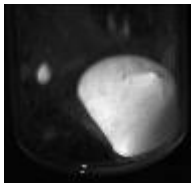
- Theory 6:
- Qualification Test Set and Routine Test Set

- **Statistical considerations on number of objects containing defects**
- **Particle selection, particle size and size uniformity**
- **Labeling of test set objects**
- **Supply/purchase of test sets**
- **Maintaining and lifecycle of test sets**
- **Sampling from rejects**
- **Defect master library**
- **Types of defects**
- **Quality requirements**

1. Prior study of particle/defect occurrence in real prod => control charting / number lots sampling
    - What type of particles/fibers, occurrence
    - This will also identify where introduced for process improvement
        - Removing the cause versus solving the problem
    - Necessary for selecting machine/supplier
        - URS and defined test sets make it possible to compare offers
2. Choosing how to build test sets and good units for testing and validation
    - Real defects versus manufactured defects
        - They should not fall apart during usage
        - They should represent the process defects found
        - They have a limit lifespan, so they should be reproducible for building new sets for later revalidation which will be far easier with manufactured defects

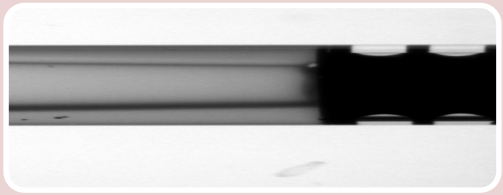
3. Artificial beds particles
   - They are completely reproducible, for 100%
   - They have exact dimensions like spheres, triangles, rectangles etc.
   - Detection limits can exactly being set
   - But their behavior in liquid motion do not resemble movement of real particles/fibers
4. Virtual defect library
   - Building a library of defect images and good units
   - The more the merrier
5. Virtual machine test
   - Having these images one can do offline configuration of machine recipes.
   - The automatic inspection machine stays in production for already validated configurations

What do? Whatever dosage form (liq or lyo),100% visual inspection required for each parenteral product for following defects:



- Glass defects
- Closure defects (caps & crimp inspection)
- Particulate matter (lyo only external)
- Fill volume *specific for liquid products*
- Cake defects *specific for freeze-dried products*
- *Cosmetics defects*

Automated Inspection of Particles in Vaccines
Vaccines Visual Defects controlled



Syr.	Vial Liq.	Lyo
- Cracks	- Cracks	- Cracks
- Particles	- Particles	- Particles
- Fill Level	- Fill Level	- Lyo defects
- Stopper	- Closure	- Closure
- Closure	- Cap Color	- Cap Color
- Flange/gripper	- Stain	- Leaks
- Stain	- scratches	- Stain
- scratches		- scratches

Visual Inspection Defect Master Library

Process rejects

Complaints

Vaccines Creation

Defects catalog

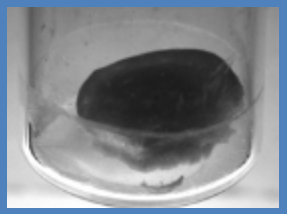
Basis for kits

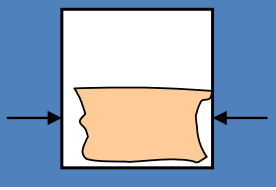
Operators certification

Machine validation

<Name>

<Root cause if known>





Description:

- Color
- Shape
- …

Instruction for defect evaluation:

- Instruction 1
- Instruction 2

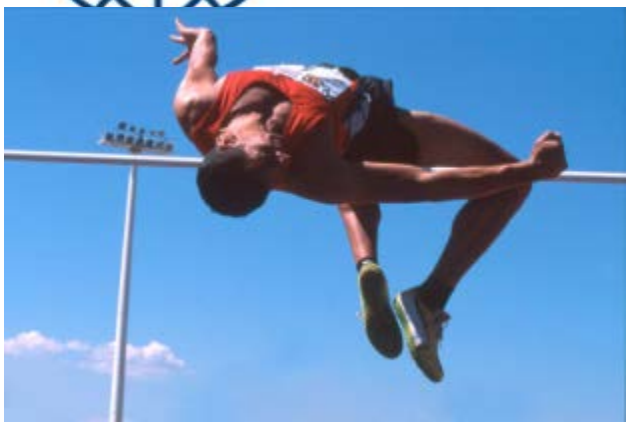
Criticality level:

Crticial – Major - Minor

- Justification 1
- Justification 2

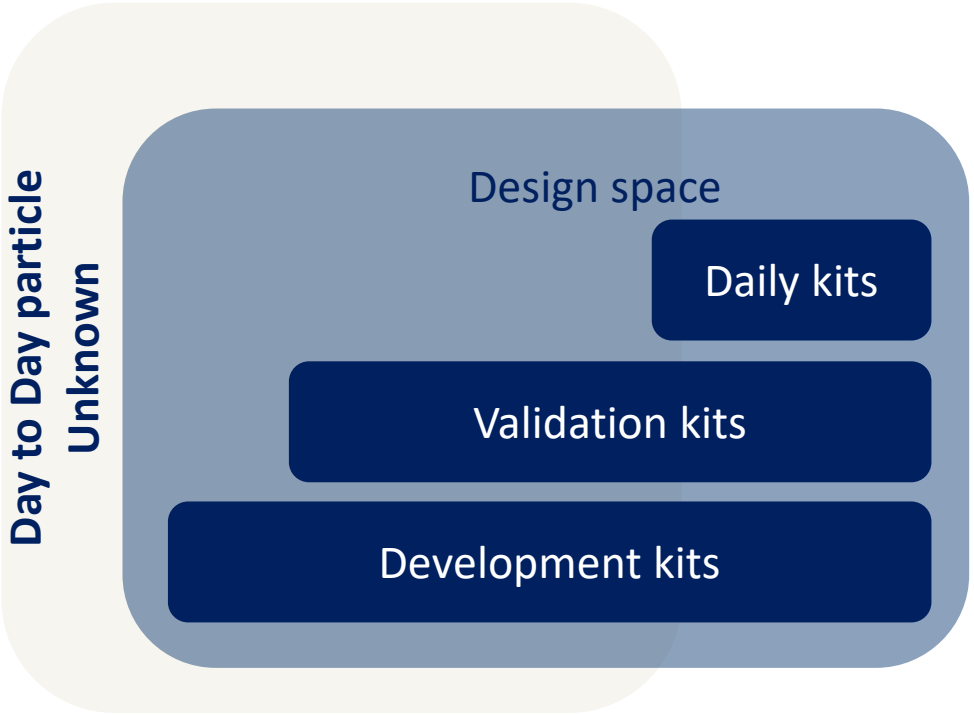
Product knowledge

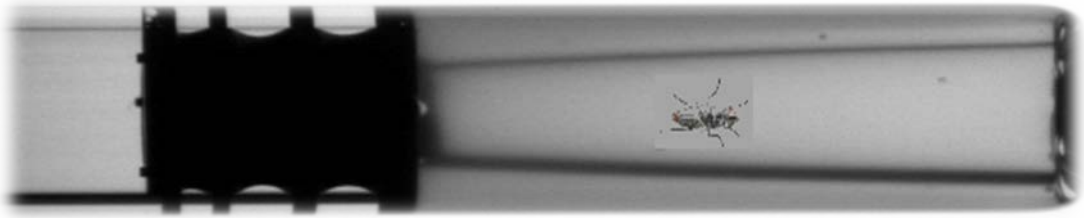
Can AVI detect unknown particles ?



Key learning:

