偏差报告
Deviation Report

PR#: 14063 Deviation No.:D-2021-0224

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: 胡, 传峰(PID-000249) 发起日期 Date Opened: 2021.05.08

简短描述 Short Description:
M1b DS2 IBI305 HIC wash阶段线性流速超出工艺规程上限IBI305 HIC wash linear flow rate beyond the upper limit of PFD00097

到期日期 Date Due: 2021.07.15 关闭日期 Date Closed:

偏差信息 Deviation Information

发现人 Discovery By: 陆波 05030014 发现日期 Discovery On: 2021.05.07

汇报人Report By: 陆波 05030014 汇报日期 Report On: 2021.05.07

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

偏差描述 Deviation Description:
2021.05.06 23:15 QA人员（20002213）审核IBI305 DS2103010批次层析系统电子数据时发现HIC wash阶段的流速波动异常。上报后纯化人员（05030014）于2021.05.07 15:50确认IBI305 DS2103010批次HIC wash步骤过程中的流速波动范围在314.1 L/hour~1170.5 L/hour，超出《贝伐珠单抗注射液M1b 3000L 纯化工艺规程》 （PFD00097）中要求HIC线性流速47~125cm/h（经换算为236 L/hour~628 L/hour）上限范围，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:

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

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

产品影响评估 Product Impact Assessment:
从《贝伐珠单抗注射液M1b3000L原液工艺验证报告》（VALR00093）可知（详见附件2），IBI305阳离子收集液即可满足原液质量标准，疏水层析步骤提供了冗余的工艺控制能力。本偏差中IBI305 DS2103010 疏水层析Wash步骤的线性流速超出工艺规程上限值，针对产品质量的影响评估已制定偏差行动项（记录ID：14095），送HIC收集液留样至QC，检测疏水层析收集液的HCP残留，DNA残留和ProA残留。对于产品质量的影响需要后续调查中进行评估。

生产/检测的影响评估 Production/Testing Impact Assessment:
IBI305工艺中疏水层析线性流速定义为CPP的依据，查阅《IBI305下游晚期工艺特性研究报告》 (IDC-PD-3-IBI305-R-002-01)（详见附件3）可知，线性流速（保留时间）主要影响的是收率及柱压。疏水层析wash过程中的柱前压力没有超过规定值上限3.5bar，wash阶段运行过程中疏水层析没有因为流速的波动而导致层析暂停。同时，本批记录DS2103010的疏水层析的收率为99.4%。本批次疏水层析收率及柱压图详见附件1，柱压和收率这两个工艺性能未受影响。wash阶段后的洗脱等步骤正常运行，未影响后续的生产活动。

其他影响评估描述 Other Impact Assessment Description:
本次工艺HIC wash步骤过程中的流速波动范围在314.1 L/hour~1170.5 L/hour，不在《贝伐珠单抗注射液制造与检定规程》 中要求HIC线性流速47~125cm/h（经换算为236 L/hour~628 L/hour）范围内。本次偏差不会触发注册的制造检定规程修改或工艺变更，故对注册无影响。

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初步影响评估附件 Initial Impact Assessment Attachment:
附件2 DS2103010 HIC wash步骤流速偏差的初步产品影响评估-工艺验证报告.docx
附件1 DS2103010 HIC wash步骤流速偏差的初步产品影响评估-HIC图谱.docx
附件3 DS2103010 HIC wash步骤流速偏差的初步产品影响评估-工艺特性研究报告.docx

偏差分级 Deviation Classification

偏差严重性 Deviation Severity:
1、从《贝伐珠单抗注射液M1b3000L原液工艺验证报告》（VALR00093）可知（详见附件2），IBI305阳离子收集液即可满足原液质量标准，疏水层析步骤提供了冗余的工艺控制能力。本偏差中IBI305 DS2103010 疏水层析Wash步骤的线性流速超出工艺规程上限值，针对产品质量的影响评估已制定偏差行动项（记录ID：14095），送HIC收集液留样至QC，检测疏水层析收集液的HCP残留，DNA残留和ProA残留。对于产品质量的影响需要后续调查中进行评估。
2、IBI305工艺中疏水层析线性流速定义为CPP的依据，查阅《IBI305下游晚期工艺特性研究报告》(IDC-PD-3-IBI305-R-002-01)（详见附件3）可知，线性流速（保留时间）主要影响的是收率及柱压。疏水层析wash过程中的柱前压力没有超过规定值上限3.5bar，wash阶段运行过程中疏水层析没有因为流速的波动而导致层析暂停。同时，本批记录DS2103010的疏水层析的收率为99.4%。本批次疏水层析收率及柱压图详见附件1，柱压和收率这两个工艺性能未受影响。wash阶段后的洗脱等步骤正常运行，未影响后续的生产活动。
3、本次工艺HIC wash步骤过程中的流速波动范围在314.1 L/hour~1170.5 L/hour，不在《贝伐珠单抗注射液制造与检定规程》 中要求HIC线性流速47~125cm/h（经换算为236 L/hour~628 L/hour）范围内。本次偏差不会触发注册的制造检定规程修改或工艺变更，故对注册无影响。

偏差发生率 Reoccurrence Probability of Deviation:
过去12个月类似缺陷回顾（关键词搜索：M1b、IBI305、HIC wash、流速、超上限），未发生类似缺陷。

偏差分级 Deviation Classification: Critical

分级的理由 Reason for Classification:
05/10/2021 06:01 PM (GMT+8:00) added by 四弟 李 (PID-000227):
该偏差对于产品质量的影响需要后续调查中进行评估，考虑到线性流速为WC-CPP，超出检定规程要求，根据SMP00090《偏差管理规程》，定义为严重偏差。

是否需要调查？ Investigation Required? : Yes

主调查人 Lead investigator: 宋, 健

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

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缺陷描述 Defect Description:
QA人员（20002213）审核IBI305 DS2103010批次层析系统电子数据时发现HIC wash阶段的流速波动异常。上报后纯化人员（05030014）于2021.05.07 15:50确认IBI305 DS2103010批次HIC wash步骤过程中的流速波动范围在314.1 L/hour~1170.5 L/hour，超出《贝伐珠单抗注射液M1b 3000L 纯化工艺规程》（PFD00097）中要求HIC线性流速47~125cm/h（经换算为236 L/hour~628 L/hour）上限范

缺陷类型分类 Defect Category: Production/Process

缺陷类型子分类 Defect Sub-Category: 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:

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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 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	DS2103010	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: 缓冲液暂存罐（1000L） 设备代码 Equipment Code MFG-M1b3-088

偏差处理措施 Deviation Action Items

PR#: 14095

责任人 Assigned To:	胡, 传峰(PID-000249)	部门 Department:	M1b DS2
截止日期 Date Due:	2021.05.10	完成日期 Completed Date:	2021.05.09
确认人 Verified By:	邓, 陈琪(PID-000209)	确认日期 Verified On:	2021.05.09

行动项详细描述 Action Description:
根据《贝伐珠单抗注射液M1b 3000L原液工艺验证报告》（VALR00093）中针对疏水层析的功能申明，将IBI305 DS2103010批次疏水收集液留样送至QC，检测HCP残留、DNA残留和Pro A残留。

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:

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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
14095	Deviation Action Items	送HIC收集液留样检测中间体质量 send reserved HIC pool sample and test intermediate quality attribute	Closed-Done
15335	Interim Investigation Report	D-2021-0224第01次阶段性报告D-2021-0224 Periodic Report 01	Closed-Done

Innovent 信达生物制药

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Initial Approval

QA Initial Review

Area QA Initial Reviewed By:	邓, 陈琪	Area QA Initial Reviewed On:	2021.05.08 19:25
Classify Completed By:	李, 四弟	Classify Completed On:	2021.05.10 18:05

Department Initial Review

Department Leader 1 Reviewed By:	康, 云	Department Leader 1 Reviewed On:	2021.05.10 21:17
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:	2021.05.10 19:40

Quality Initial Approval

Quality Approver 1 Approved By:	高, 剑锋	Quality Approver 1 Approved On:	2021.05.11 08:51
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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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: