7TH ADVANCED
GMP WORKSHOPS 2022

IPA
INNOVATION. QUALITY. GLOBAL REACH.

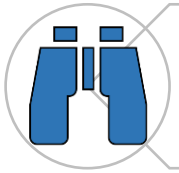
Human Error Reduction

Mr. D. B. Sridhar
Sr. Vice President, M.S.&T.
Zydus Lifesciences

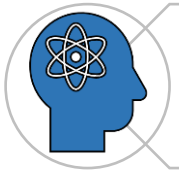
Ms. Nilanjana Basu
Sr. GM, Technical Training
Lupin Limited

Agenda

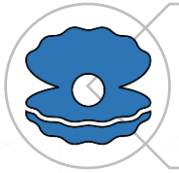
Understanding the Human Reliability



Human Error Investigation Techniques



Human Error Prevention tools /techniques



Best Practices of Human Error Reduction- Case Studies

Conclusion - Change our views on Human error

Preamble

Vicious Cycle

- Human Error
- Investigation efforts
- Holding of activity/Missed Commitment
- Re-work efforts
- Increased Workload

Preamble

What's the Problem?

Why are capable, conscientious people not always reliable?

What more can organisations do to improve human reliability?

Understanding the Human Reliability

Error

Error can be defined as… **'An act which may produce unintended results'** and when a human is involved, it is **Human Error**

Error Risk Reduction

The Error reduction process designed to…

- **Identify** the areas where human error may occur
- Identify **adverse influences** that increase the chance of error
- **Reduce** risk by addressing those adverse influences
- Systematically **increase human reliability** across the organization

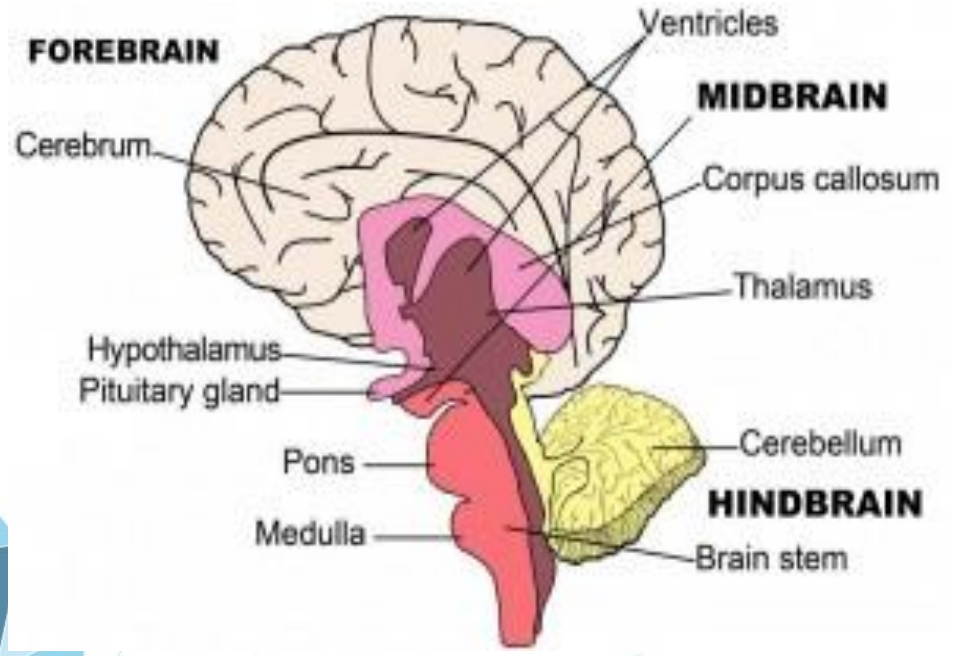
Understanding the Human Reliability

Human Reliability : Human reliability refers to the likelihood of successful human performance within specified timeframes and environmental conditions. It is critical to overall system reliability and is one factor that contributes to, or prevents, unwanted events occurring

- Focuses on '**Everyday Errors**' such as..
  - Unintended/occasional, **incorrect execution** of familiar tasks
  - **Forgetting** to act when required
  - **Failing to notice** something needing attention
- Focuses on activities and their operational context **rather than individuals**
- Aims at reducing **overall burden** of risks rather than preventing occurrence or recurrence of **specific errors**.

Understanding the Human Reliability

Human Learning – The Brain Factor



❖**Fore-brain**:

- The Cerebrum (Cerebral Cortex): associated with higher brain function such as thought and action.
- Cerebrum Is divided into two halves, Left and Right Hemispheres
- Left Hemisphere: Logical Side
- Right Hemisphere: Creative Side

❖**Limbic System**: (Emotional Brain / Childish Brain)

- Plays a role in emotionally laden memories
- It is particularly important in forming new memories, and connecting emotions and senses, such as smell and sound, to memories.

Understanding the Human Reliability

Human brain – hemispheres (Left brain vs Right brain Theory)

Left Hemisphere

Words

Language

Logic symbols

5 4 3 8 7

2/3 = 5

ABC, 123

Right Hemisphere

Different type of info processed differently

Understanding the Human Reliability

How the brain learns?

Learning = Neural Pathways = **Links**

1. When we learn, links formed

2. Learning = forming links Remembering = activating links

3. Cannot learn new unless can link to known!

4. If wrong links formed or links not formed - high chances of errors

During Learning Links needs to be created

Understanding the Human Reliability

Reticular Activating System

1.Decides ..let in ? Keep out ?

2.Works to keep things out-if thinks it already knows

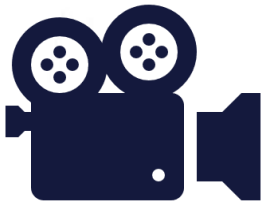
3.Adult learns if need – “unconscious incompetent”?
Need LOs or quiz to activate RAS

Reticular activating system

filters info

During Learning Links needs to be created

Understanding the Human Reliability



Video

Human Error Investigation Techniques

Investigation of Human Error – An overview

Drill Down Analysis

- To look at or examine something in depth.
- An interactive way to explore data points and view row-level data in the grid without changing the underlying query.

Spaghetti diagram

- A visual representation using a continuous flow line tracing the path of an item or activity through a process.

