

# Microbial Contamination and Control Conference





# **How Sherlock Holmes Helped Me to Improve My Root Cause Analyses**

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May 8<sup>th</sup> & 9<sup>th</sup>



## Speaker Biography



Paula Peacos, M.S. brings 30 years of practical industry experience as a microbiologist. She has worked in contract manufacturing and testing organizations as well as small, mid-size and large pharmaceutical organizations.

Paula possesses extensive experience in aseptic processing, biological API/drug substance manufacturing, cell and gene therapies and nonsterile production, both clinical and commercial, as well as microbiological laboratory management.

She has also conducted numerous compliance audits internationally as a microbiological subject matter expert. She is an experienced trainer and has developed and implemented creative, customized developmental and remedial programs both in the US and abroad.

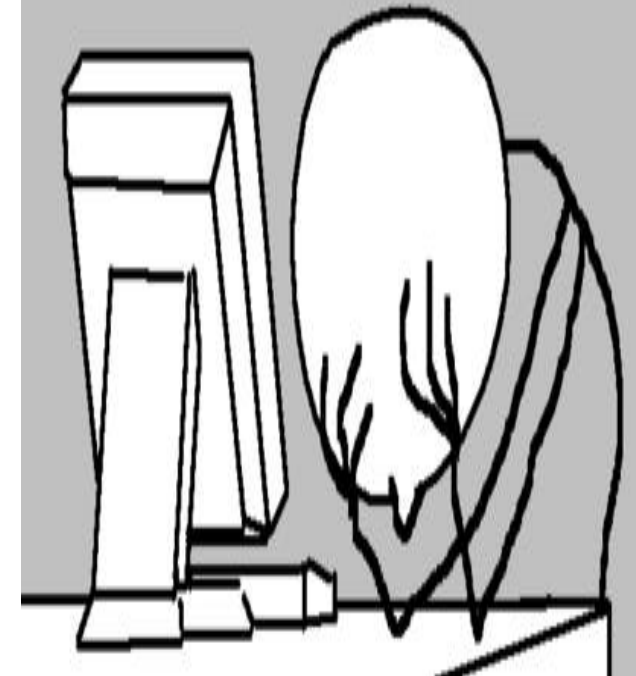
In recent years, Paula has published a number of articles, conducted technical webinars and presented at major industry meetings on topics such as data integrity, using contamination rates for trending analysis, designing and implementing robust environmental monitoring and trending programs and performing successful root cause analyses, among others.

Paula is currently employed as a Senior Consultant and Microbiological Subject Matter Expert at ValSource, Inc. She can be contacted at [ppeacos@valsource.com](mailto:ppeacos@valsource.com).

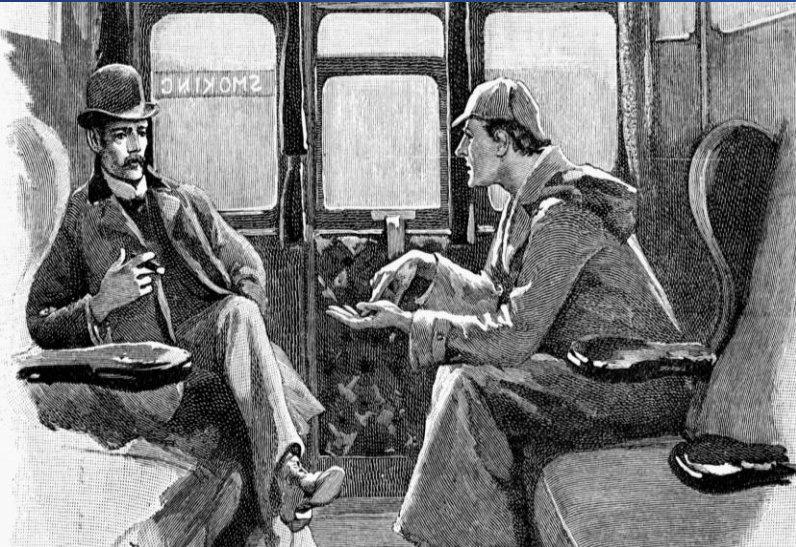


## Microbiological Data Deviation Investigations

- Time consuming
- Usually investigating a past event
- Direct evidence (the so-called “smoking gun”) is rare.
- Investigator is often under intense pressure to find the root cause as quickly as possible
- Investigative path is often unclear







## Sherlock Holmes- The World's Greatest Detective

- In 1892, “A Study in Scarlet” by Sir Arthur Conan Doyle was published.<sup>1</sup>
- In solving his cases, Sherlock Holmes:
  - Relied on logic, reasoning, and most importantly, **observation and simple common sense**
  - Identified and fully evaluated **all** available evidence, **even the most absurd**, and considered **nothing else**
  - Did not allow **bias** generated through **speculation, random hypothesis or previous experience** to determine or redirect the course of his investigations





## Sherlock Holmes- The World's Greatest Detective

Keeping some of Holmes's most famous quotes in mind will prompt an investigator to:

- Recognize and fully consider **more obscure and often overlooked sources** of potential error and deviation
- Uncover **hidden bias**
- Greatly increase the chance of finding that elusive definitive root cause





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***“The world is full of obvious things which nobody by any chance ever observes.”***

***- Sherlock Holmes, “The Hound of the Baskervilles”<sup>2</sup>***





## Constant Repetition can be Blinding



- We usually don't recognize that something has changed until we get an unexpected result.
- We fail to notice the difference because, as Holmes succinctly put it, *we see but we do not observe.*<sup>3</sup>





# Constant Repetition can be Blinding

- When an unexpected result has occurred, an investigation and root cause analysis will be initiated.
- If the operator failed to recognize the error when it occurred, how likely are they to recognize it several days later?





## The Operator Interview

- Operators are often the best source of information (and CAPA).
- Most operators will not intentionally commit an error.
- **You are looking for what they failed to observe.**







## Conducting a Successful Interview

- Keep the tone conversational as opposed to authoritarian.
- Assure the operator that you see him/her/them as part of the solution.
- Asking “did anything unusual occurred while you were performing the task” in most cases will result in an answer of “no”.





## The Method of Questioning is Key

- Ask the operator to recreate the event and describe each step of the assay.
- Ask questions like these:
  - “What was happening in the lab while you were performing the assay?”
  - Ask them what they think happened, and most importantly, **why** they think it happened.







## Real Answers from Real Operators



- “The lot numbers are so long it’s really hard to record them without transposing at least one number.”
- “I had to stop what I was doing to receive an in-process sample that Manufacturing dropped off to the lab.”
- “I had to keep stopping while I was performing the assay because Manufacturing kept calling me to ask when the results will be available.”
- “The 70% IPA wipes in the opened package I used were still pretty wet, but now that I think about it, I didn’t smell any alcohol.”



## A Word about Checklists....



- Checklists are a practical and useful tool for conducting investigations **provided they do not become a substitute for critical independent thought.**
- If checklists are employed, they should be frequently reviewed, updated and supplemented, as necessary.





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*“It has long been an axiom of mine that the little things are infinitely the most important.”*

– Sherlock Holmes, *“A Case of Identity”*<sup>4</sup>





## Consider this Scenario:



- An operator uses a commercially produced calibrated microbial suspension to perform an assay.
- The operator is required to rehydrate the organism and dispense a precise amount of the suspension onto an agar plate.
- The suspension is from a qualified lot that has been routinely used by multiple operators for some time and produces consistent results.
- After incubation, the operator finds that the calibrated suspension has yielded a count that is far lower than expected and is also well outside the normal range of variation for the lot.



## Theoretically Possible Root Causes

- The operator may have:
  - failed to fully rehydrate the organism
  - incorrectly set the amount to be drawn on the micropipette
  - held the micropipette in an improper position when drawing and/or dispensing
  - improperly secured the tip onto the micropipette, resulting in an improper draw
  - failed to fully dispensed the contents of the pipette onto the agar surface
  - failed to wipe or dab the tip of the pipette against the surface of the agar
  - used the wrong pipette type or size
- The pipette may be damaged or out of calibration.
- The suspension used could have been faulty.







We sometimes  
underestimate  
the influence of  
*little things.*

*Charles W. Chestnutt*

## Finding those “Little Things”

- In cases like these, the “root cause” will often be reported as “operator error”.
- If the procedure specifically requires the operator to perform each critical step in a particular manner, the likelihood of recurrence can be drastically reduced.



## Procedures and Test Methods

- Are they too long?
- Are the instructions clear and **executable** as written?
- Are **decisions or interpretations left up to the operator?**
- Does an operator need multiple procedures to execute a single task?
- Could there be a language barrier potentially impacting correct understanding?
- Who performs periodic review? Author or user?





## It's Not Enough To Verify Training Was Completed

- It is important to verify that
  - Training the operators received was clear and **appropriate to the task**
  - Content and method of delivery was **consistent** for all operators
  - **Trainer's ability** to effectively deliver content and verify correct understanding
  - All trained operators correctly interpreted and clearly understood the content
  - All operators are performing the task in **exactly the same manner**

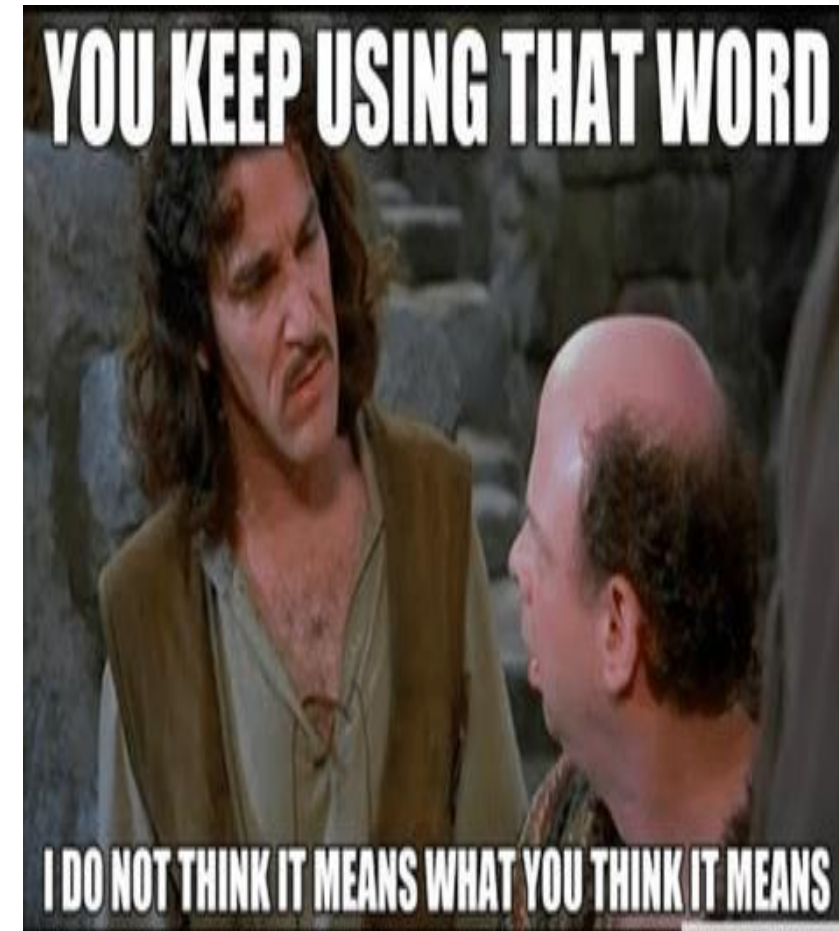






## It's Not Enough To Verify Training Was Completed

- How is comprehension measured and verified?
- Are they truly proficient?
- Errors in interpretation or understanding are often difficult to uncover.
  - **Have the operator explain the procedure to YOU.**





**“There is nothing more deceptive  
than an obvious fact.”**



**– Sherlock Holmes  
“The Boscombe Valley Mystery”<sup>5</sup>**



## The Problem with “Obvious Facts”



- We tend to accept things we believe are true without giving them due consideration.
- Failing to consider extenuating circumstances is a form of **bias**.
- **Bias** can take the investigation in the wrong direction, leading to a wrong conclusion.





## Examples of “Obvious Facts”

- “Human” vs. “environmental” organisms
  - “The organism is of human origin, so it must have been from the operator.”
  - “The organism is of environmental origin, so it had to come in on a material.”





## Examples of “Obvious Facts”

- “The vendor is qualified, and we have been using them for years.”
- “The operator is well-experienced and always pays attention to detail.”
- “The operator is new- they must have made an error.”

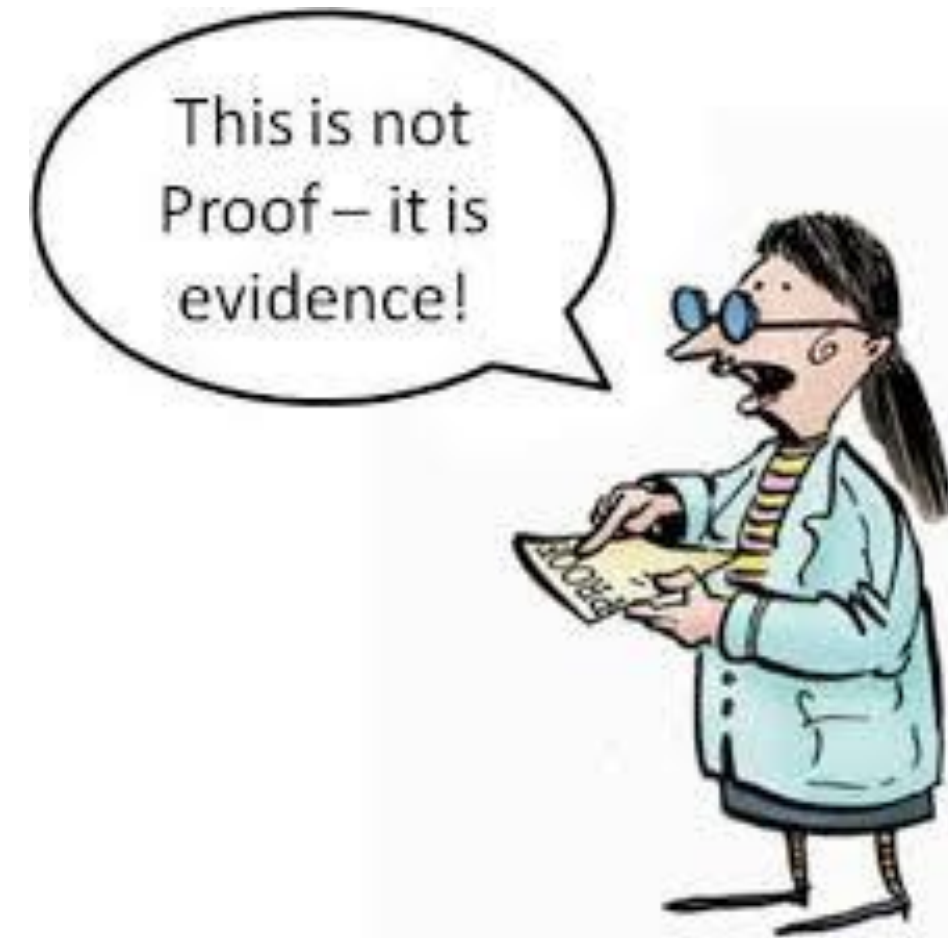
“Two of the most virulent behavioral organisms are overconfidence and an overemphasis on recent history”

~William Bernstein, M.D.



## Examples of “Obvious Facts”

- “Our sanitization methods are validated and have always been effective.”
- “The operator’s hands were clean- no growth was observed. Therefore, it wasn’t the operator.”
- “We have a validated overkill cycle, so nothing could have possibly survived.”





# Examples of “Obvious Facts”

- “We didn’t detect any contamination at any point upstream in the process.”
- “The environmental monitoring (EM) data showed no recoveries.”

People  
generally see  
what they look for  
and hear  
what they listen for.

-Harper Lee  
To Kill a Mockingbird





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***“Circumstantial evidence is a very tricky thing. It may seem to point very straight to one thing, but if you shift your own point of view a little, you may find it pointing in an equally uncompromising manner to something entirely different.”***

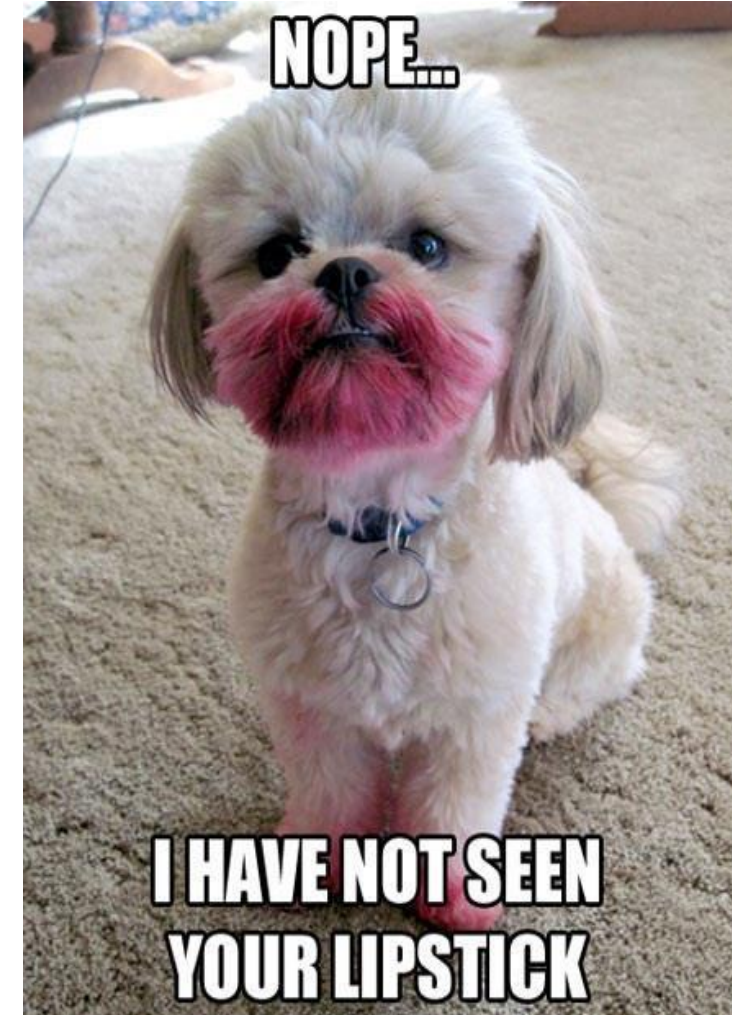
***- Sherlock Holmes, “A Study in Scarlet”<sup>1</sup>***





