偏差报告
Deviation Report

PR#: 4174 Deviation No.:D-2020-0221

Record Status: Closed-Done

基本信息 General Information

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

发起人 Originator: 陆, 志阳(PID-000109) 发起日期 Date Opened: 2020.07.27

简短描述 Short Description:
M1b DS2 150L生物反应器pH电极故障 M1b DS2 150L bioreactor pH electrode failure

到期日期 Date Due: 2020.07.28 关闭日期 Date Closed: 2020.07.28

偏差信息 Deviation Information

发现人 Discovery By: 陆志阳05020015 发现日期 Discovery On: 2020.07.26

汇报人Report By: 陆志阳05020015 汇报日期 Report On: 2020.07.26

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

偏差描述 Deviation Description:
2020.07.26 生产部人员（05020015）在细胞培养间（25D08）按照《IBI188（CD47）单克隆抗体注射液M1b3000L原液细胞培养及收获批生产记录》（BPR100411）P24“用血气分析仪检测IBI188基础培养基pH；校正pH至外测pH值”的要求对150L生物反应器（MFG-M1b3-054）进行pH校准，发现M800上不显示在线pH值，如附件1 图1所示；生产人员在进行过程校准时，M800显示“校准没有完成”，如附件1图2所示，无法按照批记录要求进行pH校准。故发起偏差。

描述的附件 Description attachment:
附件1 偏差描述附件.docx

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:
07/28/2020 02:35 PM (GMT+8:00) added by 志阳 陆 (PID-000109):
更正及时措施1完成时间，实际完成时间为2020.07.26

****
07/27/2020 10:54 AM (GMT+8:00) added by 志阳 陆 (PID-000109):
1.称量组重新申领记录,重新称量IBI188基础培养基用物料/MFG/2020.07.27
2.培养基配置组重新申领记录,重新清洗培养基配制罐，并配制IBI188基础培养基/MFG/2020.07.27
3.细胞培养组重新申领记录,将150L反应器中现有的培养基进行排废处理，并重新清洗150L反应器/MFG/2020.07.27

即时措施附件 Immediately Action Attachment:

附件5 即时措施3完成证明.pdf

附件4 即时措施2完成证明.pdf

附件3 即时措施1完成证明.pdf

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

M1b Clinical

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

产品影响评估 Product Impact Assessment:
偏差调查：
2020.07.26生产人员（05020015）在细胞培养间（25D08）操作时发现M800上pH值无法显示，而此时批记录BPR100411的P24中下一步操作指示是 “用血气分析仪检测IBI188基础培养基pH；校正pH至外测pH值”，生产人员想尝试通过批记录中校正pH的操作来完成校正，使M800显示正常。但生产人员在按照批记录要求校正pH时，M800出现了“校准没有完成”的提示。
经MST、MFG和pH电极厂家工程师排查后，发现用其他电极信号线与该电极连接时，M800上的pH值也同样不显示；另发现M800上显

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示该电极的DLI（动态电极寿命指示）为零，数据条显示为红色（如附件2图1所示DLI数值为零）。经现场人员回顾，在使用该pH电极前已按照《M1b车间pH、DO电极使用维护保养操作规程》（SOP200563）6.1.2章节所描述内容，观察并确认光学帽完好，且在DLI有效期内，并进行了记录（见附件2图2电极使用记录）。使用前pH电极校准时的DLI数据条显示正常（绿色），且校准数据无异常（见附件2图3电极校准记录）。根据厂家工程师判断，发生这种情况为pH电极故障引起。发生故障的pH电极属于质量问题，为偶发事件，后续会通过SAP系统发起报修流程，将该pH电极返厂进行调查，明确故障原因。
影响评估：
偏差发生时150L生物反应器中为IBI188基础培养基，尚未进入培养阶段。经QA、MST和MFG会议沟通，考虑到 150L反应器培养阶段需关联底通CO2进行pH控制，如果pH电极故障则培养体系pH将不能得到控制。基于pH失控的风险，故决定将150L生物反应器（MFG-M1b3-054）中培养基排掉，校准并更换新pH电极。同时重新配制培养基并对150L反应器重新进行前处理及培养基接收，按照批记录的正常流程处理完成后进行150L反应器的接种，故本次pH电极的故障对细胞培养和后续生产未产生影响。

生产/检测的影响评估 Production/Testing Impact Assessment:
N/A

其他影响评估描述 Other Impact Assessment Description:
N/A

初步影响评估附件 Initial Impact Assessment Attachment:
附件2 初步影响评估附件.docx

偏差分级 Deviation Classification

偏差严重性 Deviation Severity:
偏差发生时150L生物反应器中为IBI188基础培养基，尚未进入培养阶段。基于pH失控的风险，已将150L生物反应器（MFG-M1b3-054）中培养基排掉，校准并更换新pH电极，同时重新配制培养基并对150L反应器重新进行前处理及培养基接收，故本次pH电极的故障对细胞培养和后续生产未产生影响。

偏差发生率 Reoccurrence Probability of Deviation:
过去12个月内没有类似缺陷发生（搜索关键词：150L生物反应器、pH电极、故障）

偏差分级 Deviation Classification: Minor

分级的理由 Reason for Classification:
07/28/2020 02:54 PM (GMT+8:00) added by 祯 吴 (PID-000094):
本偏差未对细胞培养和后续生产产生影响，并且过去12个月内没有类似缺陷发生，故定义为次要偏差。

是否需要调查？ Investigation Required? : No

主调查人 Lead investigator:

不需要调查的理由 Reason for not Investigation:
本偏差根本原因明确，且未对产品质量和后续生产产生影响，故无需进一步调查。

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:

根据厂家工程师判断，发生该情况为pH电极故障引起。发生故障的pH电极属于质量问题，为偶发事件。

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

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原因描述 Cause Description:
pH电极故障

原因分类 Cause Category	原因子分类 Cause Sub-Category	原因归属部门 Cause Department
Machine	Facility/Utility/Equipment/Instrument Breakdown	M1b DS2

缺陷描述 Defect Description:
2020.07.26 生产部人员（05020015）在细胞培养间（25D08）按照《IBI188（CD47）单克隆抗体注射液M1b3000L原液细胞培养及收获批生产记录》（BPR100411）P24“用血气分析仪检测IBI188基础培养基pH；校正pH至外测pH值”的要求对150L生物反应器（MFG-M1b3-054）进行pH校准，发现M800上不显示在线pH值，如附件1 图1所示；生产人员在进行过程校准时，M800显示“校准没有完成”，如附件1图2所示，无法按照批记录要求进行pH校准。故发起偏差。

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? : No

判定重复偏差的原因 Justification for Repeat Deviation:
过去12个月内没有类似缺陷发生（搜索关键词：150L生物反应器、pH电极、故障）

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:

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受影响的部门 Impact Departments:

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

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: Other

产品代码 Product Code	产品批号 Batch No.:	数量 Quantity	处理决定 Disposition
Other	DS2007004	150L	

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: 生物反应器（150L） 设备代码 Equipment Code MFG-M1b3-054

偏差处理措施 Deviation Action Items

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

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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

相关子记录 Related children

PR#	Record Type	简短描述 Short Description	Record Status

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Initial Approval

QA Initial Review

Area QA Initial Reviewed By:	王, 淼淼	Area QA Initial Reviewed On:	2020.07.27 14:05
Classify Completed By:	吴, 祯	Classify Completed On:	2020.07.28 15:01

Department Initial Review

Department Leader 1 Reviewed By:	邓, 献存	Department Leader 1 Reviewed On:	2020.07.28 15:21
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:	2020.07.28 16:15

Quality Initial Approval

Quality Approver 1 Approved By:	高, 剑锋	Quality Approver 1 Approved On:	2020.07.28 17:16
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:

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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: