CDMO Compliance:
A Case Study from Samsung Bioepis

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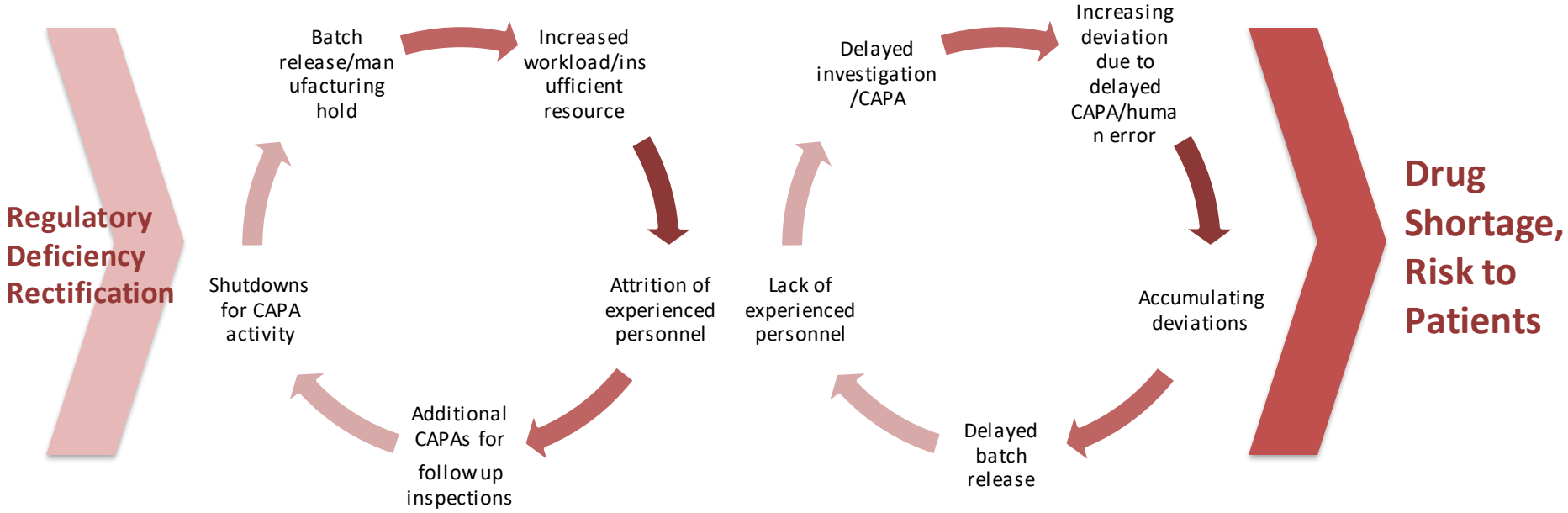
CONNECTING PEOPLE SCIENCE AND REGULATION®

Past performance does not guarantee future performance

– Especially, in GMP compliance

Aftermath of the unnoticed deficiencies – Vicious cycles until site quality improved



Lessons Learned

1. There can be an unnoticed GMP deficiency (**blind spot**) at CMO
   - If no apparent issue is detected from QMS and inspections
   - Client could not detect the deficiency due to limitations to accessible information (physical, confidentiality)

Lessons Learned

2. CMO may not have necessary knowledge and information on GMP compliance
   - CMO may not aware recent inspection trend
   - CMO may not have necessary experience for appropriate response to inspection observations
     - Deficient CAPA response may lead to regulatory actions

Lessons Learned

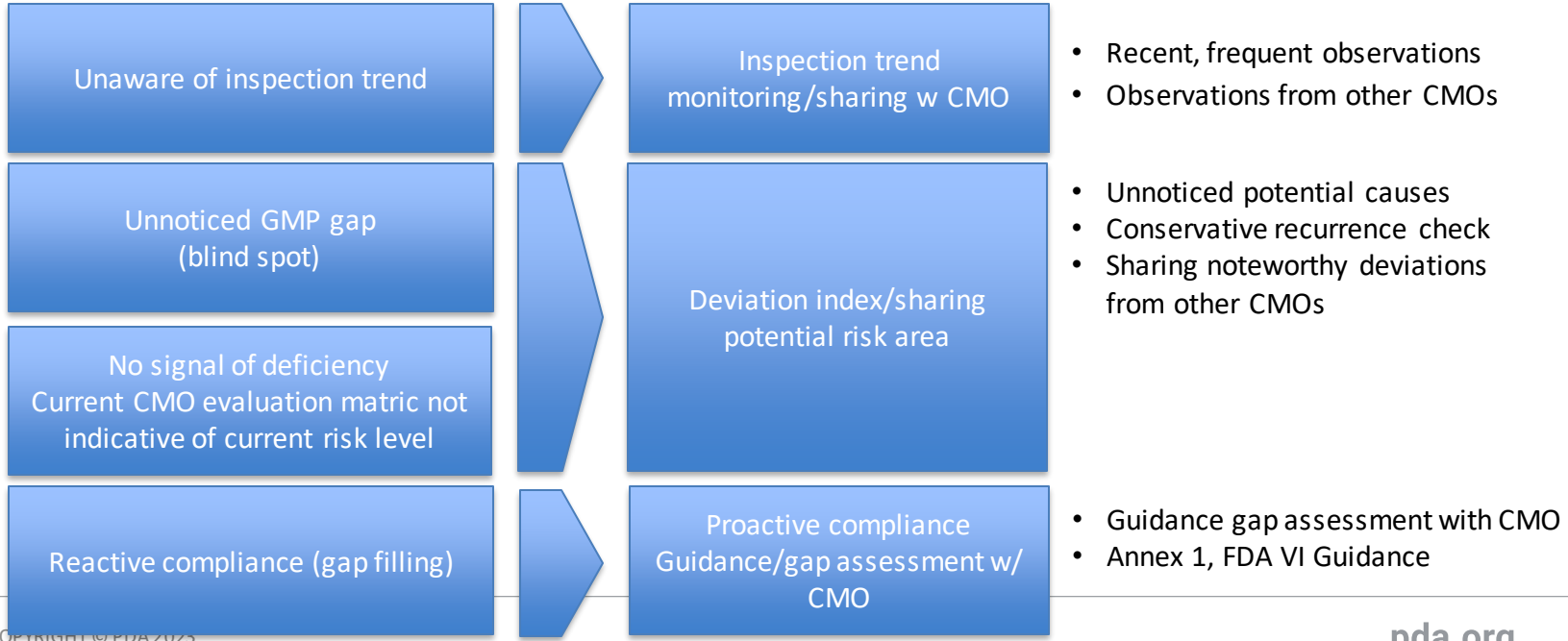
3. Client may not be able to support CMO identifying potential gaps by auditing
   - Client does not have access to/or sufficient knowledge of full operation of CMO
   - Client may not be able to be present on CMO site due to environment/condition (e.g., Covid19 pandemic)

Primary responsibility to assure GMP compliance remains on CMO, However, need collaborative efforts between client and CMO as partner to overcome limitations in detecting potential blind spots

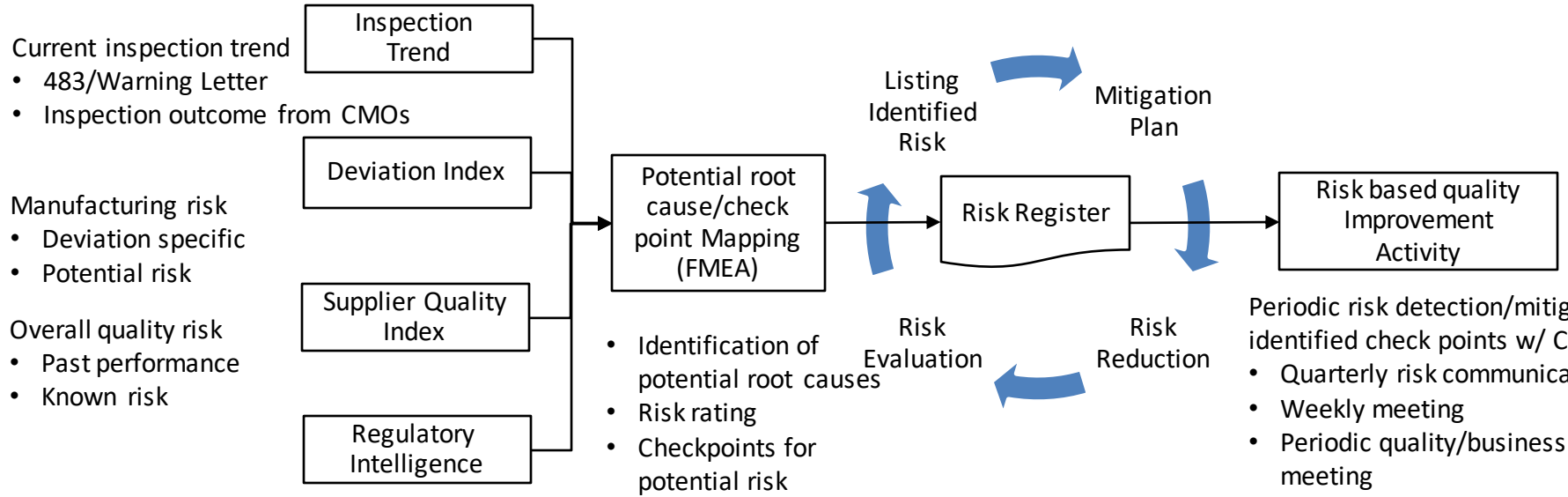
How we can support our CMO for better compliance?

An initiative to support our CMOs

- Samsung idea for improving detection of potential GMP gap to support CMO overcoming limitations – remote, confidentiality with CMO collaboration

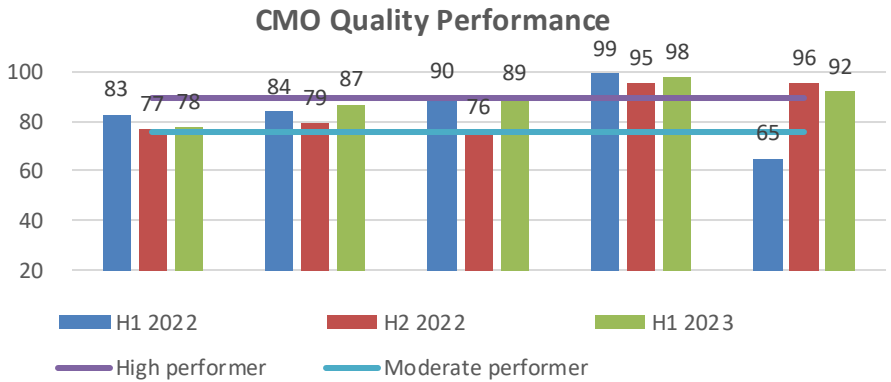


Strategy for supporting compliance of our CMOs



What if significant risk remains regardless of collaborative efforts made?

- Periodic CMO evaluation
  - 6 monthly multidisciplinary assessment of CMO performance including quality to determine whether to consider alternative options



CMO	Performance Level			Decision
	H1 2022	H2 2022	H1 2023	
1	M	M	M	
2	M	M	M	
3	H	M	H	
4	H	H	H	
5	L	H	H	

Supplier Quality Index – lagging indicator

KPI Category	Q1	Q2	Q3	Q4
Audit				
Batch record documentation				
Deviation				
PQC				
Regulatory impact				
PQR				
QAG				

GMP gap found during inspection

- Current supplier performance indicator (Supplier Quality Index) is designed to measure overall past performance

▶ Not indicating current potential risk

- Developed a new deviation focused metric to assess current potential risk associated with manufacturing

Guidance Implementation - Annex 1 example

- Collaborative/Parallel efforts with CMO from gap assessment to mitigation planning/implementation

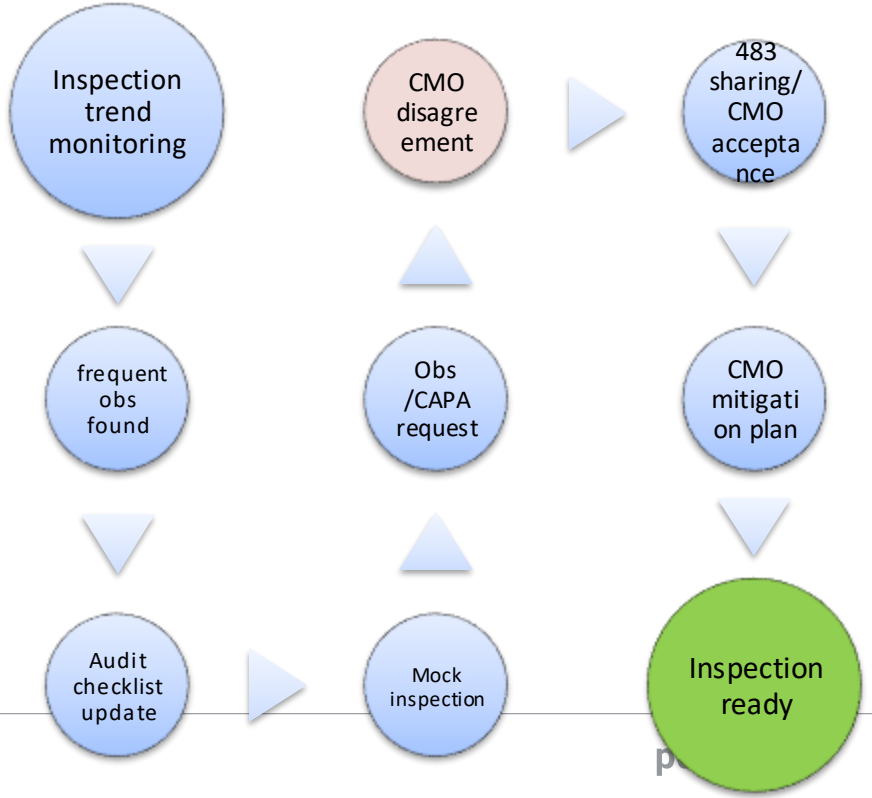
- Support provided for our CMOs
  - Questionnaire (checkpoints)
  - Onsite CMO assessment (audit)
  - Mitigation plan review
  - Consultation, financial support if appropriate

Inspection trend monitoring

- Scope: Recent inspection trends from 483, Warning Letter
- Resource: FDA website, commercial information service
- Monitoring status
  - Since Jan 2023, 40+ 483s relevant to biologics reviewed
  - 200+ check items selected (worth sharing/checking), provided for CMO review, CMO responded 68% of check items
- Use of inspection trend
  - Inspection readiness: Some successful, some not
  - CMO gap assessment for continuing improvement

Use case of inspection trend – DS CMO readiness

- DS CMO readiness for FDA inspection
  - Noticed missing periodic QA review of audit trail cited multiple times on 483s
  - Found same gap during mock inspection at CMO, but CMO was not wiling to accept the gap
  - Provided CMO the gap relevant 483 observation, requested CAPA
  - CMO acknowledged deficiency and prepared CAPA



Use case of inspection trend – DP CMO readiness

- DP CMO readiness for FDA inspection
  - Reviewed/shared 483s, observations from the same inspector from last 5 years
  - Shared the most recent observations from the same inspector (aseptic behavior-broke of first air)
    - Same observation issued (not sufficient time to improve after inspection notification)
  - 75% of observations issued was similar to previous 483s at other DP site from last 3 years

What we learned so far from the initiative

1. All efforts to support our CMO for better compliance is effective only when our CMO collaborate with us

2. Utilizing recent inspection trend for inspection readiness and continuing improvement is effective tool for better understand regulator's area of concern and maintain status of quality compliance

3. Our CMO knows themselves best, but there may be a blind spot client can support identify and mitigate

CMO response – where collaboration needed

- Initial response from CMO
  - ✗ Not willing to input resources, seen as additional work
  - ✗ Thus, some tried to charge additional service fee
  - ✗ Agreed to join assessment but with very low priority (months of lead time)
  - ✗ Rejected collaboration as they have similar internal compliance activities
- What are benefits for CMO to join this collaborative exercise?
  - ✓ Helpful to find unnoticed compliance gap (blind spot) found in other CMOs
  - ✓ If a gap is identified, it ensures time to improve (more time than finding the gap after inspection notification)
  - ✓ Eventually by maintaining robust quality compliance, CMO and client can fulfil ultimate mission – providing better quality drug to our patients

Message to industry –

Collaborative efforts to improve compliance, assuring quality/safety for patients

– Client and CMO as one team!

Message to industry – collaborative efforts!

- Due to limitation of information access for client (confidentiality and physical), CMO should take primary responsibility to maintain GMP compliance
- However, CMO should not only relying on their experience/capability to understand/operate in continuously evolving GMP environment for better quality/safety of drug
- It should be collaborative efforts between CMO and client not only for "product specific" but covering end to end manufacturing operations to identify blind spot and fill the compliance gap to assure quality and safety of drug to patients

Thank you

Session VII: Regulation of Medicines in the Post Pandemic World

Adam Thomas
Burnet Institute

Moderator

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Thank you

Closing Session

Closing Remarks

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