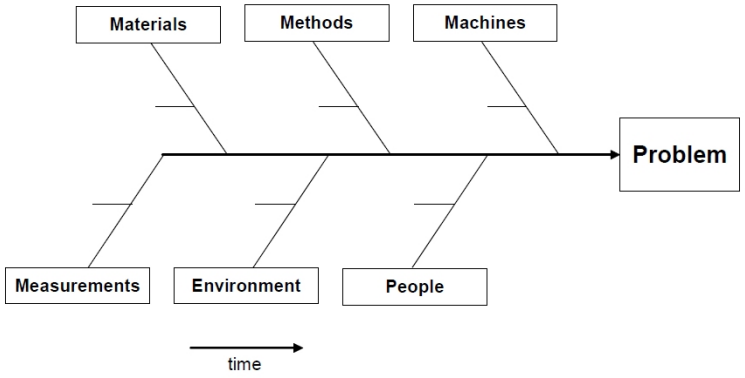
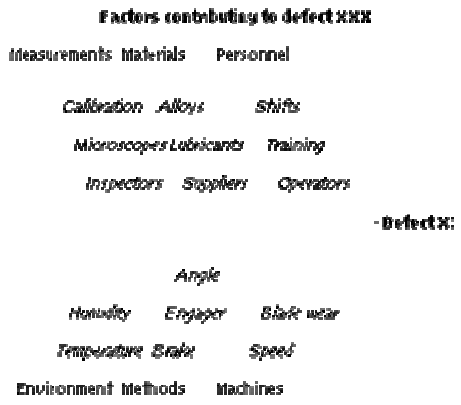
To perform a fact-based investigation for determining the root cause during the investigation is essential. The investigation shall be adequate with the significance and risk of the situation and shall include:

- A description of the situation including its impact on product quality, safety, efficacy, and purity.
- A review of all processes and/or systems that interact with or may have contributed to the cause
- Root cause investigation methodology (e.g. Fishbone, Ishikawa, Kepner-Tregoe, Fault Tree Analysis).



Fishbone diagram



Ishikawa diagram

The root cause of the situation:

- Identifying the action(s) needed to correct and prevent recurrence of nonconforming product and other quality problems.
- If validation is not required prior to implementation, a justification shall be stated.
- Verifying the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished product, either directly or via adverse impact to process performance and/or equipment effectiveness.
- The verification shall include an evaluation over a specified time period or over a number of opportunities that will assure confidence in the effectiveness of the action.

7.6 Corrective and Preventive Action Plan

A formal written plan to include the items listed below, as appropriate, must be submitted and approved by the Head of the area or Product/Process Team Leader and the Head of QA or designee, by initiation of the CAPA Form (see attachment 1). This form includes:

- A clear description of planned actions