



Root Cause Analysis and Corrective Action Plan: Update 2.0 10/1, 2014

Syphacia obvelata contamination in Barrier Unit 506, Cambridge City Indiana

Problem ID: <i>Syphacia obvelata</i> . IBU506					Response Due Date: 20 June, 2014			
Beginning June 2, 2014, a cross-functional team from Taconic executed an investigation using the 8 Disciplines (8D) Problem Solving Methodology. 8D is a standard methodology used in leading quality systems, providing a structured process for correcting complex issues. 8D focuses on analysis, corrective action and preventive action (Permanent Corrective Action).								
Step	1	2	3	4	5	6	7	8
Action	Establish the Team	Problem Definition	Develop Interim Containment Action	Identify & Verify Root Cause	Identify Permanent Corrective Actions (PCA)	Implement & Validate PCA	Prevent Recurrence	Team Closure
1	Establishing the Team and Goals: Appropriate group of people with the process/ product knowledge, allocated time, authority and skill in the required technical disciplines to solve the problem and implement corrective actions.				Team Goals: <ul style="list-style-type: none"> Ensure client risk is minimized and managed to the best extent possible. Team Objectives: <ul style="list-style-type: none"> Determine Root Cause for the <i>Syphacia obvelata</i> outbreak in IBU506. Establish containment plan, near term corrective action, and future preventive actions. Provide maximum transparency and support to clients who were impacted, and transparency/assurance to clients who were not impacted. 			
	Department	Name	Skills	Responsibility				
	Quality Assurance	Lou Cimbrello	Quality Management	Team Leader				
	Quality Assurance	Danett Revalee	Quality Management, Auditing	Cambridge City Auditing				
	Veterinary Sciences	Dr. Jeff Lohmiller	Attending Veterinarian	Investigator, liaison with client veterinary scientists				
	Operations	Kevin Behan	Operations	Operations Leadership				
	Operations	Cheryl Brannigan	Operations	Cambridge City Production Manager				
	Operations	Troy Morrison	Operations	Cambridge City Site Leader				
	Health Diagnostics	Dr. Paula Roesch	Health testing	Testing Program				
	Sales	Carole Levin	Sales operations	Coordination of Client Communications				
	Inventory	Sara Navins	Production / Inventory Planning	Analyst				
	Customer Service	Tamera Connolly	Customer Service	Care of clients				
	Genetics	Dr. Ana Perez	Genetics	Genetic testing of samples				
	Executive team	Patrick Laverty	VP Quality	Executive Liaison				

