

PR#: 3205

Deviation No.:D-2020-0162

Record Status: Closed-Done

## 基本信息 General Information

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

发起人 Originator: 刘, 浩(PID-000045)

发起日期 Date Opened: 2020.06.08

简短描述 Short Description:

M1b DS1 纯化管罐DHT超时限 Purification tube and tank DHT exceeded time limit

到期日期 Date Due: 2020.06.09

关闭日期 Date Closed: 2020.06.08

## 偏差信息 Deviation Information

发现人 Discovery By: 汪豪05030045

发现日期 Discovery On: 2020.06.05

汇报人 Report By: 刘浩05030041

汇报日期 Report On: 2020.06.05

发生部门 Occurred Department: M1b DS1

汇报部门 Report Department: M1b DS1

偏差描述 Deviation Description:

2020.06.05 21:00, 纯化人员 (05030045、20001032) 在26C15除病毒前纯化间执行DS2004003批次阳离子交换层析的管罐的使用后CIP, 准备执行Recipe: PU\_CIP\_CH0302\_T0301\_308CEX\_PR, Formula: CIP\_CH0302\_T0301\_308CEX程序时, 发现T0301罐、CH0302到T0301罐的管道、T0301罐到CH0303的管道的DHT开始时间为2020.06.04 15:47, 超过DHT时限24小时, 与《纯化管罐系统标准操作规程》(SOP200571) 6.7.5中要求“产品转移管道使用完成后应在24小时内或超出CIP有效期进行清洗”不符, 故产生偏差。

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:

即时措施附件 Immediately Action Attachment:

厂房设施名称 Facility Name:

M1b

产品所属阶段 Product Phase:

Commercial

## 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:

Recipe: PU\_CIP\_CH0302\_T0301\_308CEX\_PR, Formula: CIP\_CH0302\_T0301\_308CEX程序用于T0301罐、CH0302到T0301罐的管道、T0301罐到CH0303的管道的CIP, 该程序需在阴离子层析系统CH0303 (MFG-M1b2-006) 的CIP完成后运行。经调查发现, DS2004003批次T0332 Buffer 罐的0.5M NaOH溶液 (DS2004003-S005-01) 使用前实际溶液量 (约为4600L) 比需求量 (约为5200L) 少约600L, 该溶液用于阴离子层析系统CH0303 (MFG-M1b2-006) 的使用后CIP, 所以2020.06.04当天没有办法CH0303的后处理, 导致阴离子层析系统CH0303 (MFG-M1b2-006) 的Unit一直被占用, 无法释放, 所以Recipe:

PU\_CIP\_CH0302\_T0301\_308CEX\_PR, Formula: CIP\_CH0302\_T0301\_308CEX程序无法启动。

根本原因分析:

CH0303 Unit被占用是造成该偏差的直接原因, 而实际0.5M NaOH溶液量少于需求溶液量是导致CH0303 Unit无法释放的原因, 也是造成DHT超时限要求的根本原因。

对产品的影响评估:

《M1b生产1线清洁下游管道清洁验证方案》(VALP00023) 中管道DHT时间见附件1。

根据《M1b生产1线管道清洁验证方案》(VALP00023), 以上管道为同类设备中较难清洗的管道, 文件中规定DHT为24+4h, 实际执

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行时间DHT>35h, 此次Recipe: PU\_CIP\_CH0302\_T0301\_308CEX\_PR, Formula: CIP\_CH0302\_T0301\_308CEX程序中涉及的管道DHT时间为29.2h, 偏差涉及管道的DHT时间小于实际执行最小时间35.3h, 故此次管道清洗风险可控, 可以进行有效清洁。并且此偏差发生在产品收集之后, 对DS2004003批次产品无影响。

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

后续生产使用前, 会重新对T0301罐、CH0302到T0301罐的管道、T0301罐到CH0303的管道进行CIP和SIP, 对后续生产无影响。

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

不涉及。

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

附件1 管道DHT时间.docx

## 偏差分级 Deviation Classification

偏差严重性 Deviation Severity:

此次管道清洗风险可控, 可以进行有效清洁。此次偏差发生在产品收集之后, 对DS2004003批次产品无影响。

后续生产使用前, 会重新对T0301罐、CH0302到T0301罐的管道、T0301罐到CH0303的管道进行CIP和SIP, 对后续生产无影响。

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: 纯化管罐、DHT、超时限)

偏差分级 Deviation Classification: Minor

分级的理由 Reason for Classification:

06/08/2020 02:44 PM (GMT+8:00) added by 禎 吴 (PID-000094):

此次管道清洗风险可控, 可以进行有效清洁。偏差发生于产品收集后, 对产品无影响, 对后续生产无影响; 过去12个月内没有类似缺陷发生。

综上, 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:

本次偏差根本原因及影响明确, 无需进行进一步调查。

## 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:

CH0303 Unit被占用是造成该偏差的直接原因, 而实际0.5M NaOH溶液量少于需求溶液量是导致CH0303 Unit无法释放的原因, 也是造成DHT超时限要求的根本原因。

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

原因描述 Cause Description: 实际0.5M NaOH溶液量少于需求溶液量		
原因分类 Cause Category Others	原因子分类 Cause Sub-Category Others	原因归属部门 Cause Department M1b Supt.

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## 缺陷描述 Defect Description:

2020.06.05 21:00, 纯化人员 ( 05030045、20001032 ) 在26C15除病毒前纯化间执行DS2004003批次阳离子交换层析的管罐的使用后CIP, 准备执行Recipe: PU\_CIP\_CH0302\_T0301\_308CEX\_PR, Formula: CIP\_CH0302\_T0301\_308CEX程序时, 发现T0301罐、CH0302到T0301罐的管道、T0301罐到CH0303的管道的DHT开始时间为2020.06.04 15:47, 超过DHT时限24小时, 与《纯化管罐系统标准操

## 缺陷类型分类 Defect Category

Production/Process

## 缺陷类型子分类 Defect Sub-Category

Time Limit

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

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:信迪利单抗注射液M1b 3000L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

DS30-308DS20040033000L

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:纯化收集罐 ( 2500L )

设备代码 Equipment CodeMFG-M1b2-068

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

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:

PR#:3205

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Record Status: Closed-Done

行动项详细描述 Action Description:

纠正与预防措施 CAPA

PR#:

责任人 Assigned To:

截止日期 Date Due:

行动项详细描述 Action Description:

部门 Department:

附件 File Attachments

关联记录 Reference Records

PR#	Record Type	简短描述 Short Description	Record Status
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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:	赵, 琰	Area QA Initial Reviewed On:	2020.06.08 14:27
Classify Completed By:	吴, 祯	Classify Completed On:	2020.06.08 15:01

### Department Initial Review

Department Leader 1 Reviewed By:	康, 云	Department Leader 1 Reviewed On:	2020.06.08 16:02
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:	2020.06.08 15:13

### Quality Initial Approval

Quality Approver 1 Approved By:	周, 峥	Quality Approver 1 Approved On:	2020.06.08 16:36
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:
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### 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: