偏差报告
Deviation Report

PR#: 13819 Deviation No.:D-2021-0204

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: 江, 煜章(PID-000289) 发起日期 Date Opened: 2021.04.28

简短描述 Short Description:
M1b DS1 膜包前压力高，程序报警并HOLD,The high pressure in front of the membrane package causes the program alarm and hold

到期日期 Date Due: 2021.07.09 关闭日期 Date Closed:

偏差信息 Deviation Information

发现人 Discovery By: 刘希雨05020036 发现日期 Discovery On: 2021.04.27

汇报人Report By: 刘希雨05020036 汇报日期 Report On: 2021.04.27

发生部门 Occurred Department: M1b DS1 汇报部门 Report Department: M1b DS1

偏差描述 Deviation Description:
2021.04.27 12:56 生产人员（工号：05020036，20000222）在细胞培养间（26D08）和离心收获间（26D09）进行IBI308（二代细胞株）DS2103013 批次生产收获时，发现一级膜包前压力过高，PI-T0111-02发生HI_HI_ALM报警导致收获程序（HV_IBI308_NEW_HARVEST_PR）（Batch ID: DS2103013-020104270844）HOLD，在14:31将收获程序abort，收获程序结束。因与正常收获程序不一致，故发起偏差调查。

描述的附件 Description attachment:

是否及时上报？ Reporting in Time? : Yes

未及时上报的理由 Reason for not in Time:
NA

已采取的即时措施 Immediately Action Taken:
04/28/2021 04:07 PM (GMT+8:00) added by 煜章 江 (PID-000289):
出现报警导致收获程序HOLD后，在上报上级领导、QA、MST后，经会议讨论，于2021.04.27 14:31 将收获程序abort，以结束收获程序。（见附件1.膜包压力过高的处理） MFG2021.04.27

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04/28/2021 11:20 AM (GMT+8:00) added by 煜章 江 (PID-000289):
出现报警导致收获程序HOLD后，于2021.04.27 14:31将收获程序abort，以结束收获程序。（见附件1.膜包压力过高的处理） MFG 2021.04.27

即时措施附件 Immediately Action Attachment:

附件1.膜包压力过高的处理.jpg

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:
三级除菌滤器主要目的是降低后续工序微生物负荷，偏差发生后，三级滤器完整性检测通过，（见附件2.三级滤器完整性检测结果）说明过滤后的澄清过滤收集液的微生物限度不会受到影响，基于此，初步评估对产品质量无影响。

生产/检测的影响评估 Production/Testing Impact Assessment:
1. 出现报警导致收获程序HOLD后，经会议讨论，于2021.04.27 14:31 将收获程序abort后，收获程序正常结束。通过澄清收集液体积，蛋白含量，亲和层析柱体积，经下游MST计算得出的亲和进行3个cycle理论载量为（澄清收集液体积*蛋白含量/cycle数/亲和层析柱体积）2527.74*7.97/3/179.86=37.3，符合纯化亲和层析上样载量（23.1-53.2g/L）。因此对后续生产无影响。
2. 因膜包堵塞原因收获罐（MFG-M1b2-064）澄清收集液液位低于正常水平，约为2500kg，纯化正在上第2个cycle样时，上游操作人

偏差报告
Deviation Report

PR#: 13819 Deviation No.:D-2021-0204

Record Status: Deviation Investigation in Progress

员（20002811,05020026）发现液位即将要低于取样口（液位已降至950Kg左右），立即联系纯化告知收获罐需留有800KG的液位取样，后经与纯化人员反复沟通，为了防止液位太低取不到样品，上游操作人员于10：35紧急提前取了2袋样品备用，且纯化操作人员于10：37结束第2个cycle。程序结束后，上游操作人员（20002811,05020026）发现液位为801KG，仍可取样，且与MST沟通，前面2袋备用样品不具有代表性，于是按照《信迪利单抗注射液二代细胞株M1b 3000L上游工艺规程》（PFD00172-03）要求，于15:25在第3个cycle前重新取样2袋。（后续会建立行动项对提前取出的2袋备用样品进行废弃处理。）

其他影响评估描述 Other Impact Assessment Description:
本次偏差中，三级滤器堵塞，未执行缓冲液顶洗步骤，导致约400kg（其中缓冲罐汇总约100kg，膜包死体积约260kg）料液损失，工艺收率相较于工程批会有所降低。对工艺验证的具体影响需要进一步调查评估。