2	<p>Problem Definition</p> <p>Provides the starting point for solving the problem or nonconformance issue.</p>	<p>On Monday, June 2, 2014, an evaluation of sentinel mice from Barrier 506 confirmed positive results, identifying both ova and adult <i>Syphacia obvelata</i>. Taconic has evaluated <i>all</i> remaining locations at the Cambridge City site, and established them to <i>all</i> be <u>negative</u> for <i>Syphacia obvelata</i>, indicating the problem is isolated to a single unit.</p>
	<p>Part Number(s):</p>	<p>B6, FVB, DBA2,B6D2F1,WKY</p>
	<p>Customer(s):</p>	<p>Multiple</p>
	<p>List all of the data and documents that might help you to define the problem more exactly?</p>	<ul style="list-style-type: none"> • Client feedback. • Production reports. • Quality report and audit results. • Barrier inspection reports. • Health testing data.
	<p>Action Plan to collect additional information:</p> <p>All data was delivered in multiple iterations during the investigation period from June 2 to June 20.</p>	<ul style="list-style-type: none"> • Production, shipment data collected - S Navins. • Fecal and environmental sampling – C. Branigan • Facility Inspections – T. Morrison • Testing Results – P. Roesch • Client Feedback – C. Levin
3	<p>Developing Interim Containment Actions</p> <p>Temporary actions to contain the problem and “fix” until permanent correction is in place.</p> <p>The following containment actions were taken:</p> <ul style="list-style-type: none"> • Immediate suspension of shipments from barrier 506 and subsequent contact with clients receiving animals from 3/ 15/ 2014 to 5/30/2014. • Immediate test via fecal PCR of all 506 and all Cambridge City barrier locations. • Immediate quarantine of the barrier including incoming and outgoing materials, waste, maintenance personnel movement. • Immediate humane euthanasia and disposal of the entire barrier rodent population. • Immediate redeployment of animals from other source locations to meet clients’ needs. • Scheduled derivation of DBA/2 and WKY strains for start-up of new breeding colonies. Notified past customers of future availability of DBA/2, B6D2F1 and WKY animals 	
4	<p>Identifying & Verifying Root Cause</p>	
	<p>Possible root causes of the problem:</p> <p>Possible paths for <i>Syphacia obvelata</i> to enter the barrier were suggested in a brainstorming session with the response team.</p> <p>Based on discussions with veterinary scientists, and review of texts on the subject, the team determined that <i>Syphacia obvelata</i> into Barrier 506 could have occurred via one of 3 paths:</p> <ol style="list-style-type: none"> 1. Animals imported into the barrier (Taconic Animals). 2. Human or materials movement that accidentally transported eggs into the building. 3. Entry of a <i>Syphacia spp</i> positive rodent or insects into the barrier. <p>All three options were pursued as investigation paths in subsequent root cause analyses.</p>	
	<p>Root Cause Analysis:</p> <p>Taconic gathered additional information in the form of audit reports, facility inspection reports, and staff discussions. The team worked through Ishikawa (6M) and logic tree analysis and identified the following results for the three investigation paths:</p> <ol style="list-style-type: none"> 1. Animals imported into the barrier (Taconic Animals). Carrying <i>Syphacia obvelata</i> was ruled out as a root cause for the following reason: The barrier was populated in October 2012. Since then only incremental animals have been added from source locations (Gnotobiotic isolators) which are negative for <i>Syphacia obvelata</i>. 2. Human or materials movement accidentally transporting eggs into the building was ruled out as a root cause 	

	<p>for the following reasons: (1) A review of materials central processing (autoclaving, disinfection, sanitization) found no nonconformities or abnormalities; (2) Review of human processes, barrier entry, materials movement, aseptic techniques found no nonconformities or anomalies; (3) The spread of <i>Syphacia ovelata</i> within the three barrier rooms with the greatest prevalence in sentinel cages in room 2 indicates the likely point introduction of <i>Syphacia</i> was in room 2.</p> <p>3. Entry of a <i>Syphacia obvelata</i> positive rodent into the barrier was identified as the highest probability root cause for the following reasons: (1) IBU506 Building inspection resulted in the identification of a potential gaps where a wild mouse could have entered into the building's ductwork and subsequently through an exhaust cover into barrier room 2; (2) review of the barrier's internal pest control program indicated a lapse in controls which occurred between QA audit cycles (not detected by the auditing program); (3) inspection of the barrier identified mouse feces in and around the exhaust ductwork in room 2. Samples of these feces, tested via PCR, were found to be positive for <i>Syphacia obvelata</i>. In addition, (4) Genomic DNA isolated from the fecal material found in the IBU506 room 2 exhaust duct was tested to identify the host genus. Using a multiplex PCR for mitochondrial DNA, it was determined that the source DNA was from the <i>Mus</i> genus, however a species could not be determined. Genomic DNA was further tested using a 27 microsatellite panel. The microsatellite profile from the duct feces was unique and not consistent with any inbred line including those raised in IBU506.</p> <p>The DNA sample was also assessed for the presence of other infectious agents and these results are compatible with agents found in wild rodents. The infectious agents which were identified are more commonly reported in wild populations. In addition to <i>Syphacia</i>, the feces were positive for nucleic acids of Trichomonads, mites, <i>P. pneumotropica</i>, <i>Helicobacter</i> and MHV. All of our health testing results for IBU506 remained negative for these additional agents up to and including the health testing where <i>Syphacia</i> was identified.</p> <p>Taken together, these data are consistent with wild rodent feces and the most likely source of <i>Syphacia obvelata</i>.</p>
5	<p>Identify Permanent Corrective Actions</p> <p>The following Near-Term Corrective Actions are implemented or in process for IBU506:</p> <ul style="list-style-type: none"> • IBU506 is closed, animal free, and will not produce animals for sale for a minimum of 6 months. • IBU 506 reprocessing has begun including physical cleaning followed by steam cleaning and finally by exposure to 360 ppm chlorine dioxide gas for 4 hours to destroy any remaining <i>Syphacia</i> eggs. • IBU 506 will complete reprocessing in 2015 after complete replacement of HVAC ducts. • The barrier will be subjected to an extended screening/revalidation program. It will be sentinelized for an extended period spanning many <i>Syphacia spp.</i> life cycles with repeated animal and environmental PCR testing until a statistically robust risk assessment can be completed. • Only after this is complete, will the barrier be repopulated and production colonies restarted. <p>The following Near-Term Corrective Actions are implemented or in process for the Cambridge City Site:</p> <ul style="list-style-type: none"> • All barriers have been inspected, both structurally and for in-barrier process. Taconic confirms that there were no findings in other locations similar to IBU506. The building deficiencies and process lapses were isolated to IBU506 only. • All Cambridge City locations are subject to fecal PCR surveillance for <i>Syphacia spp</i> at a 100% sampling, weekly frequency for all sentinel cages. All locations continue to test negative weekly since June 2. 100% sampling at Cambridge City will continue for the remainder of 2014. <p>Permanent Corrective Actions (Preventive Actions) Identified:</p> <ol style="list-style-type: none"> 1. Taconic will implement an augmented auditing program, increasing random, unannounced spot checks of inside and outside barriers for condition, pest control, and general process. This is in addition to the standard scheduled QA audit program. The audits will be more frequent and include cross functional members including operations, facilities, and Veterinary Sciences staff. 2. Taconic will reinforce and augment the pest control program both inside and outside barriers, to reduce the likelihood of ingress and implement data tracking capture on relevant data (captured pests, type, number).

6	<p>Implementing & Validating the Permanent Corrective Action</p> <p>Validation of the Permanent Corrective Action will be achieved through the following steps:</p> <ol style="list-style-type: none"> 1. Auditing program demonstrating 100% compliance for all Taconic locations over a 6 month period continuing forward with periodic monitoring. 2. Continued PCR monitoring to demonstrate required performance levels and provide clients with the required confidence levels. 3. Establishment of improved metrics / surveillance in pest control program.
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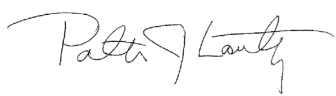
7A	<p>Preventing Recurrence in this location and others</p> <p>The permanent corrective actions and their validation (listed above) should prevent reoccurrence.</p>
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7B	<p>Review the following documents / systems</p>
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Document	Who Responsible	Completion Date	
		Planned	Status
Review and Update Pest Control SOPs	Operations and Veterinary Sciences	7/3/14	Completed 7/30/14
Review and Update Auditing Process SOP's	QA (in consult with Ops, veterinary sciences)	7/3/14	Completed 7/30/14

8	<p>Team Closure</p> <p>** Team moves to monitoring mode as of Aug 28, 2014 and disengages Sep 30, 2014. ***</p>
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Was this problem solving exercise effective? Has it been verified with a follow-up?

Yes No	Signature / Title / Date	Findings
YES	 Vice President, Quality and Business Systems	<p>Root cause was found and actions implemented are showing effectiveness.</p> <p>Pest control and audit program augmentations are complete.</p> <p>Cambridge City, and all Taconic locations test negative "-" for PCR.</p>