

THE EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES & HEALTHCARE (EDQM)



EDQM's Real Time Remote Inspections

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EDQM's GMP Assessment: Overview

On-Site Inspections

- Traditional inspection approach
- EDQM inspects about 40 sites per year

Paper based GMP Assessment

- Complementary to on-site inspections
- Up and running since 2010

Real Time Remote Inspections

- Under development
- First inspections done
- Aka **RTEMIS**

Real Time Remote Inspections: Scope

Travel restrictions, e.g. pandemic situations, safety concerns in destination country etc.

A potential regular process for sites which showed a good level of GMP compliance during previous EDQM inspections

A potential process to verify the implementation of specific parts of a CAPA if deemed necessary

If urgent GMP evaluation is needed, e.g. specific topic evaluation. In this case, the RTEMIS would not replace an on-site inspection, but allows an immediate assessment of a specific situation/aspect that might pose a risk to public health

Process flow (1)

Preparation 1/2

- More complex preparation
- Agreement on technical solutions (software/hardware)
- Connection trial: test of web conference tools and connectivity in the manufacturing areas

Preparation 2/2

- Review of larger number of documents by inspector(s) prior to the inspection in order to save time ahead of the inspection

Conduct

- Opening meeting
- Discussion of documents reviewed ahead of the inspection
- Document review/visit of manufacturing areas will be alternating
- Document review to be performed via screen sharing as well as via document camera / visual document presenter
- If needed daily wrap-up
- Closing meeting

Process flow (2)

- Follow-up is the same as for on-site inspections:
 - List of GMP deficiencies to be issued by EDQM within six weeks
 - CAPA expected within four weeks after receipt of the list deficiencies
 - Inspection report to be issued following CAPA review within 6 weeks

Essential Tools (apart from inspectors...)

Document sharing tool

web conference meeting applications

Webcams

3G/4G networks

Broadband internet

Scanner

Mobile Wifi hotspots

Document Sharing

- Done via a secure Collaboration Tool
- The data are stored on a secure EDQM server
- The inspected company is granted access to a defined folder structure to upload documents in real time during the inspection

Gear / equipment (1)

- Cell phone camera
 - Requires mobile phones suitable for hazardous areas: “intrinsically safe mobile phone” or “intrinsically safe mobile tablets”
 - Number of hardware available from different manufacturers
 - Installation of different videoconference applications
 - Example:



Gear / equipment (2)

- Head-mounted device
 - Comes also as “intrinsically safe”
 - Operating system allows different videoconference applications installation
 - Highly efficient tool
 - Example:



Gear / equipment (3)

- Document viewer

- To be used to review non-electronic documents, such as batch manufacturing records, logbooks etc.
- Functionality needed: real-time projecting
- Example:



Software Applications

- Specific web conference applications, which present the least security issues, were recommended by EDQM's IT department
- A second web conference application should always be installed:
 - as part of a back-up strategy in case problems with the primary one were encountered
 - to allow the inspectors to work in parallel, when needed
- For both applications it is recommended to install the clients on all computers/smartphones and if authorised by QA also on computerised systems that will be used as they will have more functionalities compared to the browser based use.

Main site selection criteria used in the pilot phase

- NB: criteria used will be adapted after the pilot phase

Site already inspected
by EDQM:
Knowledge of site

No negative
compliance information
in data bases

Site ideally located in
industrial areas:
communication
infrastructure

First inspections performed in 2020-2021

- Three manufacturing sites located in India
- Duration 5-6 days, approx. 6 hours per day

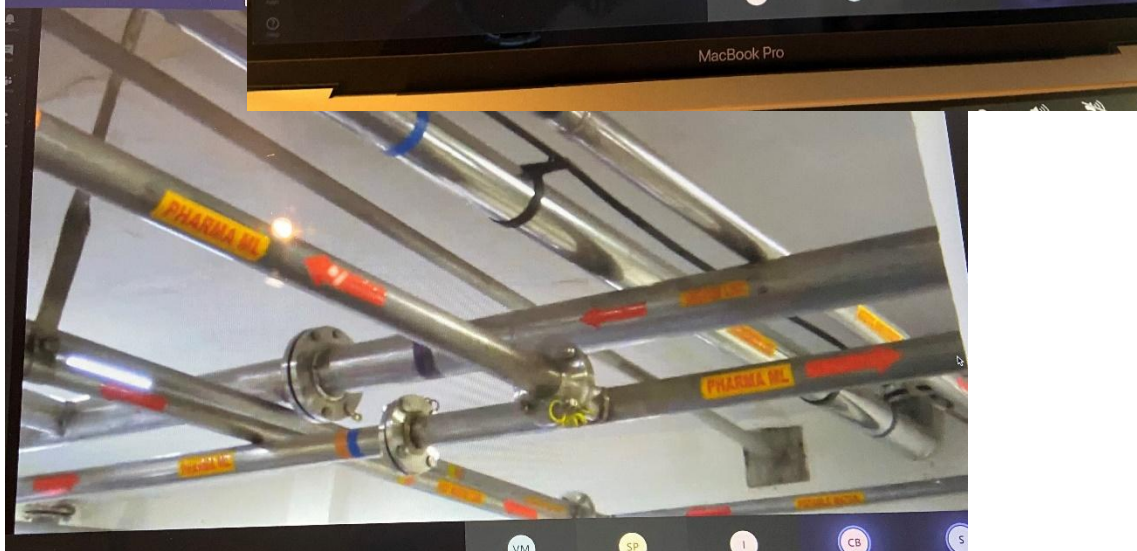
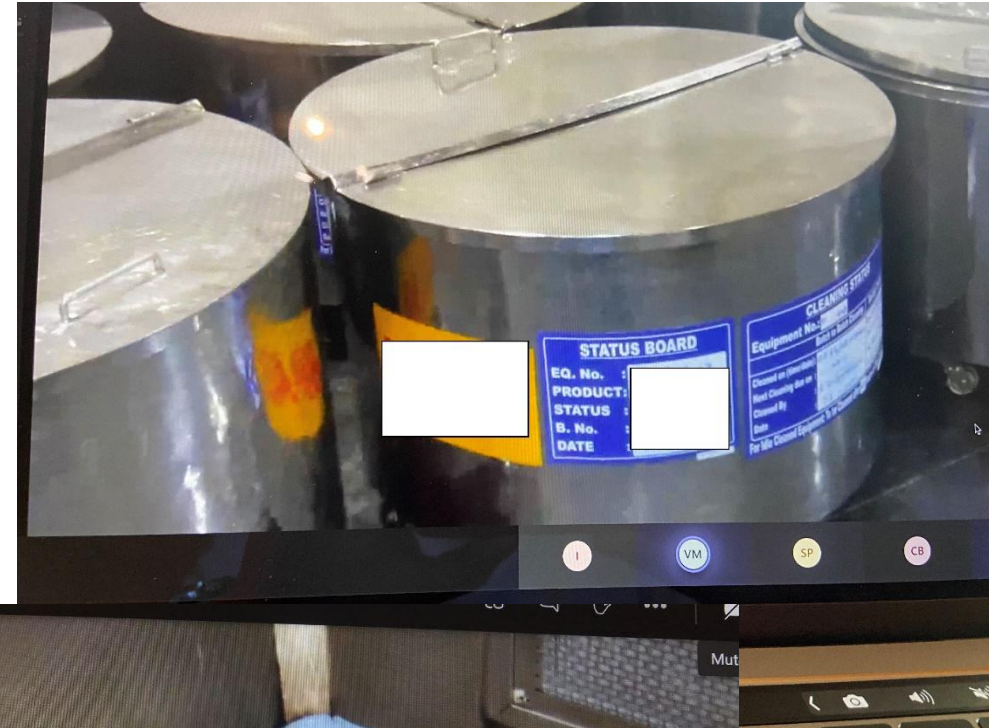
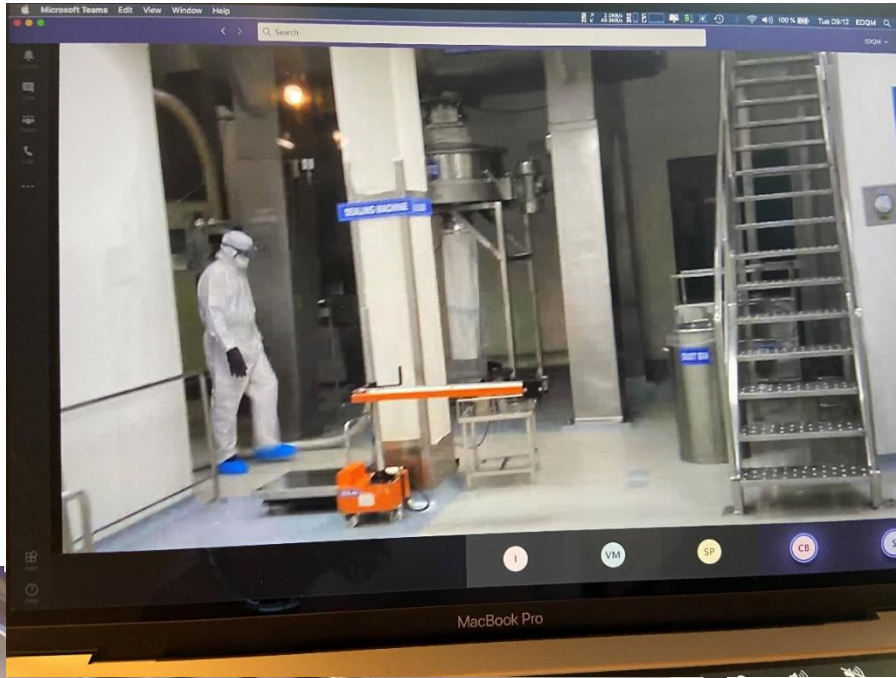
First experience gained (1)

- Connectivity test and first 3 remote inspections: successful
- Two web conference applications used, the second one when two teams needed to be set up for review of different documents in parallel
- Document viewer used for review of printed documents: results satisfactory for typed text, not always very clear for handwritten ones (in some cases it was preferable to scan and share electronically)
- Deficiencies were identified during all 3 remote inspections

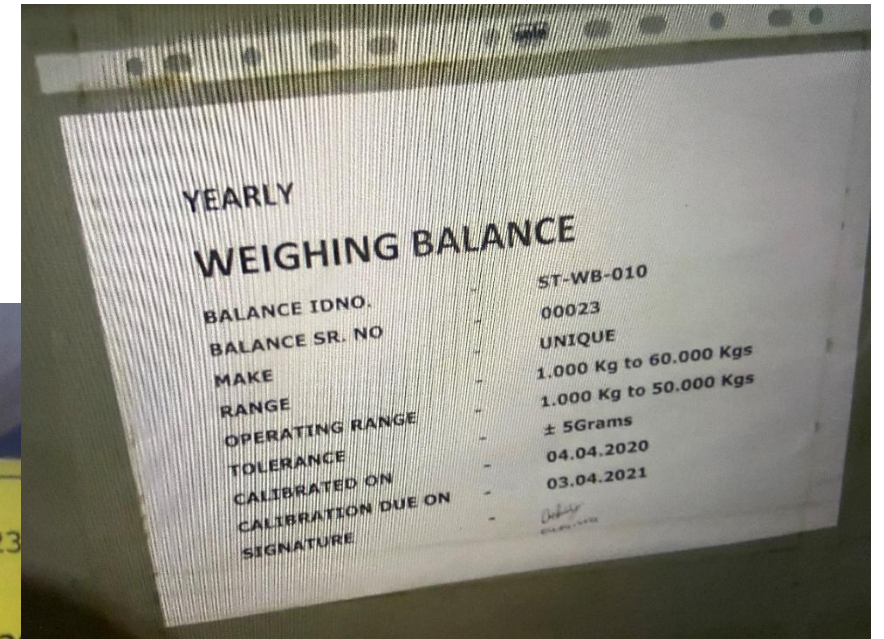
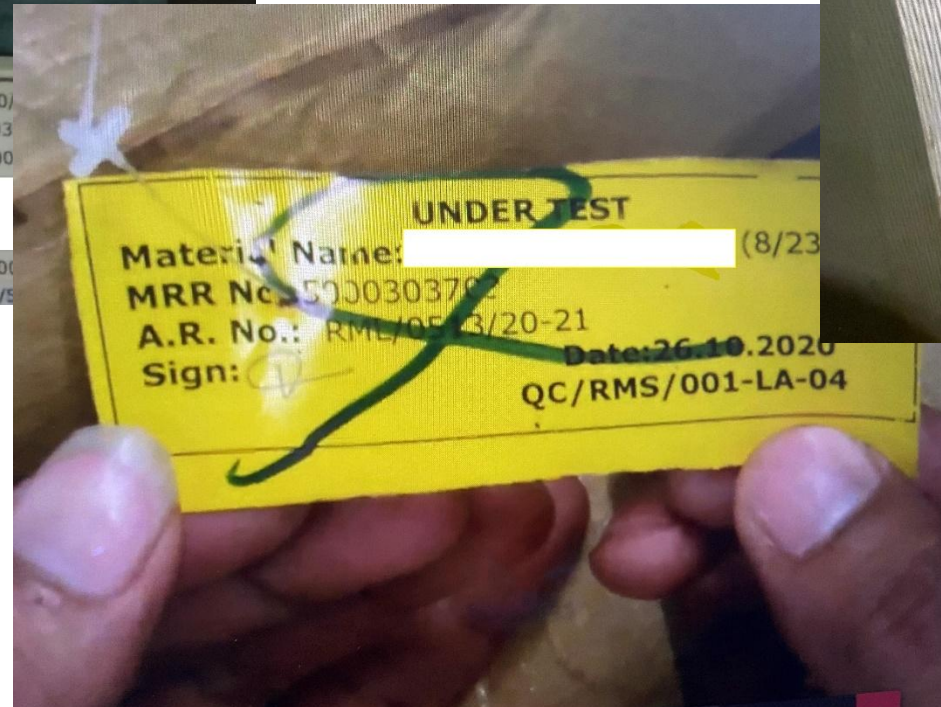
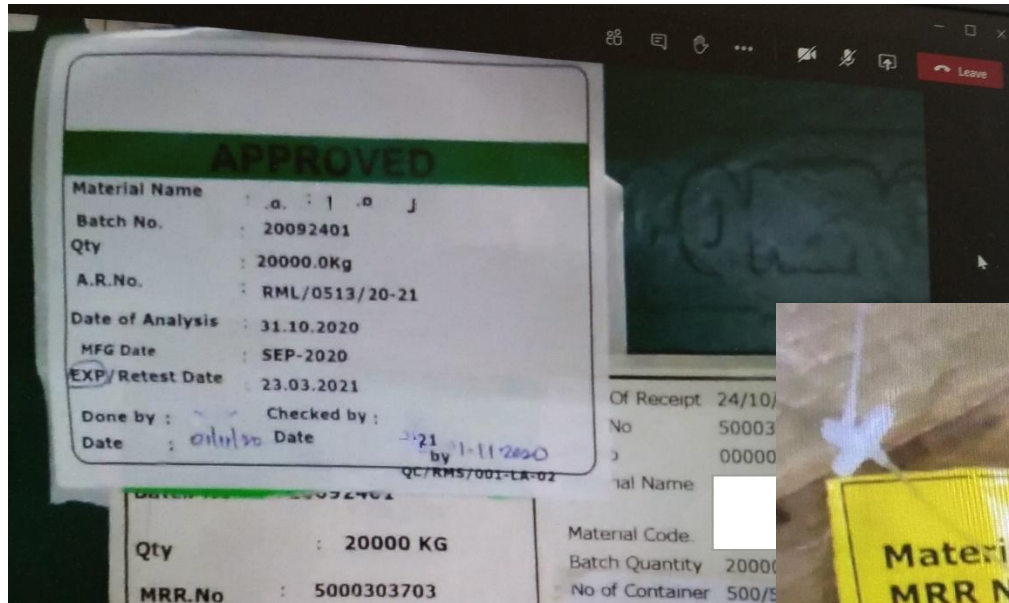
First experience gained (2)

- Head mounted camera used for site tour:
 1. Connection established in all areas visited; short interruptions in parts of clean area, usually small rooms with many walls
 2. Video quality very good; difficulties with computer screen views (suggestion: photographs could be taken by cell phone and shared)
 3. Sound quality generally good; difficult for camera operator to hear instructions in noisy areas (could be solved either by the operator receiving instructions by moving to quieter areas and/or by communicating via cell phone used by a second person nearby)
 4. Camera battery lasts ~2,5 hrs, should be taken into account when planning the site visit; the availability of a back-up battery might also be considered

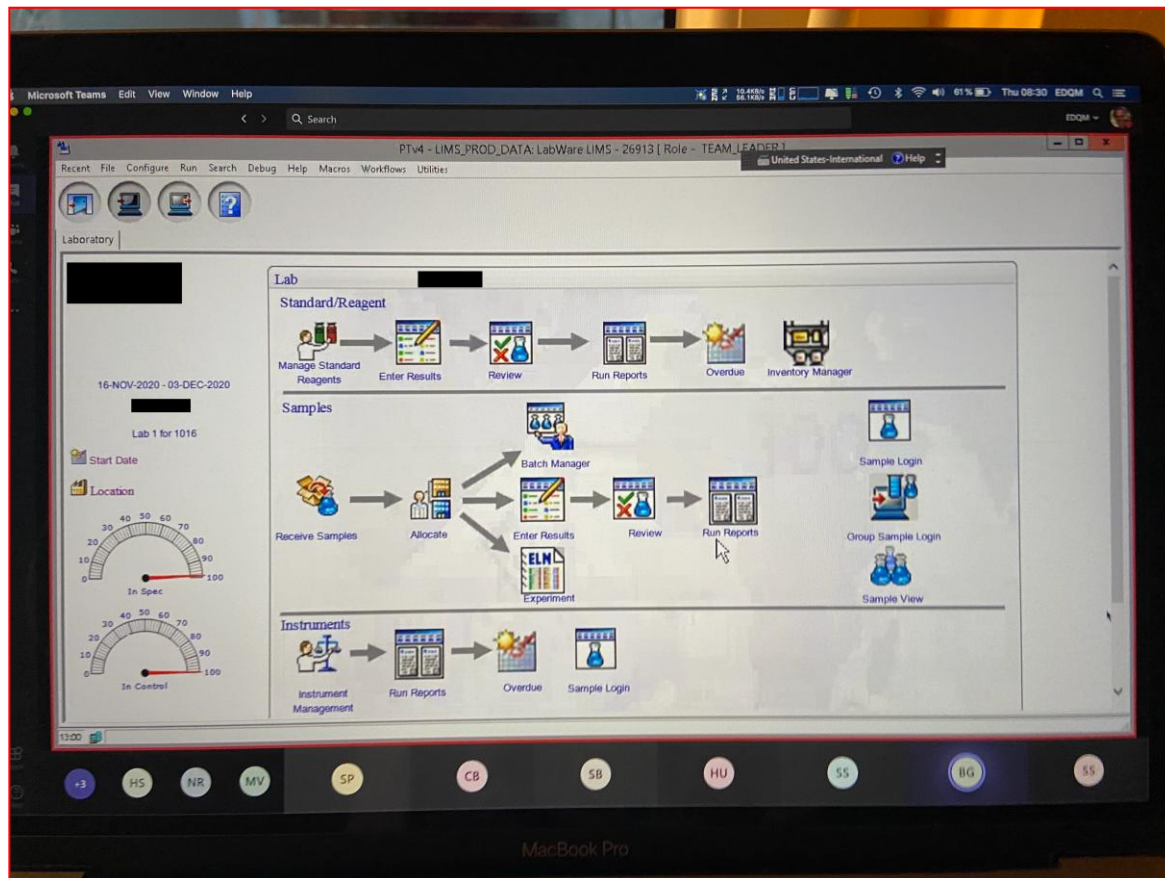
First experience gained – visual feedback



First experience gained – visual feedback (cont.)



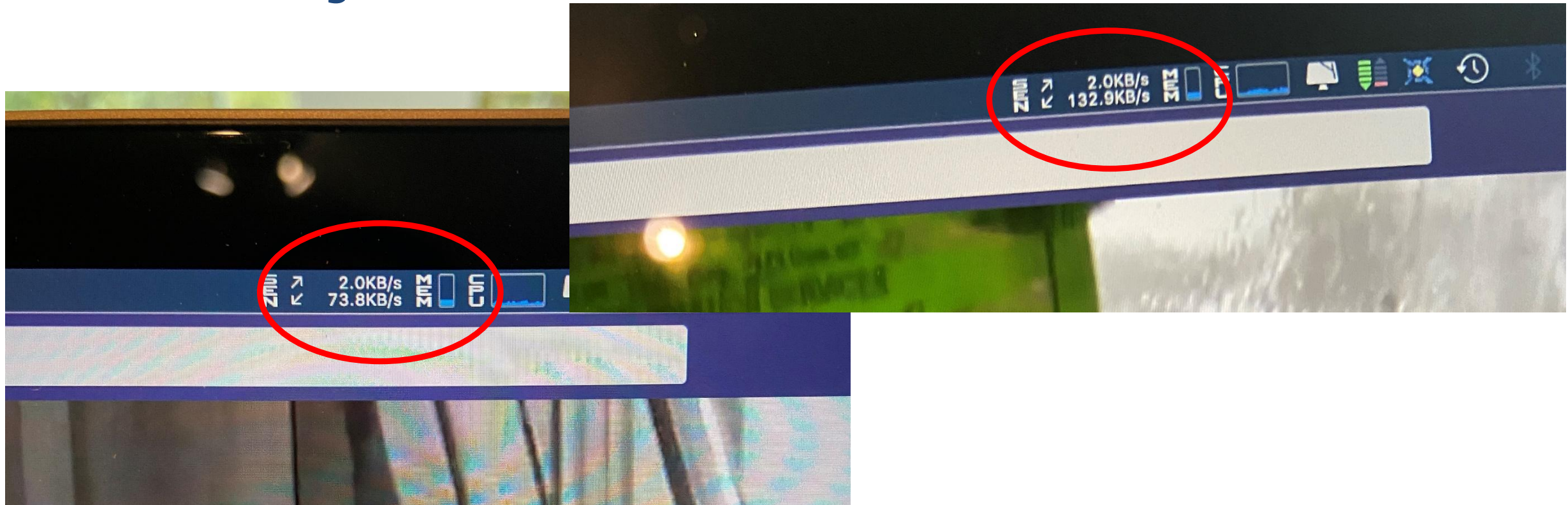
First experience gained – visual feedback (cont.)



Autoscale or fixed: From -10000.000 mAU to 100000.000 mAU	
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First experience gained – visual feedback (cont.)

- The data transmission rate should not be less than 100KB/sec in order to ensure a steady footage - easy to achieve when using broadband in meeting rooms, but a challenge when using mobile hotspots / Wifi in manufacturing areas



Considerations after the first inspections (1)

- Options for data integrity verification: controlled access to CS / retrieval of data using a stand alone computer / review of exported audit trails
- Inspectors work in parallel when needed, using both conferencing tools
- One main facilitator at firm's site: interacts with other colleagues, clarifies inspectors demands/queries, etc.
- Predefined structure of upload folder, e.g. topic wise or day wise. Sound naming of uploaded files is important

Considerations after the first inspections (2)

- High performance scanner availability to scan and send/upload documents which cannot be reviewed properly by document viewer
- In case of bad coverage, time constraints or lesser need to check in real time specific less important areas, inspectors could request the firm to take a video and upload it straight away for review

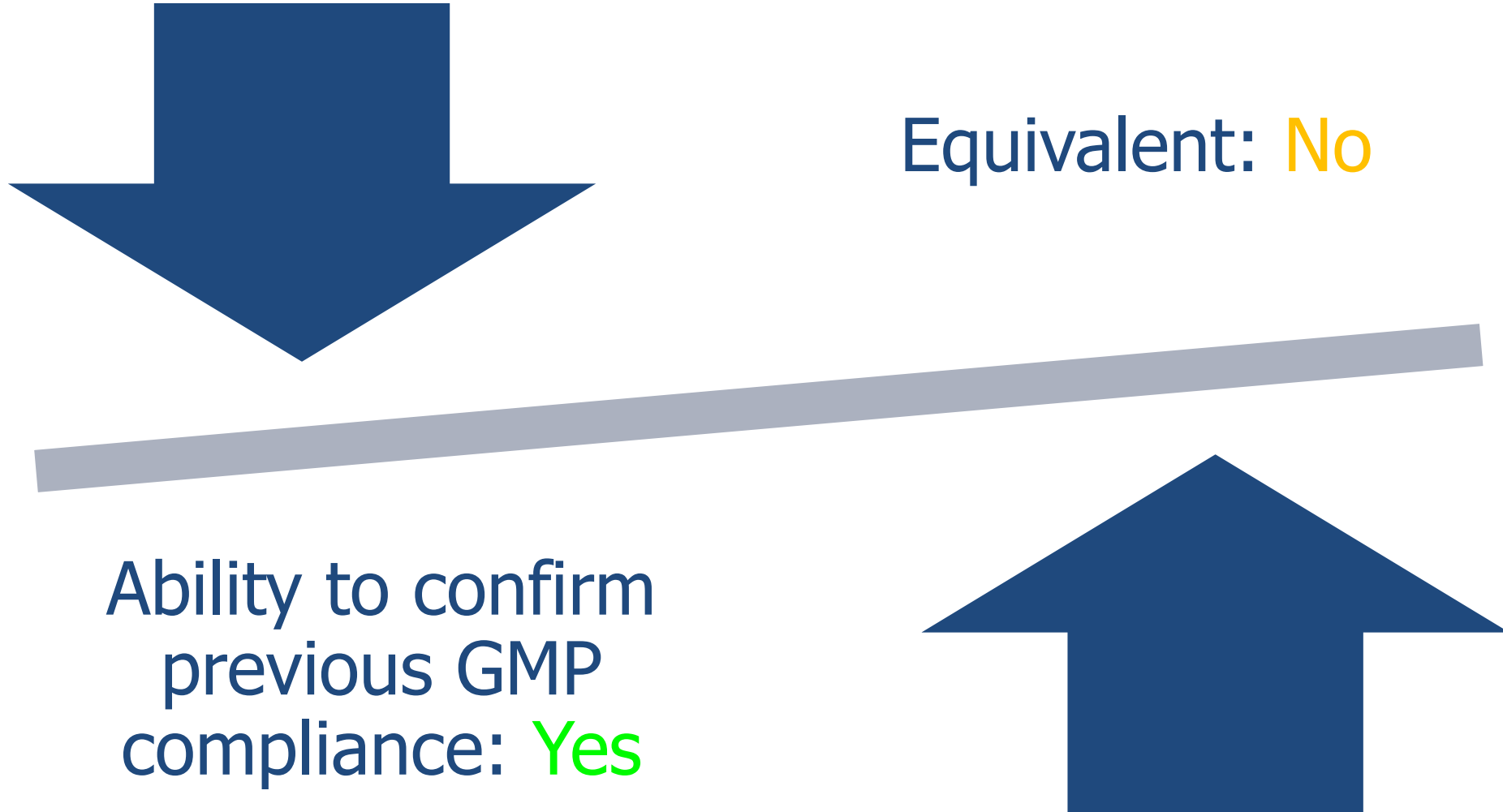
Challenges

- Technical difficulties depending on area connectivity, staff's technical experience etc.
- Not easy to substitute certain elements of on-site inspections, such as the ones of surprise and body language interpretation

Advantages

- Provides a possibility to evaluate the GMP compliance of a firm when an on-site inspection cannot be performed or is deemed of lower priority
- Allows real time interaction with the firm concerned
- Saves financial and human resources (both for the EDQM and firms)
- No travel: no carbon dioxide footprint, therefore beneficial for environment

1st Trial: RTEMIS equivalent to on-site inspections?



Summary

A new, third pillar for the supervision of the GMP compliance of pharmaceutical manufacturers

GMP
Assessment

RTEMIS

On-Site
Inspection

RTEMIS still in pilot phase – more experience needs to be gained
First impression promising

Acknowledgements

- Thomas Hecker, EDQM
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Thank you for your attention



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