# Interpreting Circumstantial Evidence

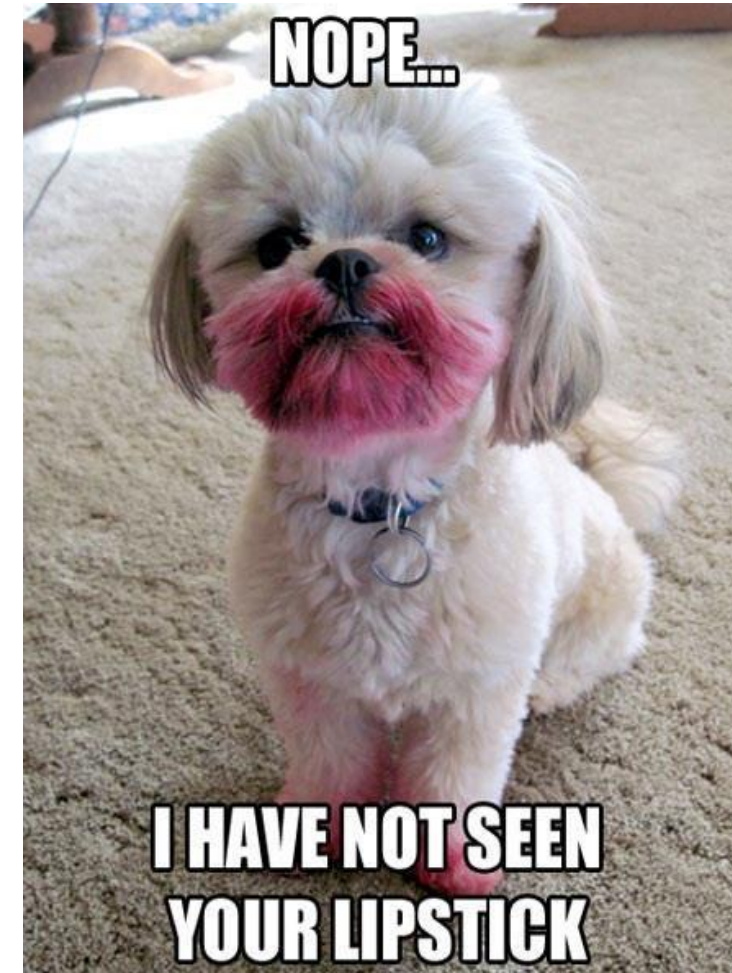
- We tend to interpret and accept or dismiss evidence **based on our own experience and similar past events.**
- Conclusions drawn by two investigators from the same piece of evidence can be completely different.
- **Two deviations that appear to be identical may have entirely different root causes.**





# Interpreting Circumstantial Evidence

- Investigations are best performed by cross-functional teams
- You need the **correct** Subject Matter Experts with **demonstrated experience**
- SMEs need to **actively participate in the investigations from the beginning.**





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***“It is a capital mistake to theorize before one has data. Insensibly one begins to twist facts to suit theories, instead of theories to suit facts.”***

***– Sherlock Holmes, “A Scandal in Bohemia”<sup>6</sup>***





## The “Obvious Root Cause”

- Sometimes we look at a deviation and assume there is no need to investigate further because the root cause appears to be obvious.
- The investigator must look at **all of the available evidence and only the available evidence.**
- It is critical not to summarily dismiss or accept any piece of evidence without thoroughly **evaluating it within the context it occurred.**





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***“It is an old maxim of mine that when you have excluded the impossible, whatever remains, however improbable, must be the truth.”***

***– Sherlock Holmes, “The Beryl Coronet”<sup>7</sup>***



## Sometimes the seemingly impossible is indeed possible...

- It is a well-known fact that although microorganisms can and do grow in sterile water at 2-8°C, the growth is usually minimal.
- It is also a well-known fact that microorganisms in general possess the ability to mutate in order to survive unfavorable conditions.
- The error in the root cause analysis occurred when the supervisor continued to pursue the “obvious root cause” even though **the documented evidence clearly suggested otherwise.**







## Defining and Justifying the Root Cause



- Compile **ALL** of the information you have gathered and draw a reasonable and scientifically sound conclusion.
- The **rationale** behind any and all decisions must be clear and scientifically justified.
- If you are ruling something out, **explain why**.
- *If you have a piece of hard evidence that does not fit your determined root cause, either your root cause is incorrect, or you have more than one cause.*
- You have an obligation to exhaust all avenues.





## Summary

- Keeping these famous quotes in mind can help one more easily and more accurately determine the definitive root cause.
- It does not, however, require a detailed root cause analysis to determine why these quotes attributed to a fictional 19<sup>th</sup> century detective still hold perfectly true more than a century later.
- In this case, the root cause is indeed truly obvious....





## Root Cause:

**Doyle was a genius.**







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# Thank you for your kind attention!





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