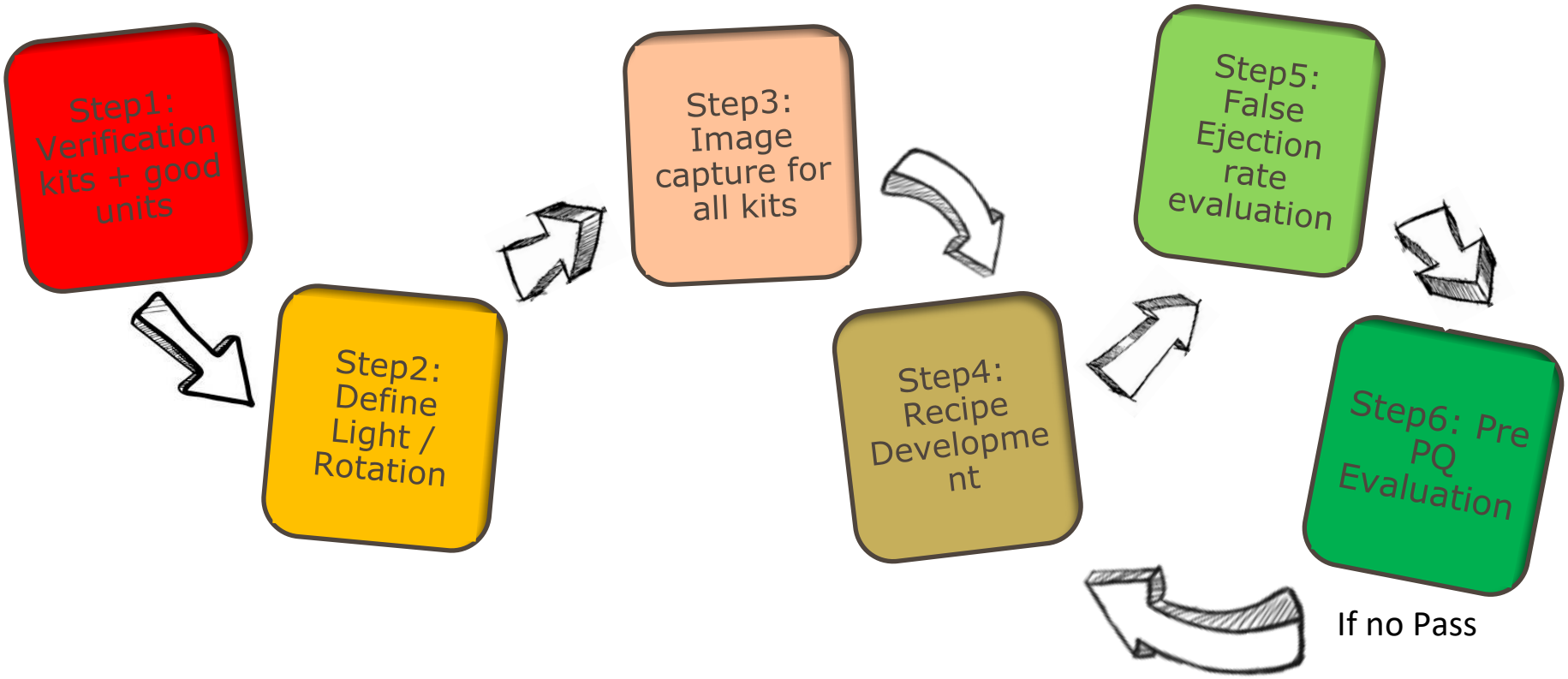
- Machine vision is designed with minimum threshold, may be compared to high jump.
- Machine vision is designed to detect defect that are outside the design space to anticipate some new defects (unknown)
- With artificial image library we can demonstrate capability of unknown detection





!Fake image!

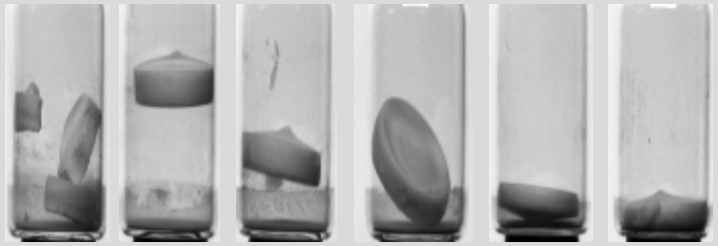
Vision Recipe development



Lyophilized Parenteral defects
Grey zone of Acceptable Imperfection

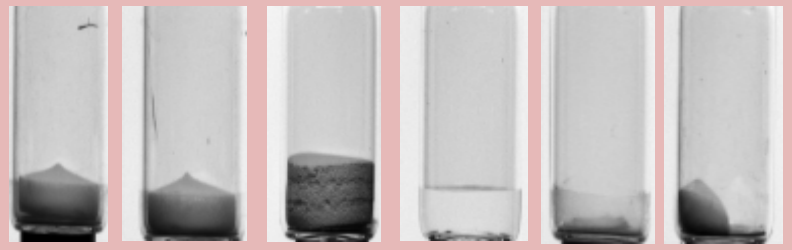
Conform

Acceptable Imperfections



broken Lifted Debris Bent Flipped Powder . . . . . .

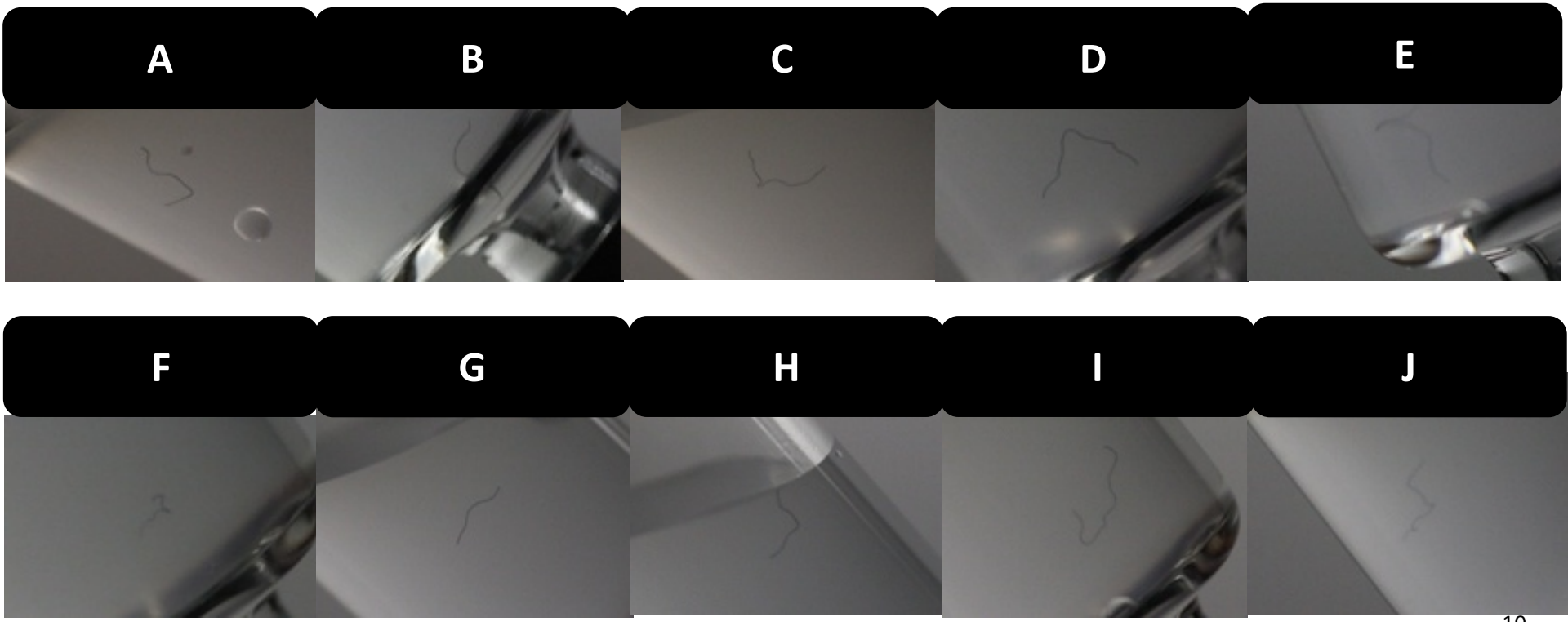
Defect



crack crack X2 dose liquid half Moon . . .

Precipitating particle:
- black
- lengenthed, type fiber
- big : 0.6 mm²

Location definition
Defect family (particle/Crack/closure)
Defect types (attributes)



Performance Qualification AVI Lyo Inspection

2 Validation Kits are used

Reference defect Kit

+ consistent defects
+ no degradation
+ stable years
+ Fixed Detection rate

- Artificial
- Gross defects

Real Defect Kit

+ Real defects

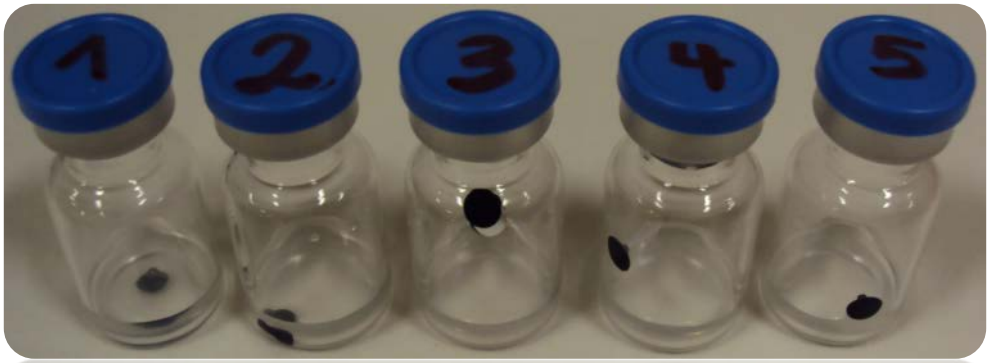
- Degrade fast
- Variability between defects
- No Detection rate limit

- Collection in production
- Manufacturing
  - Sub contracting : working instruction / DML /
  - Internal group: working instruction / DML /
  - Labelling units / UV printing➔ anti mixup
  - Back up units when broken
- Logbooks of kits
- Supply for sites
- Storage condition
- Documentation of use / line clearance
- Verification / change units
- Expiry date

SOPs
+
QA Oversight

Daily kits ?

- Daily kit test for machine functionality
- = gross defect to simulate ejection
- Not a performance evaluation only for vision system functionality of detection and rejection



Key take away:

- In this section you have learnt:

KITS	
	Statistical considerations on number of objects containing defects
	Particle selection, particle size and size uniformity
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