# 偏差报告
# Deviation Report

PR#: 5704 Deviation No.:D-2020-0304

Record Status: Closed-Done

## 基本信息 General Information

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

发起人 Originator: 张, 晓菲(PID-000133) 发起日期 Date Opened: 2020.10.07

简短描述 Short Description:
M1b DS1 培养基中有异物Foreign matter in the medium

到期日期 Date Due: 2020.10.10 关闭日期 Date Closed: 2020.10.11

## 偏差信息 Deviation Information

发现人 Discovery By: 刘志达20000271 发现日期 Discovery On: 2020.09.29

汇报人Report By: 张晓菲20000131 汇报日期 Report On: 2020.09.29

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

偏差描述 Deviation Description:
2020.09.29 13:30 M1b DS员工（20000809、20000271）在培养基间（27K18）准备信迪利单抗注射液M1b 3000L原液（批号DS2009005）种子培养基（批号DS2009005-S010-01；分装编号：-06）时发现种子培养基中存在白色异物，同一批次种子培养基（批号DS2009005-S010-01；分装瓶号：05）在2020.09.25用于该批次细胞复苏生产使用，为了调查DS2009005-S010-01批次的种子培养基存在的白色异物对培养基的质量和对已经生产的DS2009005批次细胞的影响，需发起偏差调查。
培养基中异物2020.09.29发现，2020.10.07走系统原因：2020.09.30初步判断异物；2020.10.01-2020.10.06为非工作日。

描述的附件 Description attachment:
附件1 培养基中白色异物.jpg

是否及时上报？ Reporting in Time? : Yes

未及时上报的理由 Reason for not in Time:
N/A

已采取的即时措施 Immediately Action Taken:
10/07/2020 11:07 AM (GMT+8:00) added by 晓菲 张 (PID-000133):
1.2020.09.29,M1b DS改用同批次其他编号的种子培养基。
2.2020.09.29，MST将有异物的种子培养基进行隔离。

即时措施附件 Immediately Action Attachment:

附件2 2020.09.29使用的种子培养基信息.jpg

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:
初步调查：
种子培养基（批号DS2009005-S010-01；分装编号：06）发现白色异物后，将异物取出经过目视及接触分析，异物面积很小，仅约为1mm×1mm，异物质地较硬，边界清晰，排除培养基成分析出的可能性，用刀片将异物切割，切割后仍为独立不零散的小块且边界清晰（见附件3、附件4），从颜色、质地分析，其特性应和PETG方瓶中瓶盖盖子材质有很大的相似性，认为很大可能性为PETG方瓶中瓶盖旋紧过程中，螺纹挤压掉落的塑料碎片， 该材质本身就会和培养基接触，故可以排除塑料材质成分溶出析出对培养基的影响。同时回顾了培养基过滤操作，培养基过滤过程未发现异常，过滤操作人员（人员工号：20000284、05210005）均具备上岗资质（见附件5、见附件6），且过滤用H4型号0.2μm滤器完整性检测结果合格（见附件7），故可排除培养基过滤过程异物引入的可能性。且对剩余的分装培养基进行目视检查，并未发现有同类似的异物存在。综上描述，此异物为PETG方瓶中瓶盖的塑料碎屑可能性极大，有异物的种子培养基（批号DS2009005-S010-01；分装编号：06）仅是影响到此独立分装的培养基，且分装编号：06的培养基未用于生产，所以对该整批次的培养基没有影响。
影响评估：
此外，该整批次其他分装编号的培养基所进行的细胞摇瓶扩增的数据正常（见附件8），细胞活率维持在较高水平且符合工艺要求范

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围（活率大于等于85%），细胞倍增水平除复苏代次较慢之外，其他两代次摇瓶扩增细胞活率与、密度与历史批次相比未有显著的异常。故分析认为异物批次的培养基未对该批次细胞复苏及扩增产生影响，且培养基质量未受影响。
发现异物的培养基为摇瓶及wave反应器扩增的种子培养基，细胞培养还处于种子扩增阶段，基本无产品表达，故对产品质量基本无影响。
本偏差的原因为：PETG方瓶中瓶盖旋紧螺纹挤压过程中，瓶盖中的塑料碎片脱落掉进瓶子中。

生产/检测的影响评估 Production/Testing Impact Assessment:
PETG方瓶中瓶盖旋紧螺纹挤压过程中，瓶盖中的塑料碎片容易脱落掉进瓶子中，后续实际生产过程中，操作人员在培养基配制完及使用之前，都会进行目视检查，目视检查合格之后才会用于生产中，所以使用到有塑料碎屑的培养基可能性极低。培养基中有异物对后续生产也不会造成影响。

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7 过滤器完整性测试图.PNG
附件8 与历史批次数据对比图.PNG
附件4 异物切割后照片.jpg
附件3 异物切割前照片.jpg
附件5 05210005人员上岗证.png
附件6 20000284人员上岗证.png

## 偏差分级 Deviation Classification

偏差严重性 Deviation Severity:
根据初步影响评估，该异物可能为PETG方瓶中瓶盖的塑料碎屑，发现异物的培养基为摇瓶及wave反应器扩增的种子培养基，细胞培养还处于种子扩增阶段，基本无产品表达，故对产品质量基本无影响，该整批次其他分装编号的培养基所进行的细胞摇瓶扩增正常，与历史批次相比未有显著异常。且分装编号06的培养基未用于生产，后续实际生产过程中操作人员在培养基配制完及使用之前都会进行目视检查，故对该整批次的培养基没有影响，对后续生产无影响。
综上，本次偏差对产品无影响。

偏差发生率 Reoccurrence Probability of Deviation:
回顾过去12个月内无类似缺陷发生（关键词：培养基、异物）。

偏差分级 Deviation Classification: Minor

分级的理由 Reason for Classification:
10/10/2020 05:52 PM (GMT+8:00) added by 伊婷 陈 (PID-000128):
根据初步影响评估，本次偏差对后续生产无影响，对产品无影响，原因明确，为PETG方瓶中瓶盖旋紧螺纹挤压过程中，瓶盖中的塑料碎片脱落掉进瓶子中。且回顾过去12个月内无类似缺陷发生（关键词：培养基、异物），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:
已在初步影响评估部分调查明确偏差产生原因，为PETG方瓶中瓶盖旋紧螺纹挤压过程中，瓶盖中的塑料碎片脱落掉进瓶子中，且本偏差对产品没有影响，故不需要进一步调查。

## 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:

PETG方瓶中瓶盖旋紧螺纹挤压过程中，瓶盖中的塑料碎片脱落掉进瓶子中。

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

原因描述 Cause Description:
PETG方瓶中瓶盖旋紧螺纹挤压过程中，瓶盖中的塑料碎片脱落掉进瓶子中。

| 原因分类 Cause Category | 原因子分类 Cause Sub-Category | 原因归属部门 Cause Department |
|---|---|---|
| Others | Others | N/A |

缺陷描述 Defect Description:
2020.09.29 13:30 M1b DS员工在培养基间准备信迪利单抗注射液M1b 3000L原液种子培养基时发现种子培养基中存在白色异物，同一批次种子培养基在2020.09.25用于该批次细胞复苏生产使用，为了调查DS2009005-S010-01批次的种子培养基存在的白色异物对培养基的质量和对已经生产的DS2009005批次细胞的影响，需发起偏差调查。

| 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? : No

判定重复偏差的原因 Justification for Repeat Deviation:
回顾过去12个月内无类似缺陷发生（关键词：培养基、异物），故本偏差非重复偏差。

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:

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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:

## 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

| 产品代码 Product Code | 产品批号 Batch No.: | 数量 Quantity | 处理决定 Disposition |
|---|---|---|---|
| DS30-308 | DS2009005 | 125ml | Release |

## 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: IBI308 种子培养基

| 溶液代码 Media/Buffer Code: | 批号 Batch No.: | 数量 Quantity: |
|---|---|---|
| S010 | DS2009005-S010-01 | 8kg |

## 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#:

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:

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## 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 |
|---|---|---|---|

## 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, 沛芳 | Area QA Initial Reviewed On: | 2020.10.09 08:38 |
| Classify Completed By: | 陈, 伊婷 | Classify Completed On: | 2020.10.10 18:11 |

### Department Initial Review

| | | | |
|---|---|---|---|
| Department Leader 1 Reviewed By: | 邓, 献存 | Department Leader 1 Reviewed On: | 2020.10.10 18:36 |
| 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: | 2020.10.10 18:13 |

### Quality Initial Approval

| | | | |
|---|---|---|---|
| Quality Approver 1 Approved By: | 周, 峥 | Quality Approver 1 Approved On: | 2020.10.11 13:36 |
| 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: |

### 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: