偏差报告
Deviation Report

PR#: 14247 Deviation No.:D-2021-0234

Record Status: Deviation Investigation in Progress

基本信息 General Information

厂区 Division: Innovent Biologics (Su Zhou) Co., Ltd

发起人 Originator: 周, 小华(PID-000313) 发起日期 Date Opened: 2021.05.12

简短描述 Short Description:
M1b DS2 CIP站(MFG-M1b3-114)淋洗水电导率超标 The conductivity of CIP station（MFG-M1b2-114）rinse water exceeds the standard

到期日期 Date Due: 2021.06.16 关闭日期 Date Closed:

偏差信息 Deviation Information

发现人 Discovery By: 周小华05080036 发现日期 Discovery On: 2021.05.12

汇报人Report By: 周小华05080036 汇报日期 Report On: 2021.05.12

发生部门 Occurred Department: M1b DS2 汇报部门 Report Department: MST

偏差描述 Deviation Description:
2021.05.012 15:45 MST员工（05080036）在为M1b DS2线年度清洁确认汇总数据时发现自2020.09.27至2021.05.01期间M1b 2线CIP站MFG-M1b3-114淋洗水样品出现31次电导率超1.3 μS/cm的情况，批次信息、电导率值、设备及管路和时间见附件1。根据《M1b生产2线不锈钢生物反应器清洁验证方案》（VALP00040）、《M1b 生产2线上游管道清洁验证方案》（VALP00042）和《M1b 生产2线离心机及相关CIP管道清洁验证方案》（VALP00055），在线电导率限度≤1.3 μS/cm，若超过该限度，应发起偏差流程进行调查。故发起偏差调查。

描述的附件 Description attachment:
M1b DS2设备及管路电导率超标汇总 .xlsx

是否及时上报？ Reporting in Time? : Yes

未及时上报的理由 Reason for not in Time:

已采取的即时措施 Immediately Action Taken:

即时措施附件 Immediately Action Attachment:

厂房设施名称 Facility Name: 产品所属阶段 Product Phase:

M1b Commercial+Clinical

初步影响/风险评估Initial Impact/Risk Assessment

产品影响评估 Product Impact Assessment:
根据《清洁验证主计划》（VMP00013），电导率测量是一种检测水样中游离离子物质非常灵敏的方法，而CIP100主要成分为KOH和EDTA（详见附件2）故本偏差涉及的淋洗水电导率超标推测为游离钾离子残留导致，金属残留离子会影响产品渗透压，因此上游CIP过程钾离子残留对本偏差涉及生产批次产品的影响较小。具体影响会在偏差第二部分调查中进行详细分析。

生产/检测的影响评估 Production/Testing Impact Assessment:
M1b 2线CIP站MFG-M1b3-114淋洗水样品电导率检测超标后，在本次调查第二部分建立偏差行动项：对本偏差涉及的转料管路（150L（MFG-M1b3-054）至750L（MFG-M1b3-055）管路；1000L补料罐（MFG-M1b3-059）向3000L反应器（MFG-M1b3-056）的补料管道每批次进行实时监控，若再次出现电导率超标的情况，对涉及管路重新执行CIP程序，直至检测结果合格，方可继续生产。

其他影响评估描述 Other Impact Assessment Description:
本偏差涉及的淋洗水电导率超标，可能影响M1b DS2清洁验证状态，需在第二部分进行进一步调查分析。

初步影响评估附件 Initial Impact Assessment Attachment:

偏差报告
Deviation Report

PR#: 14247 Deviation No.:D-2021-0234

Record Status: Deviation Investigation in Progress

附件2： CIP100 spec.pdf

偏差分级 Deviation Classification

偏差严重性 Deviation Severity:
对产品SISPQ的影响：
根据《清洁验证主计划》（VMP00013），电导率测量是一种检测水样中游离离子物质非常灵敏的方法，而CIP100主要成分为KOH和EDTA（详见附件2）故本偏差涉及的淋洗水电导率超标推测为游离钾离子残留导致，金属残留离子会影响产品渗透压，因此上游CIP过程钾离子残留对本偏差涉及生产批次产品的影响较小。具体影响会在偏差第二部分调查中进行详细分析。

偏差发生率 Reoccurrence Probability of Deviation:
过去12个月该区域同类型缺陷回顾（关键词搜索：M1b DS、 CIP站(MFG-M1b3-114)、淋洗水电导率超标）
PR 14066 偏差编号：D-2021-0227 M1b CIP站(MFG-M1b2-115)淋洗水电导率超标 The conductivity of rinse water exceeds the standard in M1b CIP station（(MFG-M1b2-115)）
该偏差还在调查中，级别为minor，因为该问题在二线继续发现，所以将其升级为主要偏差进行后续的调查。

偏差分级 Deviation Classification: Major

分级的理由 Reason for Classification:
05/13/2021 06:59 PM (GMT+8:00) added by 育芳 刘 (PID-000093):
该缺陷在近期为第二次发现，且需要进一步分析根本原因，根据根本原因考虑建立CAPA措施。
综上，该偏差定义为主要偏差。

是否需要调查？ Investigation Required? : Yes

主调查人 Lead investigator: 周, 小华

不需要调查的理由 Reason for not Investigation:

调查总结&根本原因分析 Investigation & RCA

调查总结 Investigation Summary:

调查附件 Investigation Attachments:

根本原因分析 Root Cause Analysis:

根本原因分析附件 Root Cause Analysis Attachment:

原因描述 Cause Description:

原因分类 Cause Category	原因子分类 Cause Sub-Category	原因归属部门 Cause Department

偏差报告
Deviation Report

PR#: 14247 Deviation No.:D-2021-0234

Record Status: Deviation Investigation in Progress

缺陷描述 Defect Description:
2021.05.012 15:45 MST员工（05080036）在为M1b DS2线年度清洁确认汇总数据时发现自2020.09.27至2021.05.01期间M1b 2线CIP站MFG-M1b3-114淋洗水样品出现31次电导率超1.3 μS/cm的情况，批次信息、电导率值、设备及管路和时间见附件1。根据《M1b生产2线不锈钢生物反应器清洁验证方案》（VALP00040）、《M1b 生产2线上游管道清洁验证方案》（VALP00042）和《M1b 生产2线离心机及相关CIP管道清洁验证方案》（VAL

缺陷类型分类 Defect Category	缺陷类型子分类 Defect Sub-Category
Production/Process	Operation

是否是重复偏差 Repeat Deviation? :

判定重复偏差的原因 Justification for Repeat Deviation:

重复偏差的原因描述 Reason of Repeat Deviation Description:

相关的重复偏差 Repeat Deviation Records

PR#	deviation#	简短描述 Short Description	Record Status

最终影响/风险评估 Final Impact/Risk Assessment

对产品质量的影响 Impact on Product Quality:

对其他批次的影响 Impact on Other Batches:

对系统/设备的影响 Impact on System/Equipment:

对验证状态的影响 Impact on Validation State:

对产品注册的影响 Impact on Product Registration:

对法规符合性的影响 Impact on Regulation Compliance:

对稳定性的影响 Impact on Stability:

对其他方面的影响 Impact on Other Aspects:

受影响的部门 Impact Departments:

影响/风险评估附件 Impact/Risk Assessment Attachment:

偏差报告
Deviation Report

PR#: 14247 Deviation No.:D-2021-0234

Record Status: Deviation Investigation in Progress

受影响的产品信息 Impacted Product Information

产品最终处置建议 Product Disposition Proposal:

产品名称 Product Name: 贝伐珠单抗注射液M1b 3000L原液

产品代码 Product Code	产品批号 Batch No.:	数量 Quantity	处理决定 Disposition
DS20-305	DS2009015	3000L	

产品名称 Product Name: 贝伐珠单抗注射液M1b 3001L原液(商业化）

产品代码 Product Code	产品批号 Batch No.:	数量 Quantity	处理决定 Disposition
DS30-305	DS2103001	3000L	

产品名称 Product Name: 贝伐珠单抗注射液M1b 3000L原液（二代细胞株）

产品代码 Product Code	产品批号 Batch No.:	数量 Quantity	处理决定 Disposition
DS01-305C-2	DS2012018	3000L	

产品名称 Product Name: 贝伐珠单抗注射液M1b 3000L原液（二代细胞株）

产品代码 Product Code	产品批号 Batch No.:	数量 Quantity	处理决定 Disposition
DS01-305C-2	DS2012017	3000L	

受影响的物料信息 Impacted Material Information

物料名称 Material Name:

物料代码 Product Code	批号 Batch No.:	数量 Quantity

受影响的溶液信息 Impacted Media/Buffer Information

溶液名称 Media/Buffer Name:

溶液代码 Media/Buffer Code:	批号 Batch No.:	数量 Quantity:

受影响的设备信息 Impacted Equipment Information

设备名称 Equipment Name: CIP清洗站 (CIP-05-06) 设备代码 Equipment Code MFG-M1b3-114

偏差处理措施 Deviation Action Items

偏差报告
Deviation Report

PR#: 14247 Deviation No.:D-2021-0234

Record Status: Deviation Investigation in Progress

PR#:

责任人 Assigned To: 部门 Department:

截止日期 Date Due: 完成日期 Completed Date:

确认人 Verified By: 确认日期 Verified On:

行动项详细描述 Action Description:

纠正信息 Correction Information

PR#:

责任人 Assigned To: 部门 Department:

截止日期 Date Due: 完成日期 Completed Date:

确认人 Verified By: 确认日期 Verified On:

行动项详细描述 Action Description:

纠正与预防措施 CAPA

PR#:

责任人 Assigned To: 部门 Department:

截止日期 Date Due:

行动项详细描述 Action Description:

附件 File Attachments

关联记录 Reference Records

PR#	Record Type	简短描述 Short Description	Record Status
14066	Deviation	M1b CIP站(MFG-M1b2-115)淋洗水电导率超标 The conductivity of rinse water exceeds the standard in M1b CIP station ((MFG-M1b2-115))	Closed-Done

相关子记录 Related children

PR#	Record Type	简短描述 Short Description	Record Status
15620	Interim Investigation Report	D-2021-0234第01次阶段性报告01 Deviation interim investigation of D-2021-0234	Pending QA Review

偏差报告
Deviation Report

PR#: 14247 Deviation No.:D-2021-0234

Record Status: Deviation Investigation in Progress

Initial Approval

QA Initial Review

Area QA Initial Reviewed By:	邓, 陈琪	Area QA Initial Reviewed On:	2021.05.13 14:53
Classify Completed By:	刘, 育芳	Classify Completed On:	2021.05.13 19:01

Department Initial Review

Department Leader 1 Reviewed By:	康, 云	Department Leader 1 Reviewed On:	2021.05.14 08:43
Department Leader 2 Reviewed By:		Department Leader 2 Reviewed On:	
Department Leader 3 Reviewed By:		Department Leader 3 Reviewed On:	
Department Leader 4 Reviewed By:		Department Leader 4 Reviewed On:	
Department Leader 5 Reviewed By:		Department Leader 5 Reviewed On:	
Area QA Leader Reviewed By:	代, 圆圆	Area QA Leader Reviewed On:	2021.05.14 08:11

Quality Initial Approval

Quality Approver 1 Approved By:	管, 国兴	Quality Approver 1 Approved On:	2021.05.14 09:42
Quality Approver 2 Approved By:		Quality Approver 2 Approved On:	
Quality Approver 3 Approved By:		Quality Approver 3 Approved On:	

Final Approval

QA Final Review

QA Final Reviewed By:	QA Final Reviewed On:

Investigator Final Review

QA Representative Reviewed By:	QA Representative Reviewed On:
Investigator 1 Reviewed By:	Investigator 1 Reviewed On:
Investigator 2 Reviewed By:	Investigator 2 Reviewed On:
Investigator 3 Reviewed By:	Investigator 3 Reviewed On:
Investigator 4 Reviewed By:	Investigator 4 Reviewed On:
Investigator 5 Reviewed By:	Investigator 5 Reviewed On:
Investigator 6 Reviewed By:	Investigator 6 Reviewed On:
Investigator 7 Reviewed By:	Investigator 7 Reviewed On:
Investigator 8 Reviewed By:	Investigator 8 Reviewed On:

Department Final Approval

Department Leader 1 Final Approved By:	Department Leader 1 Final Approved On:
Department Leader 2 Final Approved By:	Department Leader 2 Final Approved On:
Department Leader 3 Final Approved By:	Department Leader 3 Final Approved On:
Department Leader 4 Final Approved By:	Department Leader 4 Final Approved On:
Department Leader 5 Final Approved By:	Department Leader 5 Final Approved On:

Quality Final Approval

Quality Approver 1 Final Approved By:	Quality Approver 1 Final Approved On:
Quality Approver 2 Final Approved By:	Quality Approver 2 Final Approved On:

偏差报告
Deviation Report

PR#: 14247 Deviation No.:D-2021-0234

Record Status: Deviation Investigation in Progress

Quality Approver 3 Final Approved By: Quality Approver 3 Final Approved On:

Product Final Disposition

Disposition Proposed By: Disposition Proposed On:

Proposal Reviewed By: Proposal Reviewed On:

Product Disposition Approved By: Product Disposition Approved On: