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26 May 2015

Elyse Groh
St Louis University Hospital
3635 Vista at Grand
St Louis, MO 63110
USA

Incident Report # 1132C

Dear Ms Groh,

We have received your incident report regarding Delivery Set with batch no. 11501 used in SIR-Spheres® microspheres treatment on 23 February 2015. It was reported that there was a collection of spheres at the hub where C line connects to 3-way stopcock. We have reviewed this incident, and summarise the findings as follows:

> *The reported collection of microspheres in the stopcock entry from C-line was confirmed. Upon removal of the accumulated microspheres, no restrictions to the flow through any parts of the Delivery Set was observed. Potential causes of a blockage or accumulation of microspheres are a heavy concentration of microspheres being administered, coming from either the needle being pushed to the bottom of the vial and/or prolonged stoppages or interruptions to the administration process. A copy of the report is attached for your information.*

Thank you for bringing this matter to our attention. Our commitment is to continually provide the highest quality product and service to our customers. Please do not hesitate to continue to bring these matters to our attention, or to contact us should you have any further concerns.

Yours sincerely,

Heather Winslade
Global Head of RA/QA

cc. Mark Sadlowski, Regional Sales Manager, Sirtex

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Incident Evaluation

Date: 21 May, 2015

Ref: Incident Report 1132

An incident report (#1132) was received in Feb 2015, from St. Louis University Hospital, St. Louis, MO, USA.

The incident report related that during the administration of a SIR-Spheres microspheres dose, there was an accumulation of microspheres seen in the C-line entry to the 3 way stopcock.

The report specifically stated:

> *"Dr. Vaheesan did SIR Spheres dose delivery following SIRTEX protocal. Post procedure analysis revealed that 78% of dose was delivered to patient. Per the protocol at SLU this is considered an patient event. There were no patient consequences. Reason to pursue the IR is that post op analysis shows a collection of spheres at the hub where c line connects to 3 way stopcock. During air phase the first air bubble dislodged a significant amount of spheres from the 3 way stop cock. Air phase was stopped after this bubble was delivered to patient. post op analysis confirm no activity in v vial. a 2nd SS procedure that day resulted in 97% of dose being delivered to patient.*
>
> *Since so many spheres were collecting at the hub/connection of c line to 3 way stopcock it led to question that there may be a defect in tubing at this junction that was hindering the spheres traveling thru the stopcock. Especially since the next case the prescribed dose had 97% delivered and SIRTEX protocol for steps of the dose delivery were identical."*

Batch code of the Delivery Set was quoted on the incident report as 11501. This is not a valid Sirtex Batch number. 20cc Merit syringes were reportedly used.

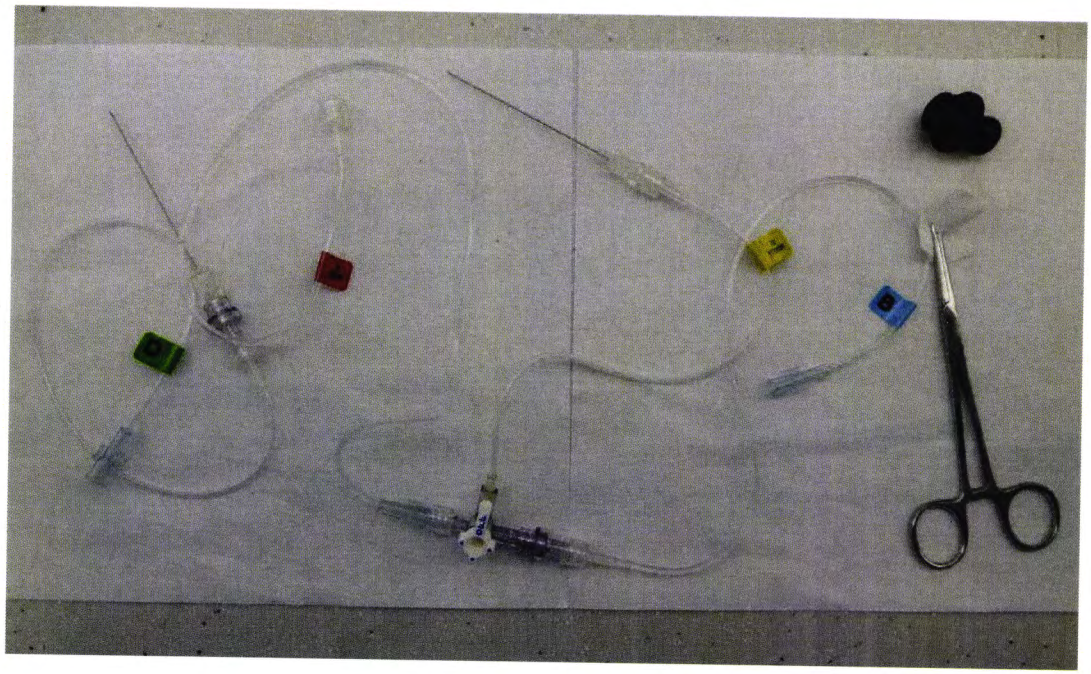
After suitable radioactive decay, the Delivery Set was returned to Sirtex, and received in May, 2015.

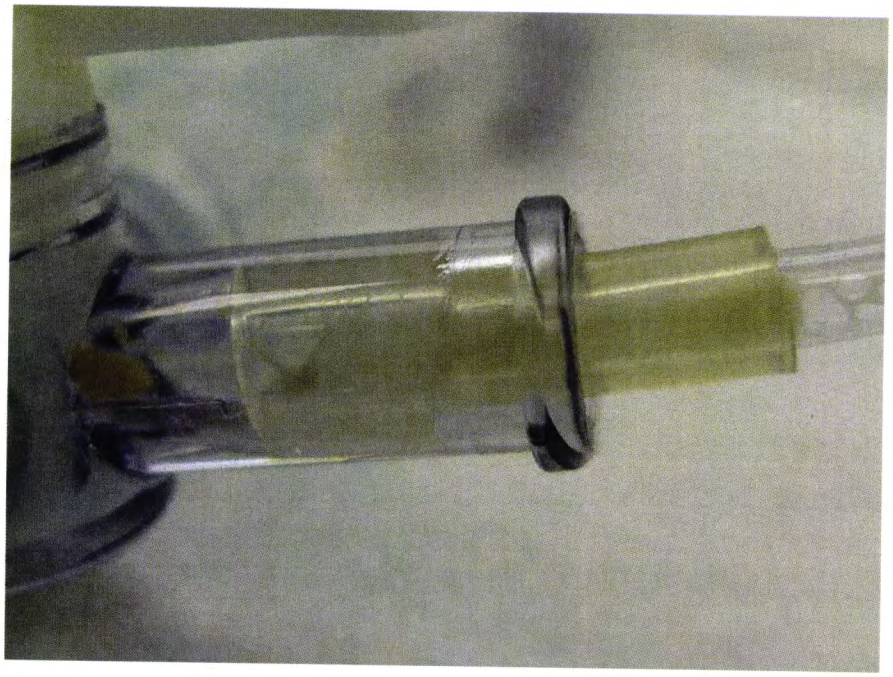
Items related to this incident, as returned included:

- A single Delivery Set complete with D-line
- A V-vial holder stopper plug

A pair of surgical forceps (not Sirtex supplied) was also included with the returned Delivery Set.

Initial inspection



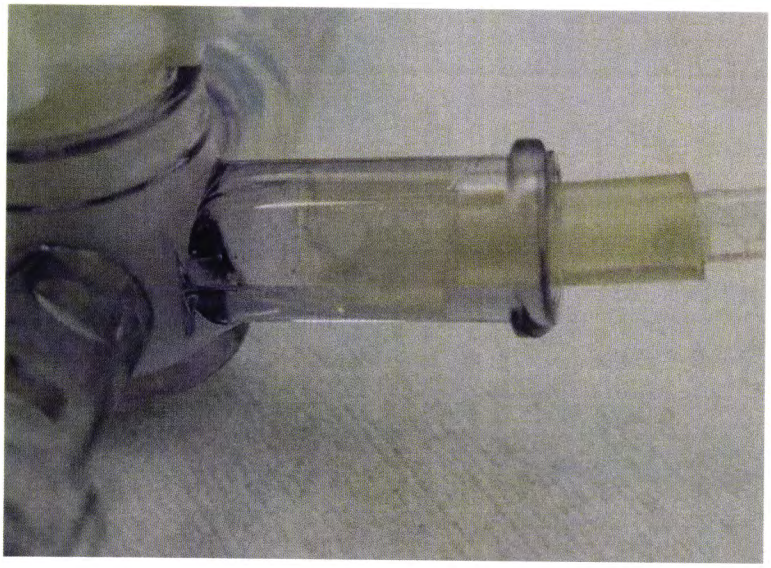


As received, the stopcock was turned off relative to the C-line. The C-line tubing appeared to be fully and firmly inserted into the 3-way stopcock. Inspection showed a small amount of microspheres remaining in the C-line entrance to the 3-way stopcock.

There was no apparent microspheres residue present in the A-line, B-line and D-line. Visible inspection did not reveal any damage or visible manufacturing or assembly faults on the entire Delivery Set.

Functional Testing

In order to replicate the reported restriction in the C-line leading to the 3-way stopcock, a 30ml syringe filled with water was attached to the B-line. The stopcock was turned to the "off" position relative to the A-line. Light to moderate steady pressure was applied to the syringe.



Water flow was established from B-line to C-line via 3-way stopcock, effectively back-flushing the C-line.

The outgoing water containing microsphere residues from C-line was collected in a separate container. The introduced water flowed through the B-line and C-line with relative ease.

The initial cluster of spheres located at the stopcock entrance to the C-line was flushed through the system and cleared without any significant resistance or back pressure being felt.

No occlusion or restriction was detected as continuous pressure was applied to the system.

Conclusion

The reported collection of microspheres in the stopcock entry from C-line was confirmed. Upon removal of the accumulated microspheres, no restrictions to the flow through any parts of the Delivery Set were observed.

The reported accumulation was easily removed and was not due to any restriction or manufacturing fault in the Delivery Set. Potential causes of a blockage or accumulation of microspheres in the Delivery Set are a heavy concentration of microspheres being administered, and/or prolonged stoppages or interruptions to the administration process.

Heavy concentration of microspheres can occur if the C-line needle is inserted too deep within the V-vial, if insufficient water is added to the drawn up dose within the V-vial, or by performing the administration process without pulsing the D-line syringe so as to slowly bring the microspheres into a dilute suspension.

Steve Yu
Quality Assurance Officer
Sirtex

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