1.0 Purpose

The purpose of this procedure is to provide principles and tools for Root Cause Analysis (RCA).

2.0 Scope

Root cause analysis is a core building block to continuous improvement efforts made at Ion Nutritional Labs. It may be required in investigations for Quality Events or process improvements, including the following:

- Non-conformances
- Deviations
- Out of Specification / Out of Trend laboratory results
- Complaints
- Adverse Events
- Audit Findings
- Risk Assessment / Risk Management

3.0 Responsibility

3.1 It is the responsibility of all employees assigned to complete a root cause analysis to follow this procedure.

3.2 It is the responsibility of Quality to keep this procedure aligned with current practices.

4.0 Definitions

4.1 **Cause** – the reason something happened. Causes of failure have sub-classifications as direct, indirect, potential, and /or root causes

4.2 **Direct Cause** – A cause clearly linked to the problem of failure

4.3 **Indirect Cause** – A cause that creates a circumstance or action that ultimately causes the problem or failure

4.4 **Potential Cause** – A cause that could be a direct or indirect cause to the problem or failure, but either was not or is not proven as a cause in the specific instance

4.5 **RCA** – Root Cause Analysis; A collective term that describes a wide range of approaches, tools, and techniques used to uncover causes of problems or failures and then analysis of those causes to determine the root cause(s)

4.6 **Root Cause** –The core or fundamental issue that sets in motion the entire cause-and-effect reaction that ultimately leads to the problem(s) or failure(s). Strict definitions of root cause restrict RCA to only one root cause; however, there are often multiple causes to a problem or failure. The root cause is the largest contributor and other causes are secondary. For the purpose of RCA, Ion Labs allows more than one cause labeled as a root cause as long as each root cause is a significant contributor to the problem or failure.

4.7 **Quality Event** – The issuance of an event number for a quality system subject to SOP QS-112 and as defined in the scope of specific SOPs associated with that system

4.8 **cGMP** – Current Good Manufacturing Practices

4.9 **CAPA** – Corrective and Preventative Action as defined in SOP QS-108

4.10 **OOS** – Out of Specification

4.11 **SME** – Subject Matter Expert

5.0 References

5.1 QS-111-F1, Form, Root Cause Analysis Form

5.2 C-105, SOP, Protocol and Report Documentation Requirements

5.3 QS-114,SOP, Quality Risk Management

5.4 QS-112, SOP, Core Quality Systems and Quality Events

5.5 C-201, SOP, Deviation and Investigation Procedure

5.6 C-501, SOP, Document Control

5.7 C-502, SOP, Record Storage, Retention, and Destruction

5.8 D-105, SOP, Out of Specification / Out of Trend Investigation

5.9 QS-101, SOP, Complaints

5.10 QS-102, SOP, Adverse Events

5.11 QS-108, SOP, Corrective and Preventative Action (CAPA)

6.0 Procedure

6.1 General Principles

6.1.1 Base RCA on scientific knowledge and the protection of the patient / customer.

6.1.2 Adjust the level of effort, formality, and documentation of the RCA to be commensurate with the level of risk.

6.2 RCA Documentation

6.2.1 For simple RCA, document the risk assessment directly in the documentation associated with the problem or failure.

6.2.2 For complex RCA, document the RCA in a report (see SOP C-105 Protocol and Report Documentation Requirements for report documentation).

6.2.3 Use form QS-111-F1 Root Cause Analysis Form to document all other RCA.

6.3 RCA Problem / Failure Sources

6.3.1 Initiate RCA in response to exception data (i.e. Quality Events that may negatively affect the quality of components, materials, products, procedures, or systems). These sources include, but are not limited to:

6.3.1.1 Complaints – SOP QS-101

6.3.1.2 Deviations – SOP C-201

6.3.1.3 OOS – SOP D-105

6.3.1.4 Audits or FDA Inspections

6.3.1.5 Product rejections / nonconformities

6.3.1.6 Recalls

6.3.2 Initiate RCA in response to non-exception data such as:

6.3.2.1 Data trending and holistic data reviews

6.3.2.2 Continuous improvement projects

6.3.2.3 Industry and regulatory surveillance

6.4 RCA Steps

6.4.1 Define the problem. The source typically defines the problem as well. If necessary, clarify the problem such that the problem or failure to analyze s clear.

6.4.2 Collect data to better understand the problem. Analyze the situation fully before moving on to identify contributing factors. Be cautious about making decisions on assumptions and theories. If possible, verify assumptions and theories with facts. Use the RCA tools as applicable.

6.4.3 Identify contributing factors. Identify as many potential causes for the problem as possible. Use the RCA tools in Section 6.5 as applicable.

6.4.4 Identify root cause(s).

6.4.5 Identify CAPA as applicable.

6.5 RCA Tools

6.5.1 5 Whys – the 5 whys method is a powerful RCA tool. This process must include individuals with practical experience with the system or process that is the source of the RCA investigation. The process simply asks the question "why" at least five (5) time. Each additional question is framed to ask why the previous why answer is true. See example in Attachment 1.

6.5.1.1 In general, ask "why" as many times as it takes to get to a root cause.

6.5.1.2 Do not ask why too many times such that unreasonable answers result. Asking why 5 times is an arbitrary number.

6.5.1.3 Search for factual answers, not opinions or guesses.

6.5.1.4 There may be more than one cause. In these cases, the 5 whys analysis may look more like a matrix with different branches.

6.5.1.5 If applicable, use this tool in combination with a Fish Bone Diagram.

6.5.2 Fish Bone Diagram – this RCA tool is also known as "The Cause and Effect" diagram. The diagram visually displays potential causes for a specific problem or effect. To construct a fishbone, start with stating the problem in the form of a question (i.e. "Why did X happen") and place it in a box at the head of the fishbone. See example in Attachment 2. The rest of the diagram consists of one line drawn across the page attached the problem statement and several lines, or "bones" coming vertically from the main line. The branches are labeled with different categories. The categories you use are up to you, but the following are good examples for manufacturing processes:

6.5.2.1 Machines (Equipment)

6.5.2.2 Methods (SOPs, Policies, Procedures)

6.5.2.3 Materials (Raw Materials

6.5.2.4 Measurements

6.5.2.5 Mother Nature (Environment)

6.5.2.6 Manpower (People)

6.5.3 Review – review of documentation and data records associated with a problem or failure may provide insight to the cause.

6.5.4 Interview – interviews of operators or individuals that observed or participated in the events that led to the problem or failure are often valuable. Additionally, interviewees that are Subject Matter Experts (SME) on a related subject may have insight into causes of the problem / failure.

6.5.5 Search – research on a subject related to the problem is similar to interviewing an SME. Solutions to the problem may already be well documented and could be referenced.

6.5.6 Other – root cause analysis is a common process to many industries. There are a number of good RCA tools available and many good training courses. Any tool or process that helps improve product quality and compliance is allowed.

6.6 Documentation Maintenance

6.6.1 All completed RCA forms will be maintained as outlined in SOP C-501 Document Control and SOP C-502 Record Storage, Retention, and Destruction.

6.6.2 When applicable, completed RCA forms will be filed with the Quality Event documentation to which it pertains (i.e. deviation, OOS, complaint).

7.0 Revision History

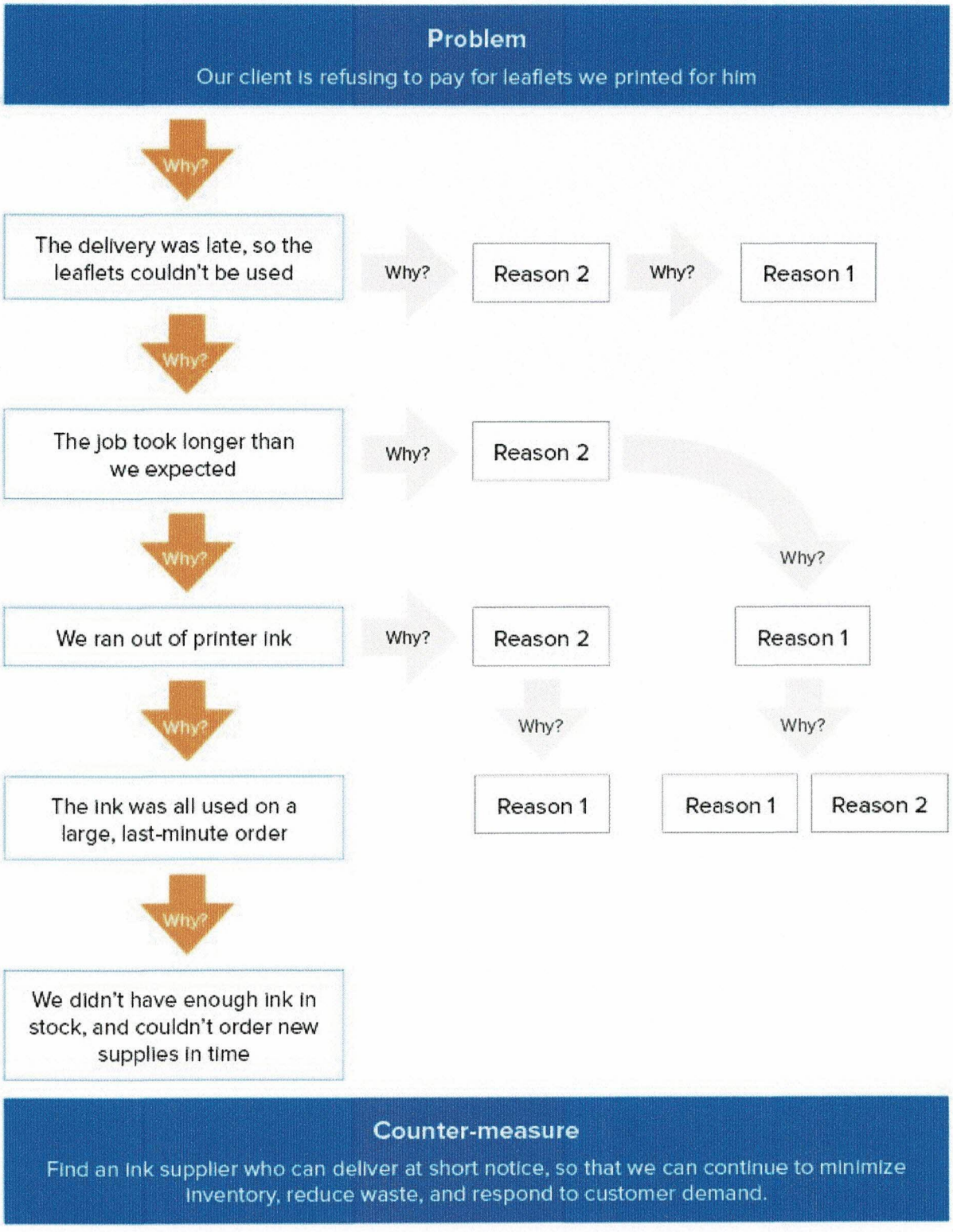
Revision	Date	Description of Changes	CCR #	By
0	01/14/20	New.	N/A	K. Burris
1	09/18/23	Scheduled review: update logo and format. Revise responsibilities. Add section for document maintenance.	CC-23-0470	K. Burris

8.0 Attachments

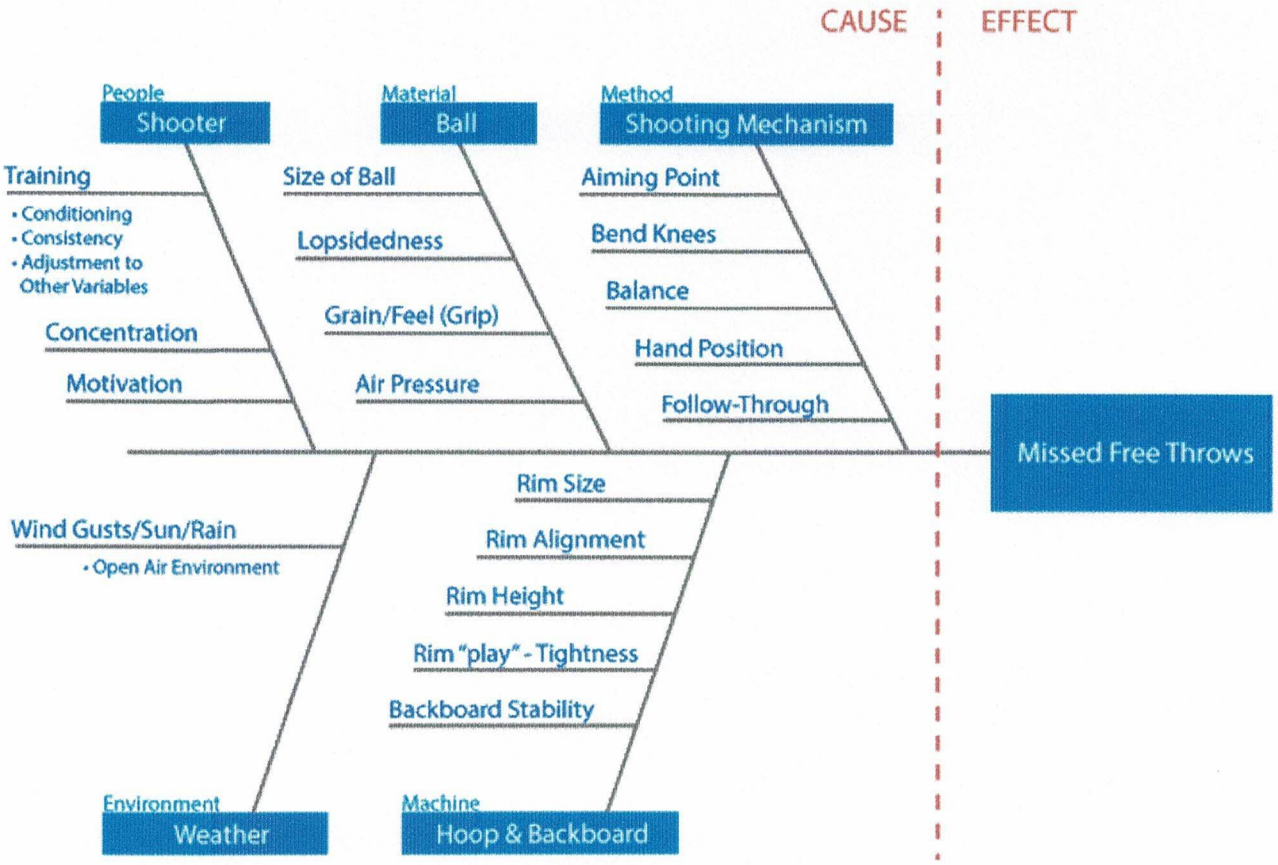
8.1 Attachment 1 – 5 Whys Example

8.2 Attachment 2 – Fish Bone Diagram Example

Attachment 1 – 5 Whys Example



Attachment 2 – Fish Bone Diagram Example



ION Nutritional Labs	Root Cause Analysis Form		
	Form: QS-111-F1	CCR No. CC-23-0470	Revision: 1

Root Cause Analysis (RCA) – Title / Description / Background

Source / Reference (i.e. DEV #, INV#, Etc.)	

Note: For complex RCA, write a report instead of using this form (see SOP C-105 for reports). For simple RCA, document the RCA directly in the source instead of using this form. Adjust the level of effort, formality, and documentation to the level of risk.

RCA– Use tools discussed in SOP QS-111 to identify potential causes and list viable causes in the RCA summary table on this form. Check all RCA tools used as applicable form the list below

5 Whys Fish Bone Review Records (specify) ______________________

Interview Observers / Operators (specify): ______________________

Interview Subject Matter Experts (specify): ______________________

Search Resources (specify): ______________________

Other (specify): ______________________

RCA Summary – Evaluate each listed cause and indicate the cause type (check all that apply). List CAPA as applicable. Note: A "Potential Cause" cause type indicates that this cause did not contribute in this instance.

Cause	Cause Type	Action Plan
☐ N/A or ☐ Cause (specify)	☐ Potential Cause ☐ Direct Cause ☐ Indirect Cause ☐ Root Cause	☐ CAPA ☐ None
☐ N/A or ☐ Cause (specify)	☐ Potential Cause ☐ Direct Cause ☐ Indirect Cause ☐ Root Cause	☐ CAPA ☐ Accept
☐ N/A or ☐ Cause (specify)	☐ Potential Cause ☐ Direct Cause ☐ Indirect Cause ☐ Root Cause	☐ CAPA ☐ Accept
☐ N/A or ☐ Cause (specify)	☐ Potential Cause ☐ Direct Cause ☐ Indirect Cause ☐ Root Cause	☐ CAPA ☐ Accept
☐ N/A or ☐ Cause (specify)	☐ Potential Cause ☐ Direct Cause ☐ Indirect Cause ☐ Root Cause	☐ CAPA ☐ Accept

Approval Signatures

Name	Title	Signature	Date
Completed By: (Initiator)			
Approved By: (Quality)			