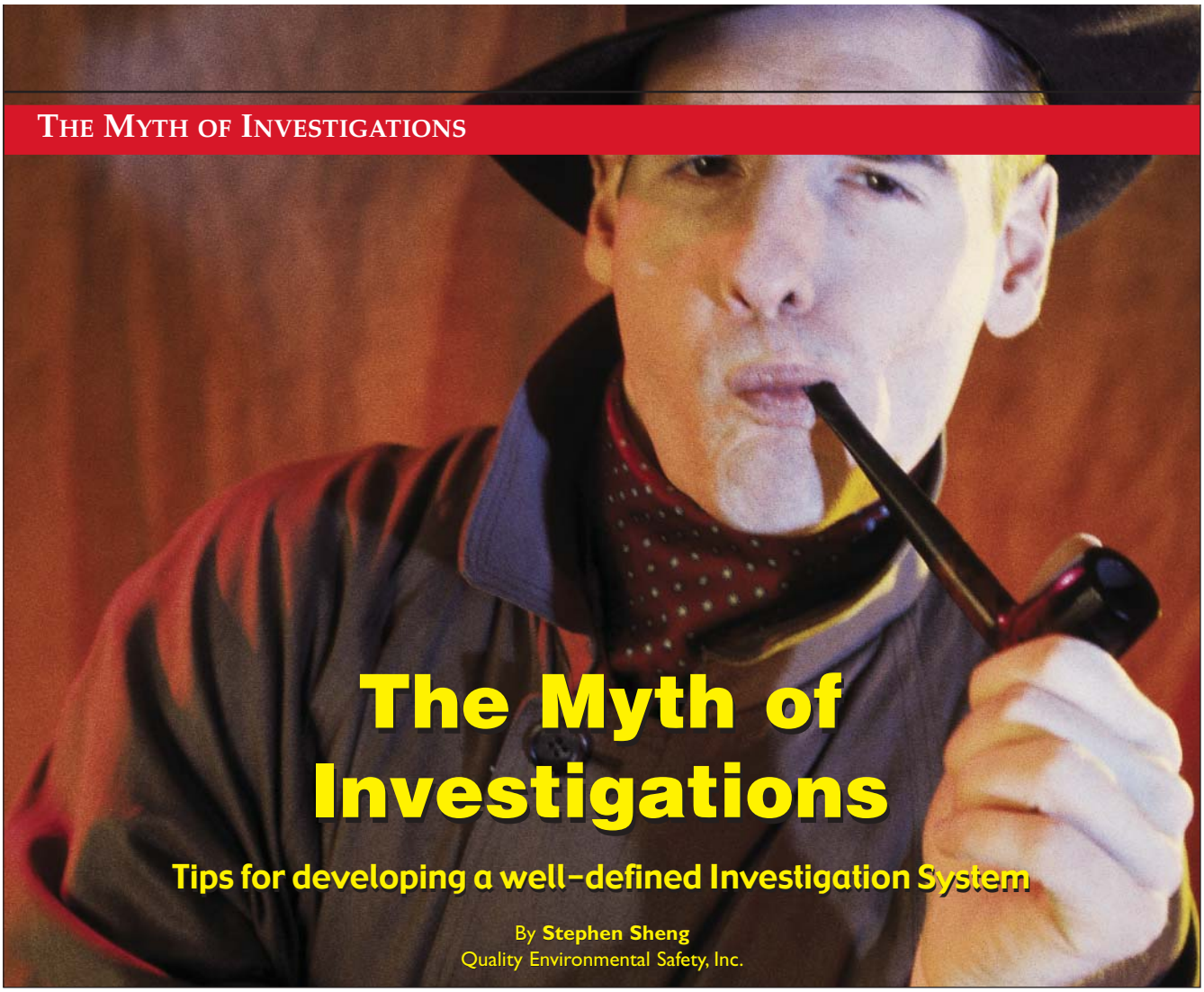


The Myth of Investigations

Tips for developing a well-defined Investigation System

By **Stephen Sheng**
Quality Environmental Safety, Inc.

THE DIFFICULTIES IN CONDUCTING TIMELY and thorough investigations make them the center of attention during most FDA inspections and ISO audits. Since investigations form an integral part of many quality systems (e.g., Deviation System, Customer Complaints Program), they could cause all of these quality systems to be dysfunctional if they are not handled properly. This is especially true for the Corrective Action and Preventive Action (CAPA) System, as poorly conducted investigations could lead to true root causes not being identified and wrong CAPAs being generated. Implementing the wrong CAPA is not just a waste of sacred resources but could also lead to bigger and more serious problems, since it means the cause of the incident has not been corrected.

However, it could bring an organization to a complete stop if every single incident were investigated, and would also potentially delay those investigations that are truly necessary. The balance between not investigating every incident and conducting timely and adequate investigations lies in the design of the Investigation System. This article will uncover the myth of investigations (when and how investigations should be conducted) and provide the path to a well-designed Investigation System.

The Incident

Investigations can result from many sources, both internal and external. Internal sources are those investigations being conducted for nonconforming materials/products, and external sources are those investigations conducted due to customer complaints. Investigations must be thorough and timely, as management decisions (business as well as quality) are often made based on the investigation results. If investigations were poorly conducted, they could be detrimental to an organization from both a compliance and financial standpoint (e.g., releasing a product that should not be released).

An incident can occur anywhere and anytime in an organization. However, not all incidents are the same nor demand the same level (i.e., length and depth) of attention. The length and depth of each investigation should be dependent on the nature of the incident encountered. Some incidents are minor in nature and do not warrant an investigation. Some incidents are major and can affect the quality of the product. The severity of each incident should be measured by:

a) Its impact on the safety, efficacy and quality of the material or product involved; and
b) Its risk as related to the statutory, regulatory and/or customer requirements.

Minor incidents should be documented on the associated quality records for future reference. Major incidents must be

Stephen Sheng is a consultant with core expertise in quality management and regulatory compliance. He is also a CQA, CQE and RAB Certified QMS Lead Auditor. He can be contacted at auditing@aol.com

thoroughly investigated based on the methodology established by the organization. Figure 1 lists some examples of minor vs. major incidents. To ensure that all major incidents are captured, the Quality Unit should review all quality records on a periodic basis. Further, trend analysis should be performed on all incidents (including minor ones) to ensure that no vital few problems exist.

Figure 1: Examples of minor vs. major incidents

Minor Incidents	Major Incidents
Documentation error like typos	Documentation error like missing records
Equipment malfunction during maintenance	Equipment malfunction during production
Damaged material containers upon receipt	Contaminated materials
No violation of cGMP or ISO requirements	Violation of cGMP or ISO requirements
Process deviation that has no product impact *	Process deviation that impacts product quality

* For incidents that have serious cGMP violations but no product impact, they should still be classified as major.

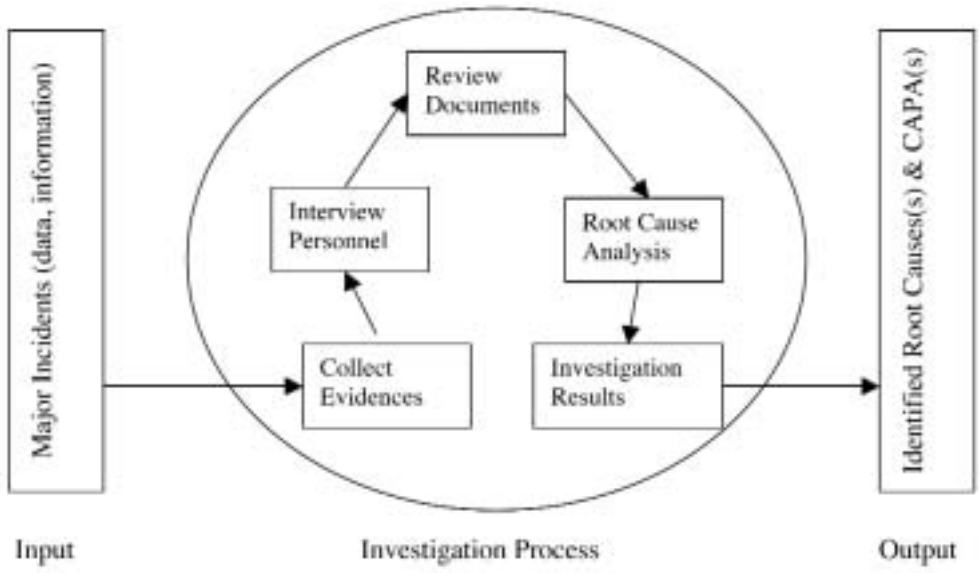
The Process

The best approach to understand a system is to map out the process. A process is defined as a "set of interrelated or interacting activities that transforms inputs into outputs"[1]. The method is to map out (or flow-chart) the required activities (or steps) of the process and to identify the interrelationship of those steps within the process. This is called the "process approach"[2] as defined in ISO 9000:2000 Standard. A simplified process model of the Investigation System is shown in Figure [2]. This process approach is also useful to improve existing systems by developing the process map (if one doesn't already exist) to reflect the established workflow and compare it with the actual process that is in use. As such, the gaps between the documented process and the actual process could be identified.

To conduct investigations that would lead to true root causes, the collection of data must be accurate and timely. Since the collected information and data are used as evidence to support the investigation results, the information and data collected must be relevant for the incident involved and must be captured and documented at the time the incident occurred. This is a critical step (i.e., information and data gathering) and can greatly affect the success of the investigation.

Information (or more specifically, evidence) can be lost or disappear if not captured in a timely manner. However, the organization cannot wait forever to secure the incident scene for gathering information. To help the operator to know which information and evidence to collect and retain for later use by the assigned investigator, an investigation template should be developed. An example of an investigation template is included as Figure 3; however, each organization should develop its own template to best suit its operational needs. The template can be divided into two parts: Part I for data collection and Part II for documenting the investigation results, identified root cause(s), and CAPAs.

Figure 2: Model of a process-based Investigation System



Investigation Techniques

Due to the time urgency and the criticality nature of an investigation, one would be fortunate to have weeks to conduct an investigation. The norm of the pharmaceutical industry to complete an investigation is 15-20 business days, counting the time from the beginning to the end: incident observed to collecting evidences/information to conducting the investigation to writing the investigation report to reviewing/approving the investigation. This is a very tight window and

Figure 3: Investigation Template

Part I – Data Collection		
Date of Incident:	Observed By:	
Product/Material/Component:	Part No.:	Lot No.:
SOP/Method:	SOP/Method No.:	Revision Level:
Record (form used):	Form No.:	Revision Level:
Equipment:	Equipment ID:	Last Calibration Date:
People (operator name):	Job Function:	Department:
Environment (facilities/utilities):		
Description (attach additional page if needed):		
Part II – For Investigator Use Only		
Investigation Summary (attach additional page if needed): Investigated By: Date:		
Identified Root Cause(s):		
Corrective Action(s): Responsible Party: Estimated Completion Date:		
Preventive Action(s): Responsible Party: Estimated Completion Date:		

Figure 4: RCA Classification/Coding Scheme (example)

Code	Description
1	**Materials (including components and products)**
1-1	Supplier performance
1-2	Material does not meet specifications
1-3	Contamination or foreign matters present
1-4	Others
2	**Methods**
2-1	Inadequate procedures, work instructions, or drawings
2-2	Inadequate test methods or specifications
2-3	Unclear process steps or parameters
2-4	Others
3	**Documentation**
3-1	Missing records
3-2	Unclear forms (need to be more specific in the information required)
3-3	Critical information (e.g., test results, approvals) not documented
3-4	Others
4	**Equipment**
4-1	Equipment malfunction
4-2	Expired calibration
4-3	Out of calibration (test results impacted)
4-4	Others
5	**People (including personnel training)**
5-1	No or inadequate training provided
5-2	Failed to follow procedures or work instructions
5-3	Human error (accident or mistake)
5-4	Others
6	**Environment (facilities, utilities, etc.)**
6-1	Utility excursion during production
6-2	Poor facility design
6-3	Old or obsolete, needs replacement
6-4	Others
7	**Miscellaneous / Others**
7-1	Natural causes (e.g., weather events)
7-2	Others

requires a systematic approach to conduct the investigation, including root-cause analysis to ensure that the time requirement can be met.

There are many problem-solving tools and root cause analysis (RCA) techniques that one can use in conducting an investigation; e.g., the "cause and effect (fishbone) diagram"[3] and the "fault tree"[4] technique. To ensure consistency among different investigators, the Quality Unit should review all those different tools and techniques and select the methodology (this can be a combination of various tools and techniques) that best fits the organizational needs.

An investigation is only considered complete and adequate when it contains all the necessary information and data (i.e., input), investigation results, including root-cause analysis (i.e., process), and the identified root cause(s) and CAPA(s) (i.e., output). To provide consistency in the investigation process and to ensure that similar outcomes would be concluded if different investigators were used, each investigation should, at a minimum, review the following aspects as they related to the incident:

a) Materials – any materials, components, and products involved;
b) Methods – procedures or test methods followed/used;
c) Documentation – the records used;
d) Equipment – the equipment that caused or affected by the incident;
e) People – work performance and training of the operator or operators involved;
f) Environment – facilities, utilities and environmental conditions impacted; and
g) Miscellaneous – like natural forces and uncontrollable factors (e.g., weather events).

Based on the methodology chosen, the investigator should be able to identify the root cause(s) of the incident and classify it (or them) into one of the seven key categories defined in Figure 4. This classification scheme is good for trend analysis and continual improvement of the manufacturing processes and quality systems. Sub-categories should be developed to further pinpoint the true root cause within each category. The coding scheme can ease up the tracking and trending purposes especially when automatic system is used.

A manual or automatic system should be in place to track all opened and closed investigations. An automatic tracking system will be helpful if the organization is dealing with a large amount of investigations and/or have multiple divisions/locations. The tracking system can be used to track other items like CAPAs and to provide notification when an investigation is overdue.

Figure 5: Characteristics of a good investigator

Personal Attributes	Professional Attributes
Sound judgment	Diligence
Good listener	Integrity
Able to communicate at all levels	Impartiality
Objective and open-minded	Honesty
Diplomatic	Commitment

Qualification of Investigators

Investigations are too critical to be taken lightly, but many times, people with limited experience and skills are assigned as investigators by an organization. This is a guarantee for failure. Investigators, like auditors, must possess a special set of characters and professional ethics as listed in Figure 5. In addition, the organization must establish a qualification process to train and qualify investigators. Providing the training and the skill sets required is an important factor to ensure a successful investigation. Each potential investigator should be knowledgeable and/or training provided on the following:

a) Knowledge of the process and the product involved;
b) Regulations (e.g., cGMP) and the requirements (e.g., ISO, customer) involved;
c) Problem-solving tool(s) identified by the organization;
d) Report-writing skills (e.g., technical writing); and
e) Use of the tracking system if an automatic system is involved.

Monitoring

There must be a mechanism to monitor the continual performance of the Investigation System and the individual investigators. The following are some tools that one can use to track and trend the performance of:

Process

a) Metrics (e.g., number of overdue investigations, cycle time)
b) Trend analysis
c) Internal audits

Investigators

a) Metrics (e.g., productivity)
b) Performance review
c) Internal audits

One of the key focuses during most FDA inspections and ISO audits is on the CAPA System and one cannot have an effective CAPA System without an effective Investigation System. A well-designed system must have:

- a well-defined process that lists all the required activities and their interrelationships;
- a systematic-approach to conduct the required activities;
- a qualification process for the personnel performing the activities; and
- a monitoring process to ensure that the System is functioning properly and for continuous improvement.

We hope that the elements discussed above provide the structure and foundation for the readers to set up a customized process that will meet the needs of their operations. ■

References

1 ISO 9000:2000, "Quality management systems – Fundamentals and vocabulary," Geneva: International Organization for Standardization, 2000.

2 ibid.

3 Evans, James R. and Lindsay, William M., "The Management and Control of Quality – Fourth Edition," Cincinnati: South-Western College Publishing, 1999.

4 Wilson, Paul F., Dell, Larry D., and Anderson, Gaylord F., "Root Cause Analysis – A Tool for Total Quality Management," Milwaukee: ASQC Quality Press, 1993.