Hanna Soinio** (Computer System Validation Team Lead at Bayer Oy), **Mirka Laavola** (Senior Inspector at the Finnish Medicines Agency), **Mia Sivén** (Associate Professor of Sustainable Pharmacy at the University of Helsinki), and Pekka Mikkola from DAIN Studios. Each panelist shared their perspectives on the current and potential applications of AI in pharmaceutical manufacturing.

Hanna highlighted the use of AI for data analysis and documentation, noting that AI could significantly expedite the creation of validation documents and improve data quality. She also emphasized the importance of maintaining data integrity and IT security when implementing AI solutions.

Mirka discussed the regulatory perspective, pointing out that while AI offers numerous benefits, it also poses risks if the data used for training models is incorrect or biased. She stressed the need for cooperation between regulators and the industry to ensure that AI applications are both innovative and compliant with regulatory standards.

Mia focused on the research and development phase, where AI can handle large datasets and identify patterns that might not be apparent through traditional methods. She also highlighted the potential for AI to enhance sustainability in pharmaceutical manufacturing by optimizing processes and reducing waste.

Pekka provided insights into the practical applications of AI, such as using AI to predict issues in manufacturing processes and improve operational efficiency. He also raised concerns about Europe's position in the global AI landscape, emphasizing the need for robust regulatory frameworks that support innovation while ensuring safety and compliance.

Collaborative Reflections

An interactive session using Miro was conducted during the webinar, where participants were invited to reflect on the presentations and share their views on various topics related to AI and computerized systems in pharmaceutical manufacturing. They were encouraged to provide insights on how AI is currently used in their work, potential applications, and the challenges they face. This session aimed to gather diverse perspectives and foster a collaborative discussion on the future of AI in the industry.

A Collaborative Path Forward

The LifeFactFuture webinar underscored the transformative potential of AI in pharmaceutical manufacturing. However, it also highlighted the need for a balanced approach that fosters innovation while ensuring patient safety and regulatory compliance. The discussions emphasized the importance of collaboration between industry and regulators to navigate the complexities of AI implementation effectively.

This was the first public event of the LifeFactFuture project. A second event focused on the regulation of medical devices is currently in planning.

As the LifeFactFuture project continues to explore the futures of life science manufacturing, events like this webinar play an important role in enabling more opportunities for conversation and collaboration. By bringing

together diverse perspectives and expertise, the LifeFactFuture project is well-positioned to speed up the introduction of digital solutions and more efficient utilization of data and to make Finland the most attractive place in the world for investments in data-driven life science manufacturing.

Tero Villman, Mikkel Stein Knudsen & Keijo Koskinen
Finland Futures Research Centre, University of Turku

The basics of the text was formulated using AI.

SOME KEY REFLECTIONS FROM MIRO

Reflections on presentations and discussions

Excellent that we will have revised regulations. The risks can be quite high with new technologies, a conservative approach is understandable.

Were the best practices of other regulated areas reviewed so that pharma is not re-inventing the wheel in AI regulations and usage of cloud environments?

It's still important we find new ways on how to inspect compliance for more complex solutions. Validation methods for AI solutions can not be the same as for CS's.
This requires new skills from auditors that they are inspecting things that are critical from patient safety point of view and having less focus on fitting old ways of working into advanced solutions (e.g. having more trust in human manual performance than electronically derived data).

AI black box paradigm is not an issue from a regulatory perspective

Good reminder of the importance of URSs

Do regulators and manufacturing use the same language?
Do we need a 3rd language as a bridge?

Let's not treat AI/ML as one, traditional regression for predictive maintenance is very different from LLMs.

Reflections on current usages of various systems

AI Validation	Machine Learning	Self Learning AI
Ensuring data quality	Quality control	ML Models are used for supporting human, so it is human decision eventually anyway
Testing and verification	Camera systems	
Validation and qualification testing and documentations, regular calibration cycles	Following MLOps practices	
SOP exists, but not yet validated any AI solution		

FULL EVENT AGENDA

Wednesday 05.02.2025 at 12.00–15.00 (online in Teams)

The LifeFactFuture consortium organizes webinars related to life sciences sector regulation. This topic is relevant to all companies in the field, from manufacturers to technology solution providers. Since the regulations for pharmaceutical manufacturing differ significantly from regulation of for medical device manufacturing, we will be holding two separate and targeted regulation workshops.

The first event will focus on issues related to pharmaceutical manufacturing. The webinar will specifically focus on the update to Annex 11 of the GMP regulation which pertains to the use of computerised systems. This covers all aspects of digital solutions for which companies must comply with within their GMP-related activities. Annex 11 is currently being updated, and the emerging regulation, including new sections on AI and ML, will be sent for public hearing soon (likely by end of 2024). During the webinar, the head of the EMA working group drafting the new regulation, ***Ib Alstrup*** from the Danish Medicines Agency, will present it. This is important information, as it dictates what is and what is not allowed in pharmaceutical operations.

PROGRAM

12.00 'The Futures of Life Science Manufacturing – Introductions from the LifeFactFuture consortium': ***Toni Ahlqvist*** (UTU), ***Sara Gambier*** (Bayer) and ***Pekka Mikkola*** (DAIN Studios)

12.15 'The New GMP Annex 11: Changes and Cases', presentation by ***Ib Alstrup***, Danish Medicines Agency

12.45 Q&A and discussion with Ib Alstrup

13.15 'Reflection Paper on the Use of Artificial Intelligence in the Lifecycle of Medicines', presentation by ***Elina Asikanius***, Finnish Medicines Agency (FIMEA)

13.30 Short break

13.40 Interactive Miro session: Reflections, cases, and impacts for your own work – computerized systems and AI in pharmaceutical manufacturing

14.10 Panel discussion with ***Hanna Soinio*** (Bayer Oy), ***Mirka Laavola*** (FIMEA), ***Mia Sivén*** (University of Helsinki), ***Pekka Mikkola*** (DAIN Studios) and ***Toni Ahlqvist*** (UTU).

14.45 Summary and closing the event

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