Root cause analysis

- A systematic method of understanding root causes contributing to human error

Complacency

- A feeling of being satisfied with how things are and not wanting to try to make them better. Major contributor to errors!

Training /Knowledge deficit

- Qualification for respective task
- SOP awareness
- Training on current procedure
- Technical know-how

Human Error Investigation Techniques

Investigation of Human Error – Understanding the Causes

- **Human Failure:** Refers to any deviation occurred due to human error.
- **Human Violation:** Refers to a deviation that is made deliberately.
- **Human Factor:** Any factor that influences human behavior at work in a way that can affect the output of the process.

- There are three primary elements viz. **task complexity**, **behavioural characteristics** and **error prone situations** that are potential triggers to human errors
- In addition, there are multiple Human Error Precursors that too contribute to occurrence of

Human Error Precursors

Task Demands:
- Time Pressure (in a hurry)
- High Workload (memory requirements)
- Simultaneous, multiple tasks
- Repetitive/ monotonous actions
- Correct Interpretation (of instructions and situations)

Individual Capabilities:
- Unfamiliarity with task
- Lack of knowledge/proficiency/experience
- Lack of effective communication
- Inadequate problem-solving skills
- Lenient attitude for critical task
- Illness / Fatigue

Work Environment
- Distractions / Interruptions
- Changes / Departures from routine
- Confusing displays or controls
- Culture of accepting workarounds
- Unaddressed personality conflicts

Human Nature
- Stress (limits attention)
- Habit patterns
- Assumptions (inaccurate mental picture)
- Complacency / Overconfidence
- Mindset (“tuned” to see)
- Inaccurate risk perception (Pollyanna)
- Limited memory

Human Error Investigation Techniques

Risk Review of Human Error – Check for Error Producing Conditions

Clarity of instructions in procedure

- Is there an approved SOP in place for the task?
- Does the existing SOPs provide all encompassing elaboration?
- Does the SOP mention handling deviations, if any, in the task/activity
- Approved procedure is available but not used often/always
- No startup checklist, for beginning of day/shift work. Reliance on memory (and not procedure) for identifying areas that need attention/check.
- No unambiguous visual indication of point reached in work sequence.

Could fatigue play a role in this failure?

- Person is working for long hours more frequently
- Not enough breaks from work /no tasks rotation
- Shiftwork rotation…
- Staff shortage
- People pressured to work (to cover staff shortage)
- Extremes of physical environment

Was training adequate?

Was supervision adequate?

Was the relevant person experienced?

Was there any sign of negligence?

Was the infrastructural support for job delivery adequate, e.g., hardware design?

- Layout of the work area not matched to process or natural sequence of activities
- Working surfaces overcrowded, where location is important
- Several similar containers (bins, folders, etc.) used to keep items separated
- Background color of working surface provides poor contrast
- Screens, equipment displays, labels and documents etc. too far away to see easily
- Things that need to be handled or adjusted are too far away to reach easily.

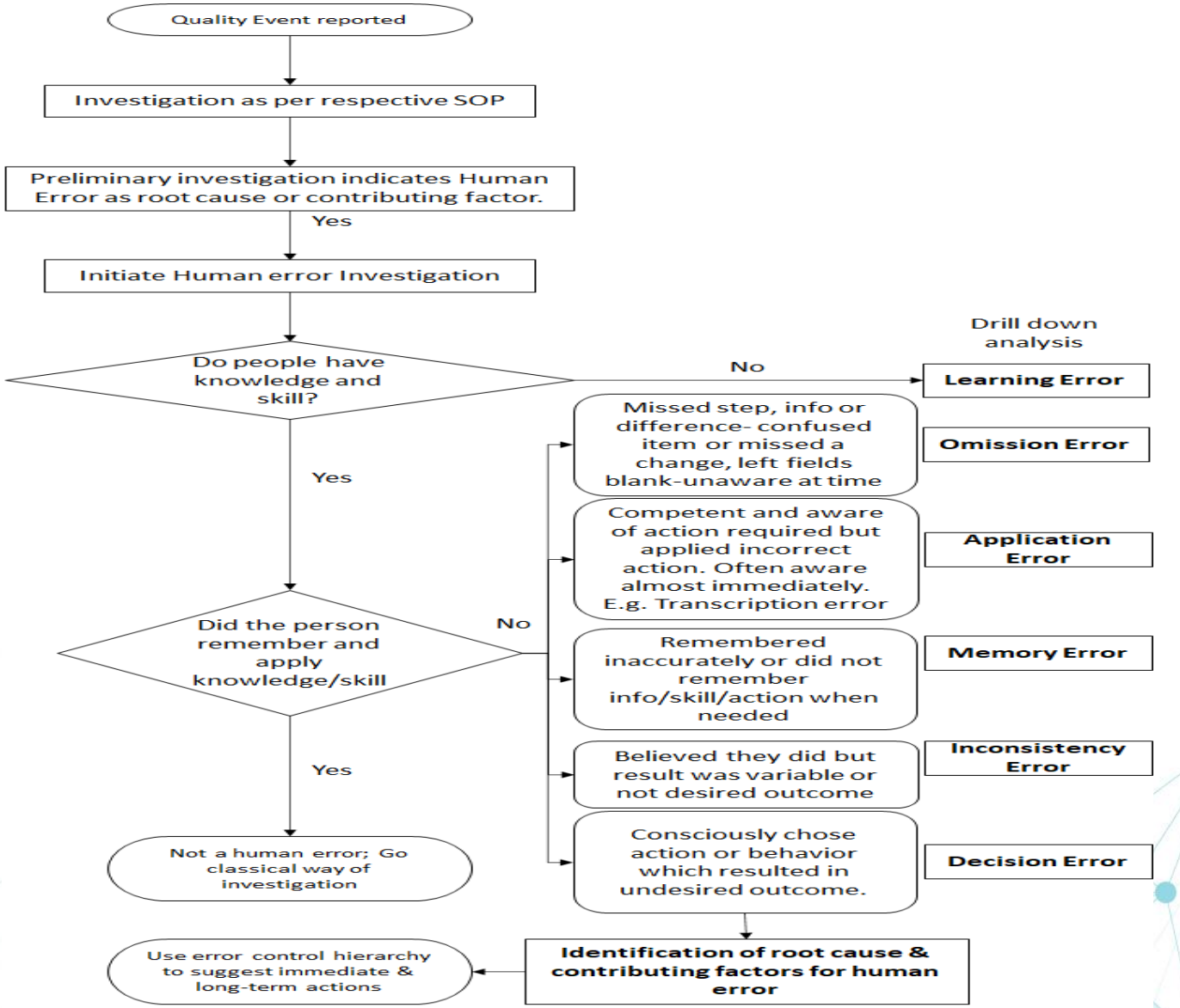
Human Error Investigation Techniques

Human Error Categorization

Learning	**Do not know** (lack skill or knowledge, or insufficient understanding of consequences)
Memory	**Knows, but does not remember** (unable to use skill or knowledge at time/situation required)
Inconsistency	**Knows, but variability in method/standard** (inconsistent performance/results)
Application	**Knows, but applied incorrect action/info** (slips, wrong outcomes, transcription errors)
Omission	**Knows, but missed a step/ action** (missing info/step, used wrong item)
Decision	**Wrong decision given situation/info** (inappropriate decisions&/or behavior)

Take Picture of the area when error Happens, it helps to understand

Human Error Investigation Flow



Further drill down analysis can be done using specific checklists for respective type of error

Remediation of Human Error

Derivation of good practices : Concept

Hierarchy of Actions: five main error management strategies:

- ✓ **Error Prevention:**

  Aims at avoiding the occurrences of errors.

- ✓ **Error Reduction:**

  Aims at minimizing both the likelihood and magnitude of error.

- ✓ **Error Detection:**

  Aims at making errors apparent as quickly and as clearly as possible and therefore enabling recovery. An error can be:

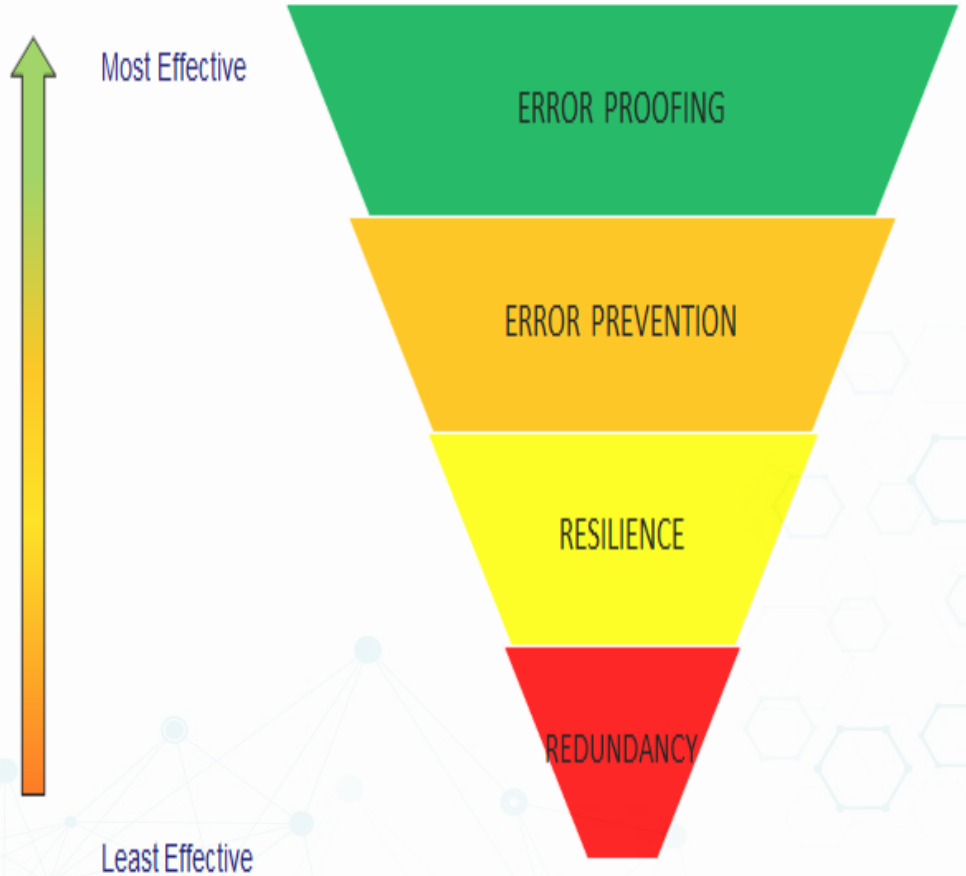
  - Detected by the person that committed the error (self-monitoring).
  - Detected by another person.
  - Detected by system e.g., an alarm.

- ✓ **Error Recovery:**

  Aims at making it easy to rapidly recover the system to its safe state after the error has been committed.

- ✓ **Error Tolerance:**

  Aims at making the system as robust as possible towards error.



Human Error Prevention tools/techniques

Mistake proofing model (Poka-Yoke)

Five principles or methods of mistake proofing:

1. Elimination: To eliminate an error-prone process step by redesigning the product or process.

2. Replacement: To substitute for more reliable process step to improve repeatability.

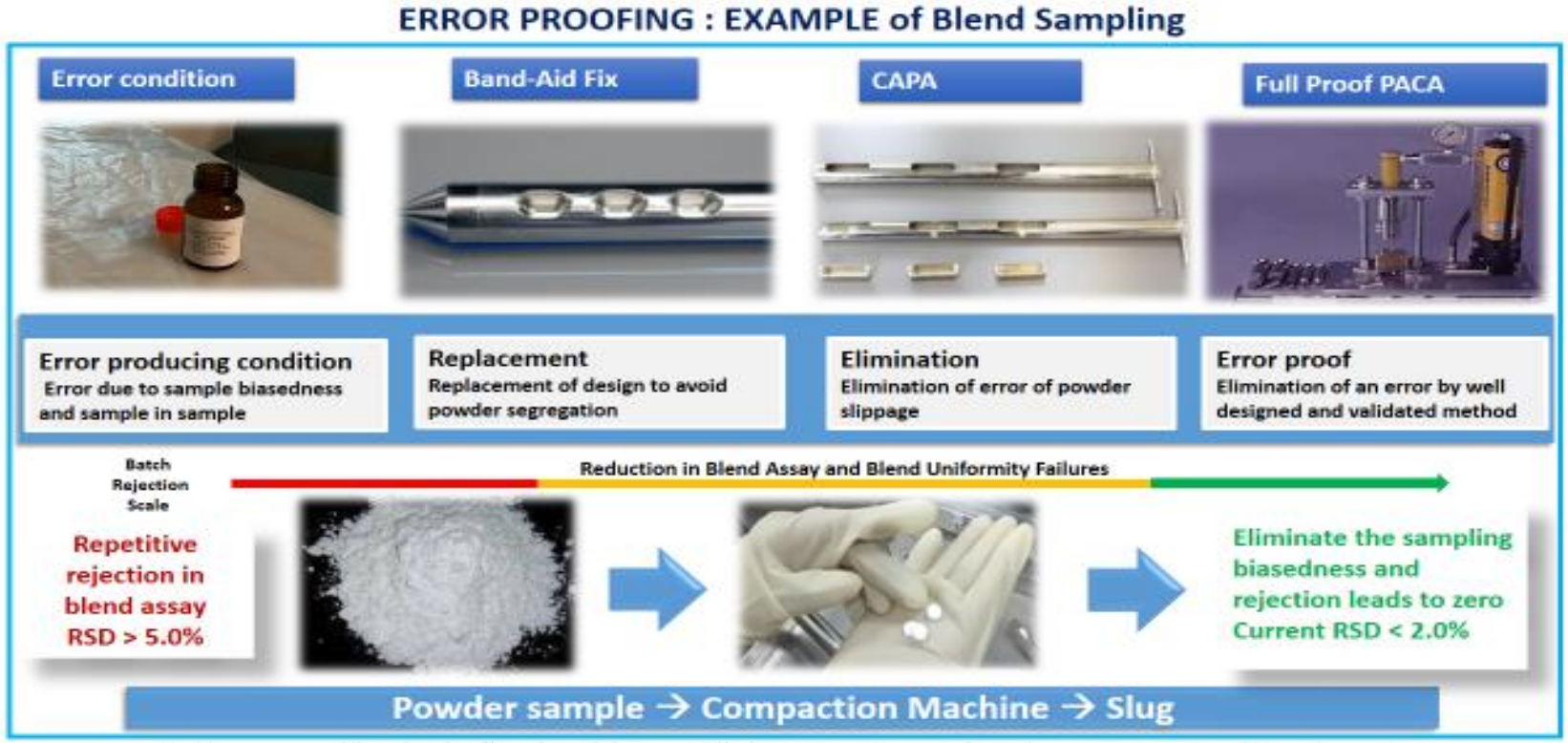
3. Simplification: To redesign the process so that it become easier for execution.

4. Detection: To identify a mistake before further processing in order to correct the defect.

5. Mitigation: To minimize the effects/mistake or to reduce the impact of an error or defect.

Example : Blend sampling in the form of slug instead of powder

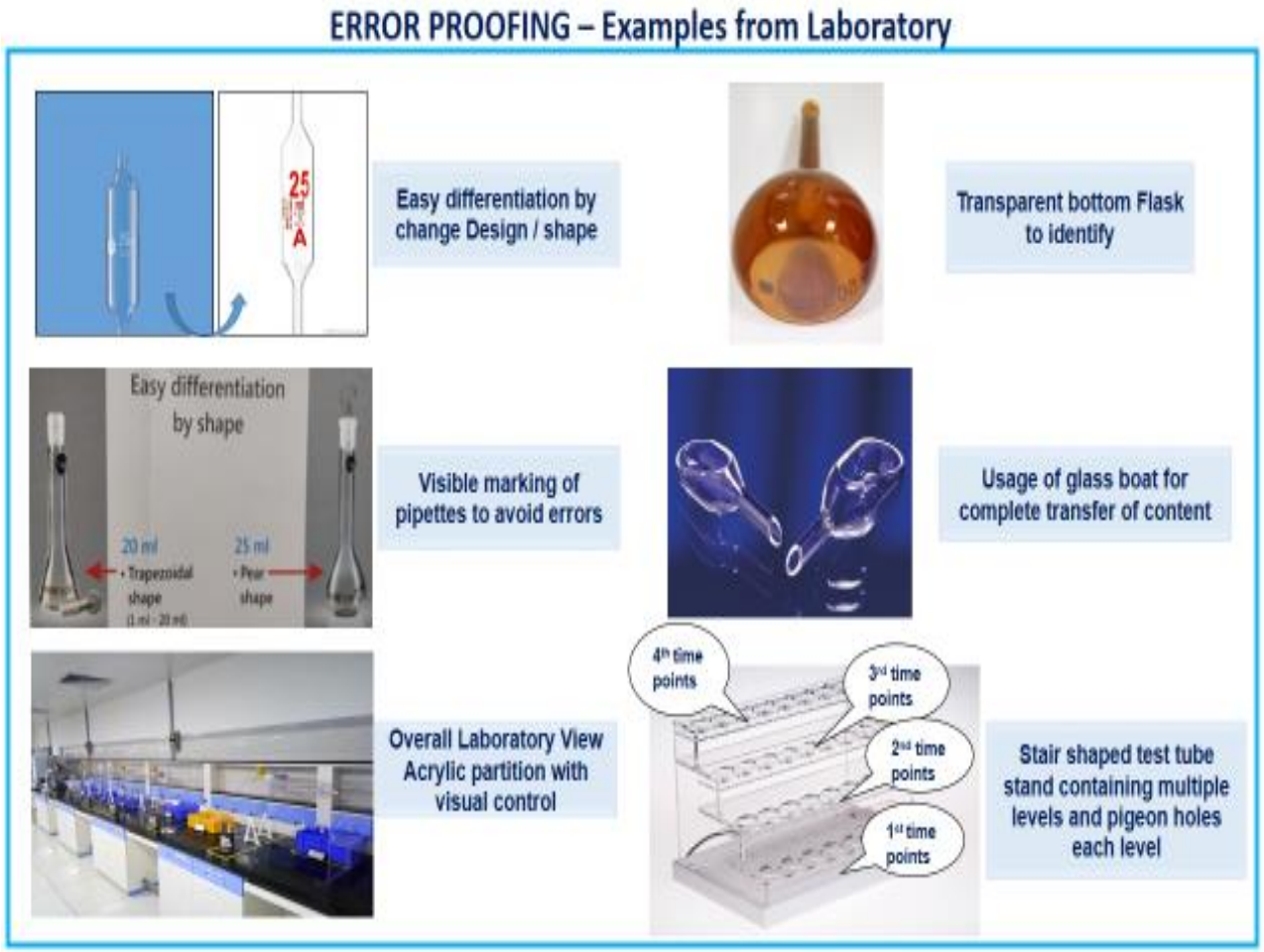
Slug sampling in powder form may lead to sampling bias i.e. Segregation during sampling or sample handling, Sample in sample etc. To avoid the issue of sampling bias, blend sampling is performed in the form of slug using compaction machine. The quantity of slug formation is kept as quantity required for QC testing that avoids probability of error due to sample in sample.



Human Error Prevention tools/techniques

Mistake proofing in day-to-day analytical activities:

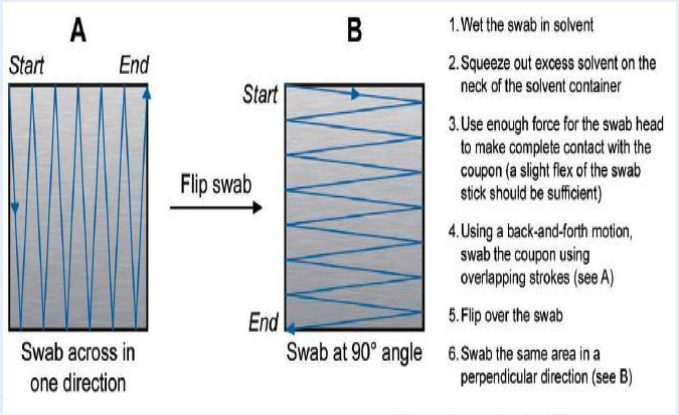
Action	Application
Usage of single row test tube stand	To avoid solution interchange in profile dissolution test
Different colour rings inserted to the volumetric flask of different time point	To avoid interchange of volumetric flasks in profile dissolution test.
Partition affixed on the desk of analyst	To avoid interchange of glassware / solution
Storage facility with segregation of cleaned pipettes	To avoid interchange or wrong selection of pipette
Affixing printed labels on volumetric glass wares	To improve label legibility & longevity.



Best Practices of Human Error Reduction- Case Studies

1 Sampling Error

Error Description	Inadequate swab sampling from equipment surface. Cleaning Validation protocol was devoid of the clause to perform zig-zag swabbing
Error Category	Inconsistency Error
Recommendations	Enhancement of CV protocol to include clause for zig-zag swab sampling in equipment surface along with pictorial depiction (Error Prevention Model)



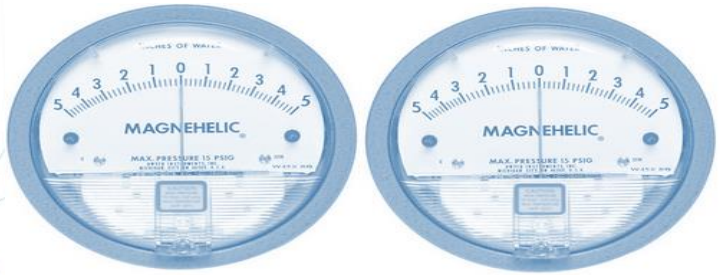
2 Visual Inspection Error

Error Description	Performing visual inspection of equipment surface cleanliness without inspector qualification.
Additional Information	Learning Gap (as the inspector wasn't trained and qualified on inspection of equipment surface for its cleanliness) and procedural inconsistency for allowing personnel to inspect without prior qualification.
Error Category	Learning Error
Recommendations	Inspector qualification procedure was prepared, and SOP was revised to incorporate a clause to perform inspector qualification prior to deployment for visual inspection activity (Error Prevention Model).

Best Practices of Human Error Reduction- Case Studies

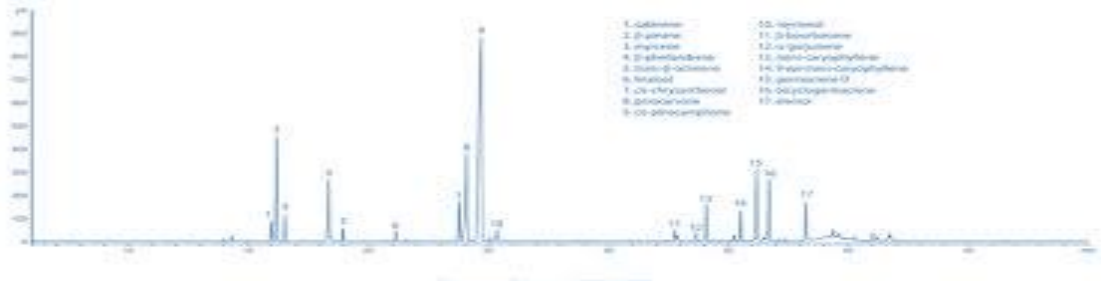
3 Forgot to check the parameters

Error Description	Operator forgets to check the environmental conditions of the manufacturing suite prior to commencement of the unit operation.
Error Category	**Memory Error**
Recommendations	Usage of attention activator and a note was added "R*ecord temperature and %RH prior to commencement of operation*" in Batch Manufacturing Record. **(Error Prevention Model) OR** Implement BMS for online data monitoring **(Error Proofing Model)**



4 Wrong Result Reported

Error Description	Wrong interpretation of chromatograms due to absence of reference chromatograms in STP.
Error Category	**Inconsistency Error**
Recommendations	Reference chromatograms attached to the STPs and training imparted to analyst. **(Error Prevention Model)**



Best Practices of Human Error Reduction- Case Studies

5 Missing Second Check

Error Description	"Verified By" sign missing in cleaning checklist of Pressure vessel
Additional Information	Operator who was responsible to verify the activity inadvertently missed to sign in the "Verified By" column of cleaning checklist as he was engaged to help the other operator in cleaning activity
Error Category	**Omission Error**
Recommendations	Implementation of digital platform for cleaning execution **(Error Proofing) OR** Redesigning of checklist in HER (Human Error Reduction) Format with Gray background for non-executable instructions and White blanks for recording observations during execution. **(Error Prevention)** ***with consent from site/company management***

6 Analyst Error

Error Description	Response ratio was not achieved as per specified criteria i.e., obtained similarity factor 0.97 against limit 0.98 to 1.02.
Additional Information	The incident occurred because the analyst had not dipped the inlet filter in rinse bottle properly.
Error Category	**Omission Error**
Recommendations	HPLC verification checklist appended to ensure all the lines are dipped properly in the Mobile Phase/Rinse line/ fill wash with their respective solution and the pictorial representations of precautionary measures have been fixed in work benches as a job aid. **(Error Prevention Model).**

Best Practices of Human Error Reduction- Case Studies

Investigation of Human Error – Process of Error Risk Reduction

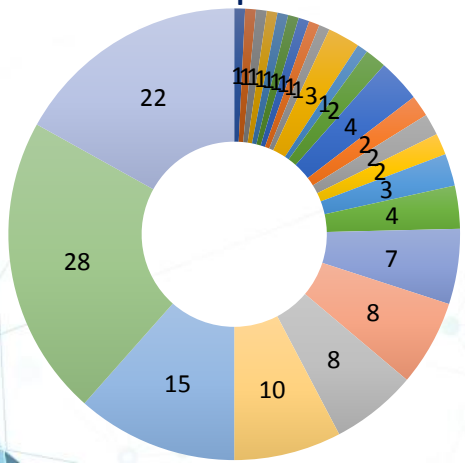
Blue	Red	Yellow	Green	Purple
Make clear what happens	Risk Review	Understand causes	Toolbox error reduction	Continuous reliability improvement
Making activities and their context explicit	Identification and assessment of risk of errors	Identification of risk influencing factors	Elimination or reduction of risk influencing factors	Continuous improvement in human reliability

Best Practices of Human Error Reduction- Case Studies

Blue

Problem Identification

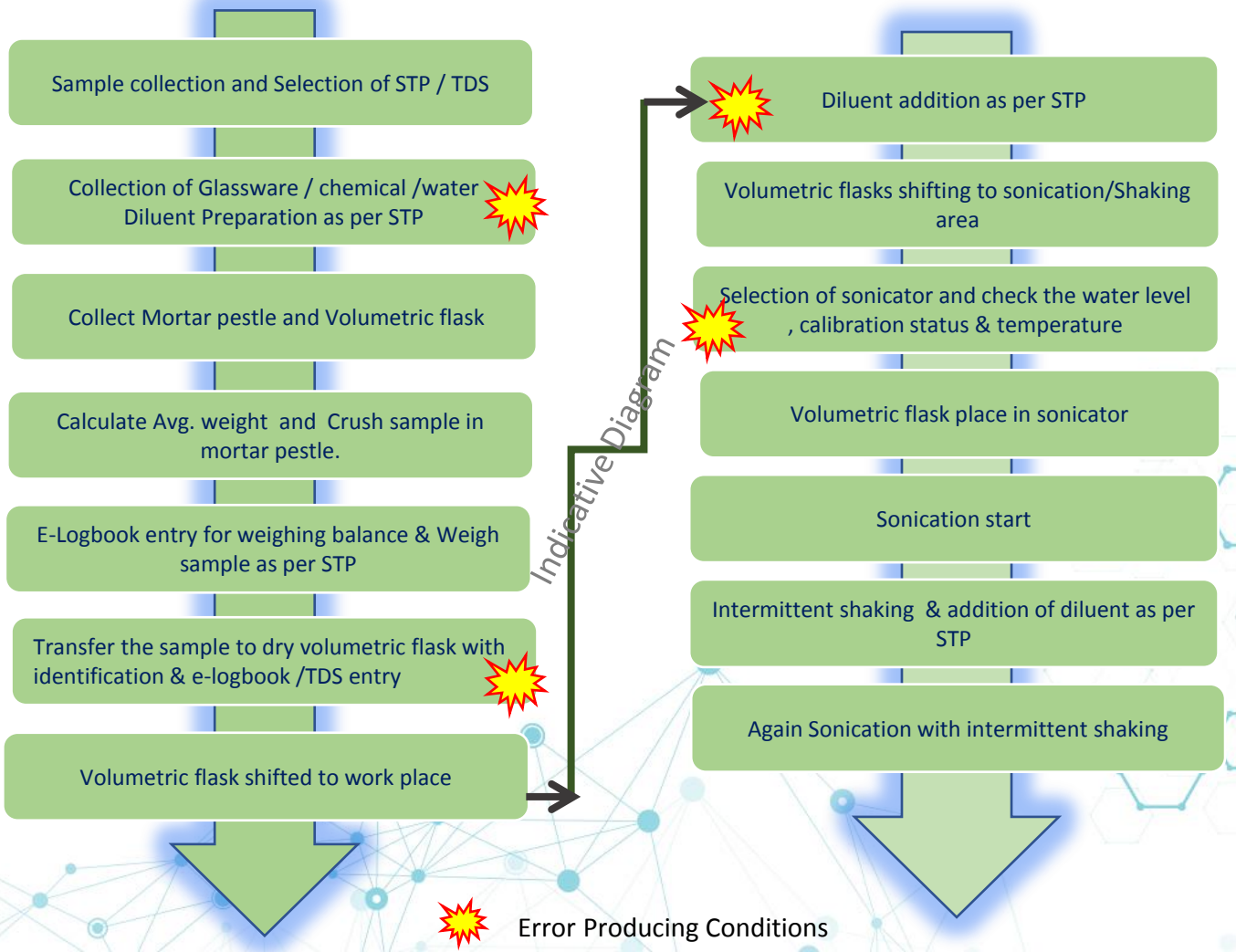
- Total 37% Invalid failure was reported in a year at one of the Mfg. site
- Brainstorming exercise done for identification of causes for higher OOS/OOT/Deviation
- Identified that **28** and **22** failure are due to **Dilution** and **Transcriptional error** respectively which is approximate **13 %** of total number of failure reported in a year



Red

Detailed understanding the process – workflow

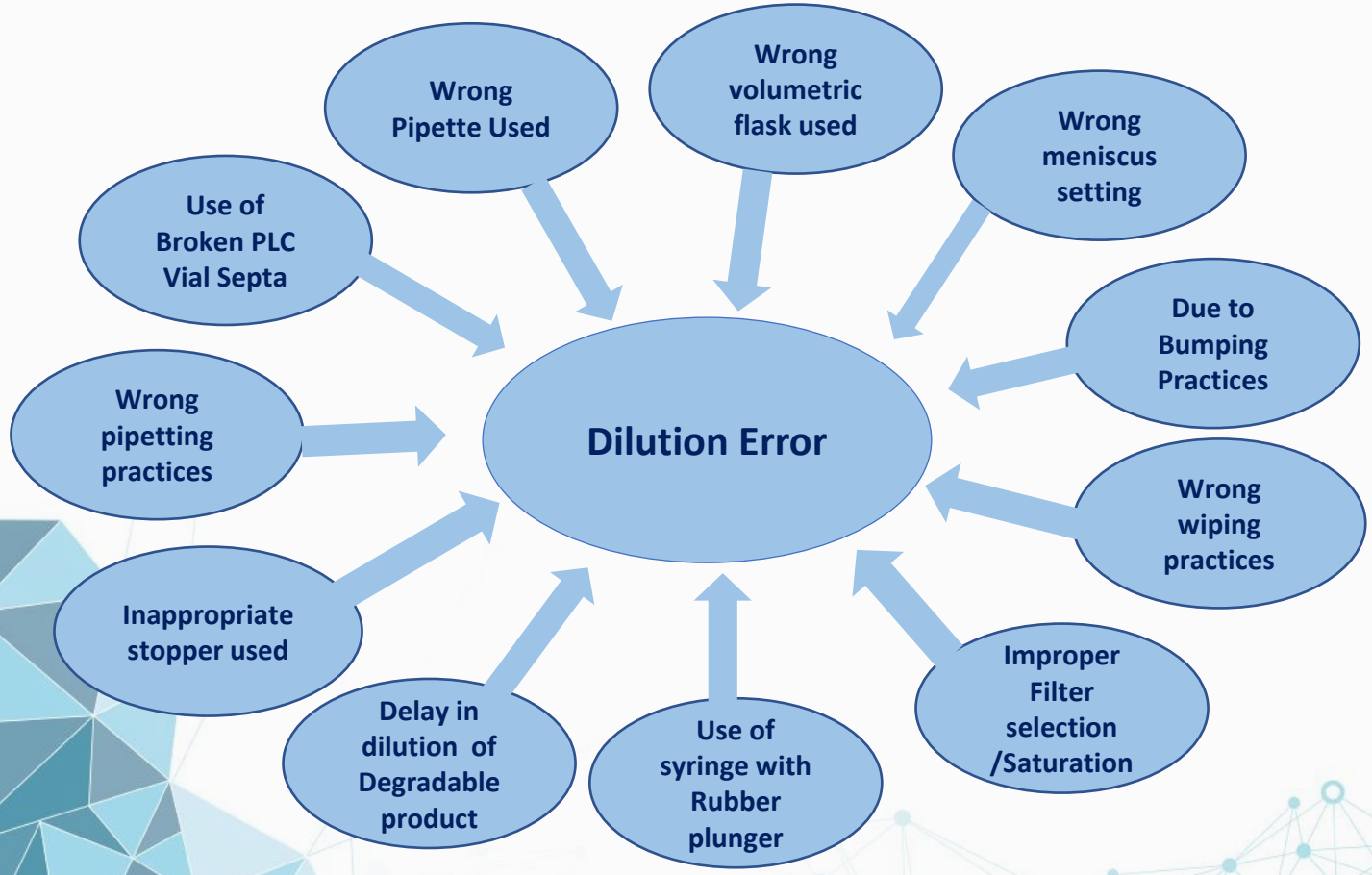
Process steps – Dilution & Potential Risk Areas



Best Practices of Human Error Reduction- Case Studies

Yellow

Potential Risk Identified



Best Practices of Human Error Reduction- Case Studies

Green

Elimination of Error Producing Condition – Good Practices implementation

Error Producing Conditions	**Working surfaces overcrowded, where location is important, (for example various grades of items in separate piles). Information must be remembered whilst other tasks are carried out, before being used.**
Concerns in Lab	During Analysis due to insufficient space to keep STP at working place , analyst refers and keeps STP on top shelf during analysis. There is restricted issuance of STP in order to have a control on traceability. As a result, one STP gets referred by 3 analysts at a time and execution largely depends on Short Term memory which fails at times.

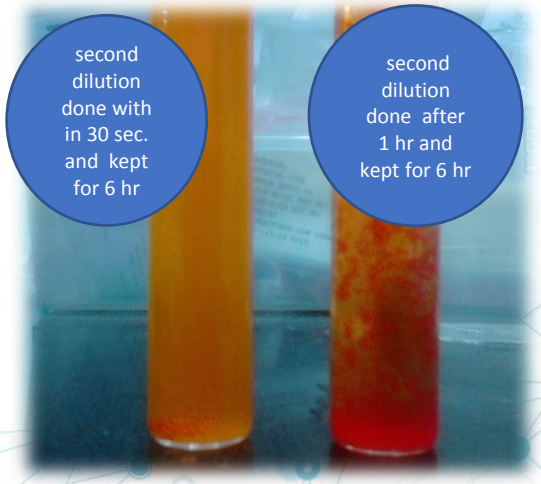
Evidences

Good practices:

- SDMS(Soft data management system:Omnidocs) implemented for storage of specification/STP
- 2 Computers provided in each QC Lab , analyst/reviewer can refer STP any time from Online system
- List of Total Specification/STP with Reviewed date shall be maintained

Error Producing Conditions	**Qualitative descriptions used where precision is needed, e.g. soon/warm**
Concerns in Lab	STP has mentioned freshly prepared sample to be injected . Some time analyst is unaware about how soon the second dilution is to be made . Delay in second dilution results in degradation of solution.

Evidences



Good practices:

- Standard testing procedure included note of risk indicating parameter regarding Freshly prepared sample .
- Special Precaution note shall be issued in case of highly sensitive product.

Best Practices of Human Error Reduction- Case Studies

Green

Elimination of Error Producing Condition – Good Practices implementation

Error Producing Conditions	**Similar Appearance - e.g. same color/style/shape of packaging, clear, colorless liquids, white powders, etc.**
Concerns in Lab	1. Wrong Volumetric flask (VF)/Pipette may be selected due to same appearance e.g. 5 mL pipet instead of 4 mL pipet and vice versa, 200mL VF instead of 250 mL VF, 75 mL VF instead of 100mL VF etc. 2. Methanol and Acetonitrile are being used in large volume in QC for mobile phase preparation and both bottles are having same shape /colour label , analyst gets confused and may use wrong solvent . 3. Pipette used with broken/damaged ends/tips may vary amount delivered in pipetting, may result in lower/higher results. Similarly uses of broken/inappropriate stoppers may leads to spillage of mother solution and may change the concentration of stock solution.
Evidences	

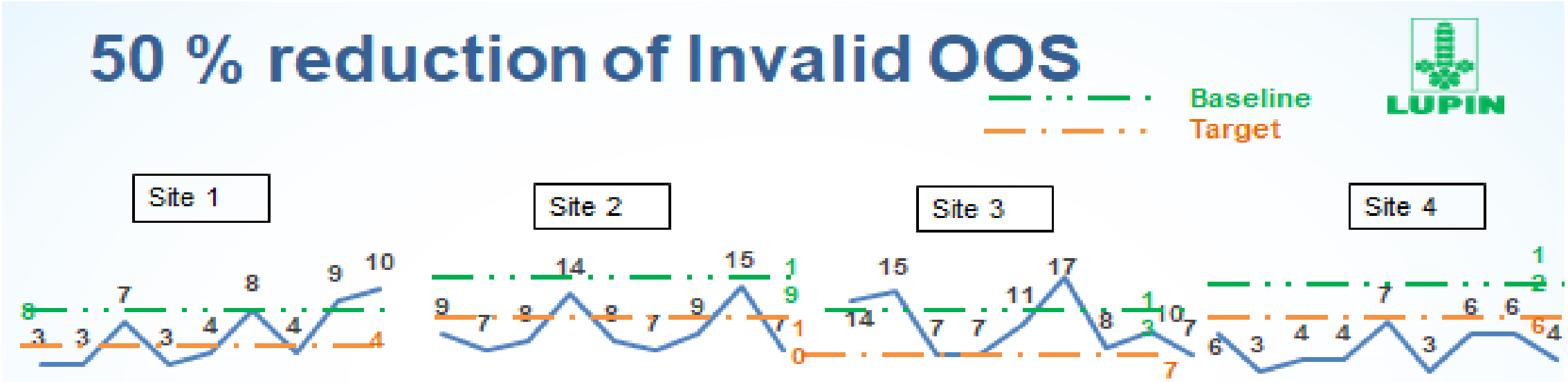
Good practices:

- Glassware marked with ring. Different shape for look alike glassware procured
- For Acetonitrile and Methanol solvents bottle supplier informed to differentiate the labeling
- Both solvents procured from different make for easy identification
- Glassware are coated with thin film that prevent breakage of Pipette at tip .Special treatment at Tip Coating.

Best Practices of Human Error Reduction- Case Studies

Purple

Continuous Reliability Improvement – A snapshot of project outcome



Error reduction methodology applied for Human Error Investigation

Project taken up at 4 major manufacturing sites

Target taken to reduce invalid OOS by 50%

Clear shift of baseline

Target achieved and is sustained

Sustenance of Human Reliability

Approach for continual improvement of human reliability

Once an area attains accepted level of human errors, multiple measures can be taken to sustain the human reliability

Conducting periodic survey to gather information about perception of stakeholders on error reduction initiatives along with contemporary challenges. This will also throw light on emerging vulnerable area.

Before and after comparison of error reduction to see if the failure rates are reduced/maintained.

Area to area comparison on error reduction initiatives/metrics in governance forum.

Conclusion - Change in views on Human error

To achieve continued success in reducing risk of human error, a well-designed strategy that includes the following kinds of processes amongst others

- **Visibility**: Managers to have meaningful and comprehensive understanding of error risk and their potential consequence
- **Awareness**: The workforce understands how to identify and address risk of error
- **Measurement**: Measurement of cause and consequences of error to be factored in driving new improvement projects
- **Handling**: Assessment on whether handling of failures help in long term error reduction through review of identified metrics
- **Empowerment**: Provision of time and resources needed to address error and empowerment of workforce to apply them
- **Deployment**: Knowledge based development and proactive application of well-founded know how

Conclusion - Change in views on Human error

Successful application of these approach in an organization, may lead to a transformational change happening and Improvement in human reliability

Reactive Approach	Proactive Approach
Focus on Individuals	Focus on activities
Toolbox fix	System improvement
Error avoidance	Reliability Enhancement

"85% of the reasons for failure to meet customer requirements are related to deficiencies in systems and processes rather than the employee. The role of management is to change the process rather than badgering individuals to do better"
Mr. Edward Deming

Acknowledgements

- Dr. Ranjana Pathak (Mentor) = Dr. Reddy's Lab.
- D. B. Sridhar (Sub Group Head) : Zydus Life sciences Ltd.
- Nilanjana Basu
- Manoj Gera - Zydus Lifesciences Ltd.
- Narendra Deshpande - Lupin Ltd.
- V Sneha Shree - Dr. Reddy's Lab.
- Yogita Bhanwaria - Dr. Reddy's Lab.
- Raju Tukra - Sun Pharma Ind. Ltd.
- Vaibhav Swaroop - Sun Pharma Ind. Ltd.
- Sanjay Ghare - Cipla Ltd.
- Ankit Pandey - Cipla Ltd.
- Sweety Shah - Torrent Pharmaceuticals Ltd.

Q & A

Thank You