初步影响评估附件 Initial Impact Assessment Attachment:
附件2.三级滤器完整性检测结果.docx

偏差分级 Deviation Classification

偏差严重性 Deviation Severity:
1.三级除菌滤器主要目的是降低后续工序微生物负荷，偏差发生后，三级滤器完整性检测通过，（见附件2.三级滤器完整性检测结果）说明过滤后的澄清过滤收集液的微生物限度不会受到影响，基于此，初步评估对产品质量无影响。
2.出现报警导致收获程序HOLD后，经会议讨论，于2021.04.27 14:31 将收获程序abort后，收获程序正常结束。通过澄清收集液体积，蛋白含量，亲和层析柱体积，经下游MST计算得出的亲和进行3个cycle理论载量为（澄清收集液体积*蛋白含量/cycle数/亲和层析柱体积）2527.74*7.97/3/179.86=37.3，符合纯化亲和层析上样载量（23.1-53.2g/L）。因此对后续生产无影响。
3.因膜包堵塞原因收获罐（MFG-M1b2-064）澄清收集液液位低于正常水平，约为2500kg，纯化正在上第2个cycle样时，上游操作人员（20002811,05020026）发现液位即将要低于取样口（液位已降至950Kg左右），立即联系纯化告知收获罐需留有800KG的液位取样，后经与纯化人员反复沟通，为了防止液位太低取不到样品，上游操作人员于10：35紧急提前取了2袋样品备用，且纯化操作人员于10：37结束第2个cycle。程序结束后，上游操作人员（20002811,05020026）发现液位为801KG，仍可取样，且与MST沟通，前面2袋备用样品不具有代表性，于是按照《信迪利单抗注射液二代细胞株M1b 3000L上游工艺规程》（PFD00172-03）要求，于15:25在第3个cycle前重新取样2袋。（后续会建立行动项对提前取出的2袋备用样品进行废弃处理。）
4.本次偏差中，三级滤器堵塞，未执行缓冲液顶洗步骤，导致约400kg（其中缓冲罐汇总约100kg，膜包死体积约260kg）料液损失，工艺收率相较于工程批会有所降低。对工艺验证的具体影响需要进一步调查评估。

偏差发生率 Reoccurrence Probability of Deviation:
过去12个月未发生类似缺陷（搜索关键词：膜包，压力，报警）

偏差分级 Deviation Classification: Minor

分级的理由 Reason for Classification:
04/29/2021 05:41 PM (GMT+8:00) added by 怡菁 王 (PID-000230):
该偏差对产品质量未造成影响，且过去12个月未发生类似缺陷，故定为次要偏差。

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:

偏差报告
Deviation Report

PR#: 13819 Deviation No.:D-2021-0204

Record Status: Deviation Investigation in Progress

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

缺陷描述 Defect Description:
生产人员在细胞培养间（26D08）和离心收获间（26D09）进行IBI308（二代细胞株）DS2103013 批次生产收获时，发现一级膜包前压力过高，PI-T0111-02发生HI_HI_ALM报警导致收获程序（HV_IBI308_NEW_HARVEST_PR）（Batch ID: DS2103013-020104270844）HOLD，在14:31将收获程序abort，收获程序结束。因与正常收获程序不一致，故发起偏差调查。

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:

偏差报告
Deviation Report

PR#: 13819 Deviation No.:D-2021-0204

Record Status: Deviation Investigation in Progress

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: 信迪利单抗注射液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
DS01-308B-2	DS2103013	NA	

受影响的物料信息 Impacted Material Information

物料名称 Material Name: Other

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

物料名称 Material Name: Other

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

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: 设备代码 Equipment Code

偏差处理措施 Deviation Action Items

PR#: 13905

责任人 Assigned To:	江, 煜章(PID-000289)	部门 Department:	M1b DS1
截止日期 Date Due:	2021.05.06	完成日期 Completed Date:	2021.05.03
确认人 Verified By:	王, 杨晨(PID-000263)	确认日期 Verified On:	2021.05.05

偏差报告
Deviation Report

PR#: 13819 Deviation No.:D-2021-0204

Record Status: Deviation Investigation in Progress

行动项详细描述 Action Description:
经与MST沟通确认，前面2袋备用样品不具有代表性，由生产人员将前面取出的2袋样品倒入通向灭活罐的水池处理。

PR#: 14251

责任人 Assigned To:	姜, 润滢(PID-000074)	部门 Department:	MST
截止日期 Date Due:	2021.05.17	完成日期 Completed Date:	2021.05.16
确认人 Verified By:	王, 杨晨(PID-000263)	确认日期 Verified On:	2021.05.31

行动项详细描述 Action Description:
为降低三级滤器堵塞风险，增加澄清过滤工序收率，在PPQ3生产过程中，发起变更，并联一个三级滤器，以增加三级滤器总面积。

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
13949	Urgent Change Control	M1b生产1线 PH_DF_TREAT phase FQ_SP3上限参数修改 High limit revise of FQ_SP3 in phase PH_DF_TREAT.	Closed-Done

相关子记录 Related children

PR#	Record Type	简短描述 Short Description	Record Status
13905	Deviation Action Items	提前取出备用样品的处理 Disposal of spare samples taken out in advance	Closed-Done

偏差报告
Deviation Report

PR#: 13819 Deviation No.:D-2021-0204

Record Status: Deviation Investigation in Progress

14251	Deviation Action Items	发起变更，在信迪利单抗二代细胞株PPQ3澄清过滤并联一个三级滤器 Initiate CCR and adding another third filter in clarification	Closed-Done
15168	Interim Investigation Report	D-2021-0204第1次阶段性报告 first periodic report of D-2021-0204	Closed-Done

Innovent 信达生物制药

偏差报告
Deviation Report

PR#: 13819 Deviation No.:D-2021-0204

Record Status: Deviation Investigation in Progress

Initial Approval

QA Initial Review

Area QA Initial Reviewed By:	王, 杨晨	Area QA Initial Reviewed On:	2021.04.28 16:18
Classify Completed By:	王, 怡菁	Classify Completed On:	2021.04.29 17:44

Department Initial Review

Department Leader 1 Reviewed By:	康, 云	Department Leader 1 Reviewed On:	2021.04.29 18:45
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:	2021.04.29 18:16

Quality Initial Approval

Quality Approver 1 Approved By:	管, 国兴	Quality Approver 1 Approved On:	2021.04.29 19:12
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#: 13819 Deviation No.:D-2021-0204

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: