Inspections and Regulatory Harmonization Alternative Tools

Workshop Session 2 – 26th January 2022

U.S. FOOD & DRUG ADMINISTRATION

Inspections and Regulatory Harmonization

Alternative Tools

from a regulatory perspective

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Regulations for inspections

- 601.20(a): A biologics license application shall be approved only upon examination of the product and upon a determination that the product complies with the standards established in the biologics license application and the requirements prescribed in the regulations in this chapter

- 601.20(b)(2)(c): No product shall be licensed if any part of the process would impair the assurances of continued safety, purity, and potency

- 600.20: Inspections shall be made by an officer of the Food and Drug Administration having special knowledge of the methods used in the manufacture and control of products

Alternative tools

- Alternative tools include
  - Assessment of records and other information requested under section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act
  - Voluntary Remote Interactive Evaluation (RIE)
  - Review of inspection reports by inspectorates under a Mutual Recognition Agreement (MRA) and confidentiality agreements

- These alternative tools are **not** considered inspections

- 483 under Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) is not issued

Remote Interactive Evaluations (RIE)

A new tool?

Video conferences

Screen sharing records

- "Guidance on Remote Interactive Evaluations of Drug and Bioresearch Monitoring Facilities" – Published April 2021
  - *Voluntary* assessment of a facility where drugs are manufactured, processed, packed or held that uses remote interactive tools such as live stream or prerecorded videos
  - An RIE will not constitute an inspection
- FDA is assessing challenges with IT, infrastructure and equipment; regulatory strategies and limitations; establishment capabilities

Pros and Cons of Alternative tools

- Pros
  - Evaluation of a facility when travel is not feasible
  - Prioritize which establishments to perform on-site inspections
- Cons
  - The firm controls the camera and thus, regulators see what the firm wants to the regulators to see
  - Regulators can not use all their senses
  - Time difference


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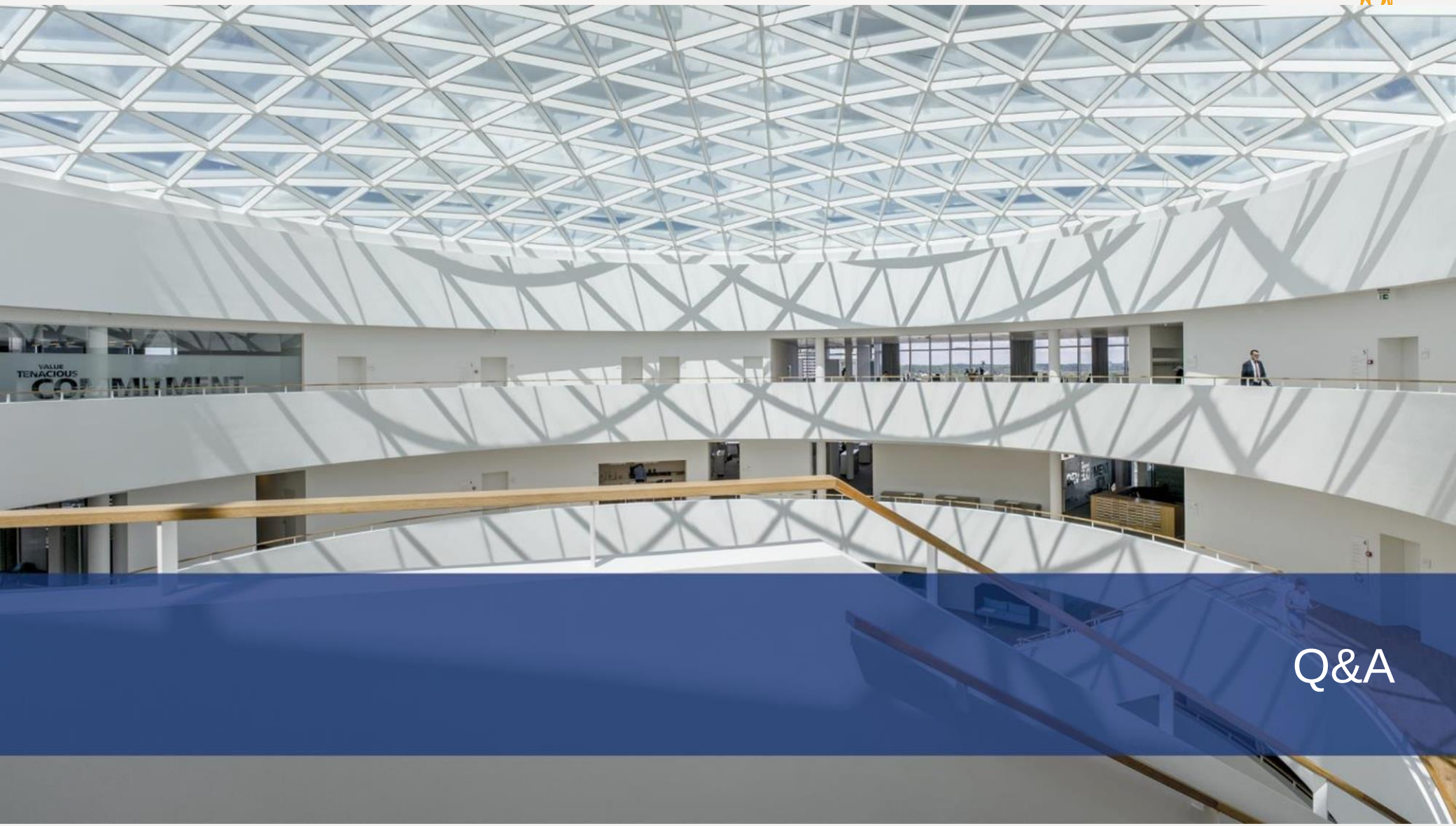


Q&A

Inspections and Regulatory Harmonization: Alternative Tools

26 January 2022
WCBP Workshop

Søren Thuesen Pedersen
Novo Nordisk A/S
Quality Intelligence and Inspections

The Novo Nordisk Quality Mission:

Agenda

Inspections and Regulatory Harmonization: Alternative Tools:

As seen from a European pharmaceutical company

The burning platform after 11th March 2020

We need a ‘standardized’ way through this!

We needed to engage with peers and regulators

Activities started (almost immediately) in:

- BioPhorum (BPOG) Working Group on Remote Inspections (Guidance is in the link)
- IFPMA Task Force on Remote Inspection (PtC is in the link)
- BIO Inspection TF focus on remote inspections (USA)
- EFPIA Manufacturing Quality Expert Group, MQEG (Inspection survey is in the link)

- First question: Can we engage regulators to use each orthers work where applicable (Reliance) ?

Podcast

- BioPhorum Webinars – BioPhorum

BioPhorum introduces – developing good practices for remote inspections in the Covid era

09th June, 2021

In normal conditions, regulatory inspections and audits are conducted on-site, however, travel and social restrictions due to the Covid-19 pandemic have forced regulatory inspections and audits of affiliates to be conducted remotely.

This is a very different way of working and a multi-company collaboration, comprising subject matter experts from 29 BioPhorum members, has shared case studies and discussed the practical factors that make remote inspections and audits effective. Learning from post-inspection feedback from inspectors has also been shared. This experience has been captured in *Peer to peer practical guidance on remote inspections and audits*.

In this podcast, a member of the collaboration, Søren Thuesen Pedersen, Senior Director of Quality Intelligence and External Affairs at Novo Nordisk, talks to Dawood Dassu, BioPhorum Fill Finish Lead.

Remote Inspections in Novo Nordisk 2020-2022:

- Russia
- Denmark
- Notified Body
- Korea

Lessons learned in Novo Nordisk

- Very, very resource intensive:
- Number of documents requested prior, during and after to the inspection vs. reviewed
- Requires a lot of practical coordination and rehearsals (IT platform, WebEx)
- Mapping of Wi-Fi!

- Inventions: Use of phones vs. scanning equipment
- The very ‘fancy’ optical equipment can be a help but in many instances a smartphone will do
- Trade secrets!
- Use of Affilate Offices. Good and bad aspects.
- Translation is critical.
- Pre-recorded videoes are labor intensive (Expert needs to be present at inspection too) vs. real-time streaming

Worth noticing on remote assessments

1. MHRA Putting patients first: A new era for our agency Delivery Plan 2021-2023:

"Pilot voluntary 'pre-inspection' checks to fast track new applications for manufacturing licences and piloting the use of consultants as 'compliance monitors' in remediation cases by Q3, 2021/22; roll out of automated inspection reports and identify new risk-proportionate approaches with our international partners by Q4, 2021/22; embed file-sharing platforms for remote inspections and visual technology capabilities as a standard part of inspections in 2022/23."

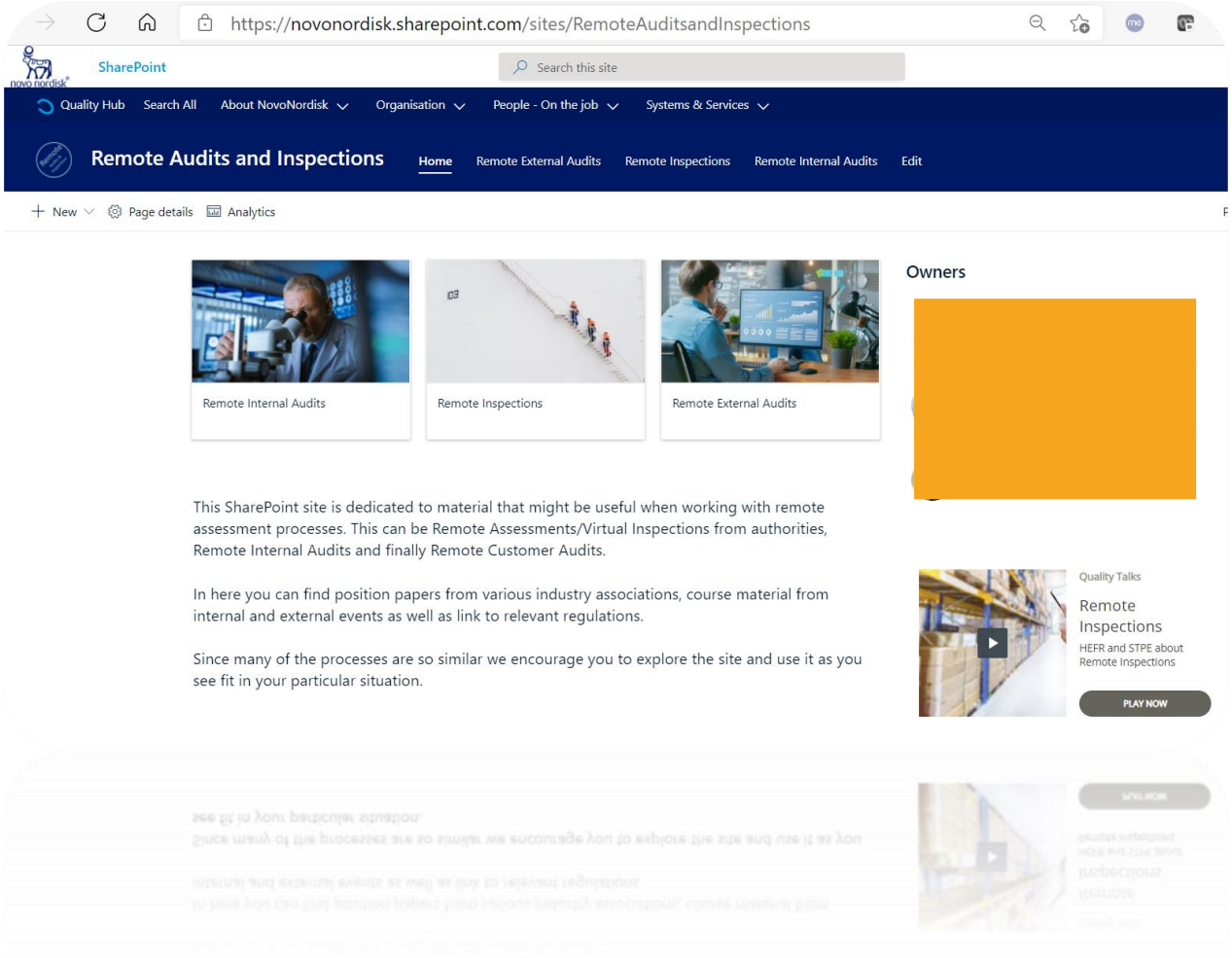
2. ICMRA: Summit Report 1.-2. December 2021

- PQKMS: Two pilots have been developed: one on collaborative assessment between regions for post-approval change management protocols striving to achieve common outcomes, and the other one on hybrid inspections, where one region is physically performing the inspection on site and one or more other participating remotely.

- Digital transformation of GCP and GMP inspections and clinical trials

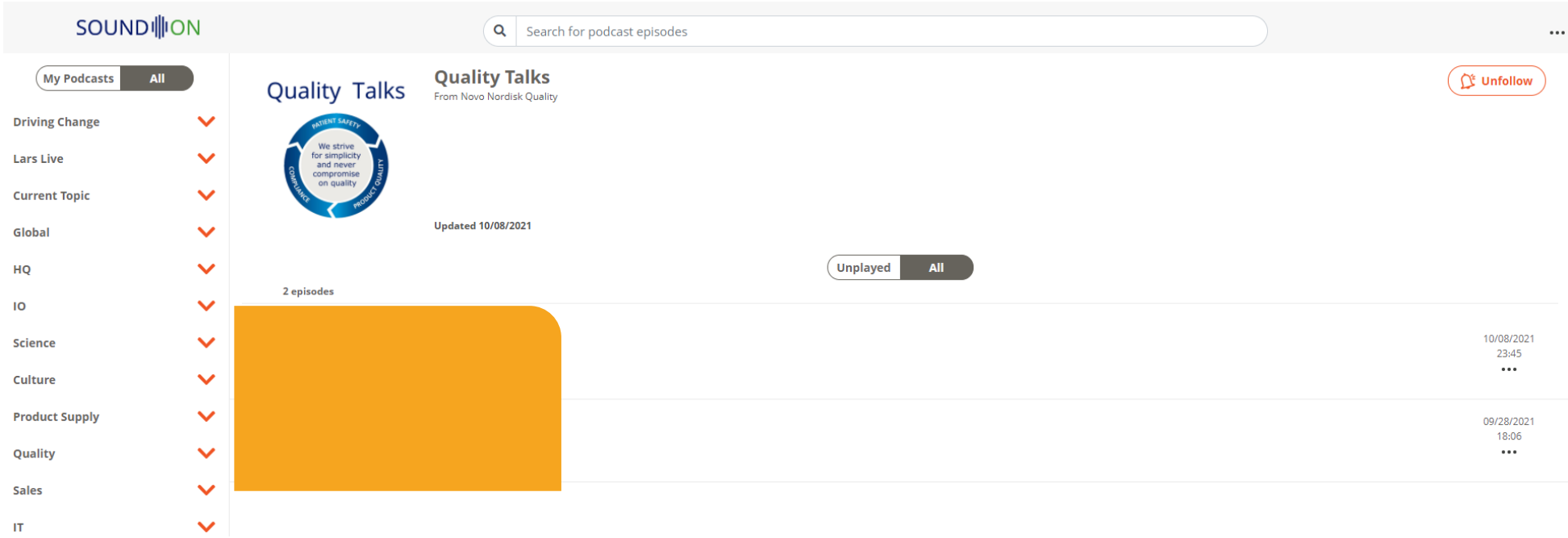
Novo Nordisk Sharepoint site

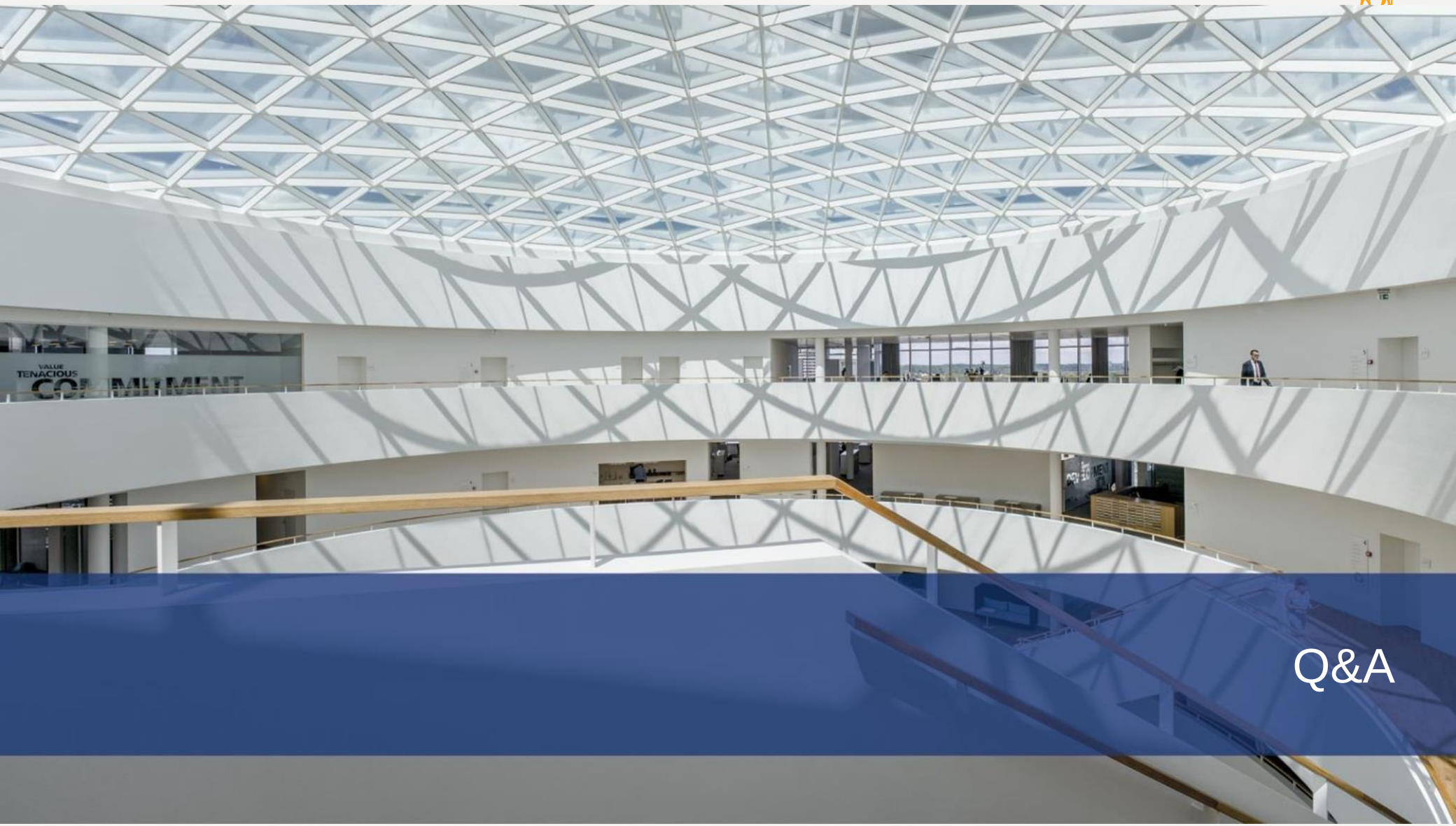
We gather all information about remote assessment in one site



Our new Podcast series in Novo Nordisk Quality Talks

- Remember to ”Follow” (Like and subscribe)





Q&A

Remote assessments

Isabelle Lequeux

Regulatory Lead, Regulatory and Partners

CONNECT
COLLABORATE
ACCELERATE™

Background

28 companies and 30 senior subject matter experts came together

to face the new 2021 requirement for biomanufacturers to face remote assessments for site certification or product licensing

The team **shared experience** and know-how on how to best to facilitate remote assessments to avoid delays and inefficiencies

A **good practice paper** was delivered, with useful practical advice to help which is in line with the individual guidance from Health Authorities

In general, industry experience of remote assessments is positive, but **securing confidentiality remains a challenge**, and there is significant increase in documentation requests and translations, ‘out-of-office’ hours Q&A and time zone differences does put a burden on colleagues

As the pandemic ebbs and flows **there remains uncertainty** as to what the Health Authority plans are for remote assessments

1 The more effective remote assessments involved a pre-work with the Inspector team

- **Clarify the purpose** and scope of the assessment
- **Set the appropriate timelines**, noting that additional preparation time is required for remote inspections, and more documents may be requested
- **Agree the stages** of the assessment (opening meeting, updates, meeting breaks, document review, Q&A, and closing meeting)
- **Align on how inspectors will provide periodic updates** (e.g. daily wrap-ups, daily check-out lists)
- **Confirm how data will be delivered** to the inspectors (which system(s) will be used)
- **Align on the format** - how documents will be provided and how the virtual (video) facility tour will be conducted (e.g. live or recorded). Decide balance between document review, presentations and simulation of an on-site experience
- **Align on the language** of the assessment and any translation needs. Note that 'live' translation can be difficult during a remote assessment
- **Agree on communication pathways** for any questions or clarifications on documents – Decide when it will be acceptable to provide an overview/response letter rather than submitting an entire document

2 Some good practices during remote inspections

- **Use and agreed plan for responsibilities** covering decision making and information flow (a RACI model is a useful tool for this)
- **Assign a moderator** for the virtual conference inspection rooms. Control the number of internal observers on the call (place control on chat threads) just as you would with an on-site inspection
- **Conduct daily wrap-up meetings** with the inspectors and reconciliation meetings with the internal inspection team
- **Have an IT technical expert** on standby
- **Have key documents translated** in advance (simultaneous translations are difficult)
- **Prepare storyboards** to clarify or introduce topics; with diagrams and photographs ready to explain any technically complicated topics
- **Expect inspectors to want to stop and zoom** in on features to allow them to absorb what they see, As the field of view is narrower on video, They may also ask to move the video forward or backward – they are in control
- **Directly check with inspectors** go know if a question has been fully answered or a document review completed – prepare to be flexible
- **Be mindful that it isn't possible to talk** the inspector through documents as happens during an on-site inspection

3 Available IT has been used to date, and new VR tools are being tested

- **Meeting conferencing platforms** (e.g. MS Teams, Google Meet, Zoom, WebEx, etc.
- **Document-sharing platforms** (e.g. OneDrive or EngageZone)
- **Document cameras** (e.g. ELMO) Video-enabled devices (e.g. smart glasses, cellphones, tablets)
- **Supporting equipment and applications** – Video-stabilizing equipment (e.g. gimbal, selfie stick) – Audio enhancers (e.g. microphones used to reduce noise in high-traffic areas) – Cameras suitable for solvent-rich API facilities

Questions to the Audience

- *From your point of view, what are the key challenges of remote assessments (industry perspective and regulatory perspective)?*

- *How are our organizations responding to these challenges?*

- *Are remote assessments here to stay or will they disappear when site visits and the physical presence is back on a routine basis? Is there a place for remote assessments besides audits/inspections/evaluations?*

- *Are inspections needed as often as they take place? Could we rely more on the work carried out by other regulatory agencies? Can we utilize existing Mutual Reliance Agreements (MRA's) in a better way? What are the main blockers to reliance on a GMP inspection by a Pharmaceutical Inspection Co-operation Scheme (**PIC/S**) member to be accepted by another PIC/S member?*