SKANalytix PDA – Manage your isolator

PDA
Parenteral Drug Association

CONNECTING PEOPLE SCIENCE AND REGULATION®

SKANalytix - 4 Life Sciences

skan

SKANalytix Orbits & Packages

SKANalytix Orbits & Packages

Active
- Trace Analysis
- H_2O_2
- O_3

Persist
- Material resistance
- Acids & Bases
- Solvents
- Oxidants
- Surfactants

***in*Silico**
- CFD Flow field
- CFD Particle tracking

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Beside a variety of technical options
we provide service packages along
the entire lifecycle time of our Isolators
to maximize the support for our customers.

Clean
- CLEAN Mapping
- CLEAN Check Isolator & Air
- CLEAN Check Material
- CLEAN IP Indicators & Prints

Persistance

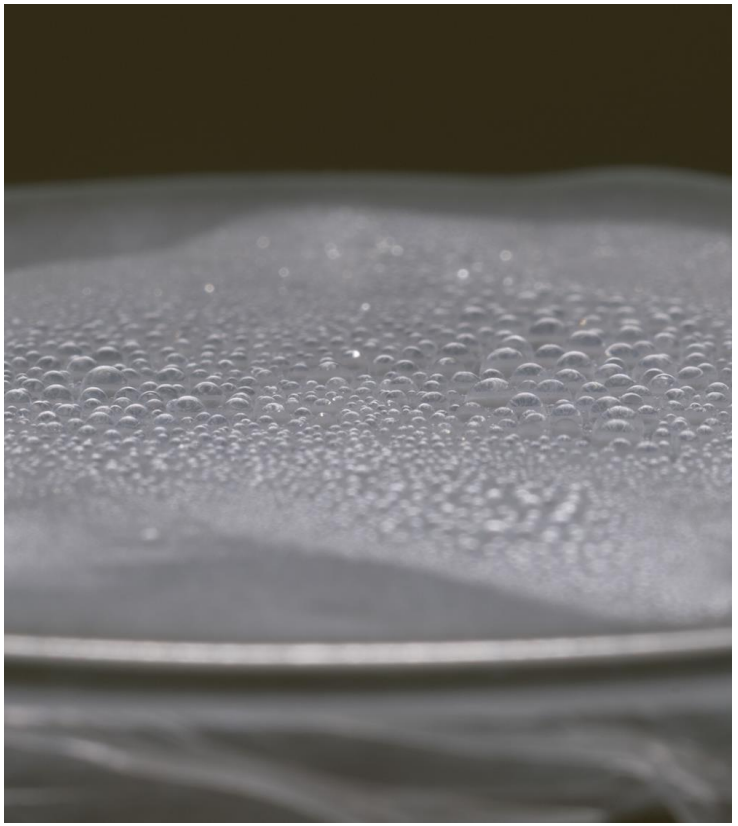
Any material used for the construction of equipment for aseptic processes must be easy to be decontaminated, show good persistence to various chemicals and should not be deteriorated by direct or indirect action of microorganisms. Similarly, suitable cleaning agents for all surfaces must be defined.

- Chemical resistance
- Biological resistance
- Surface decontamination

Diffusion and Absorption

H_2O_2 can be absorbed by different materials or even diffuse through them. To protect samples, suitable packaging needs to be selected. For equipment, materials of construction need to be used that do not absorb H_2O_2 or gas out quickly.

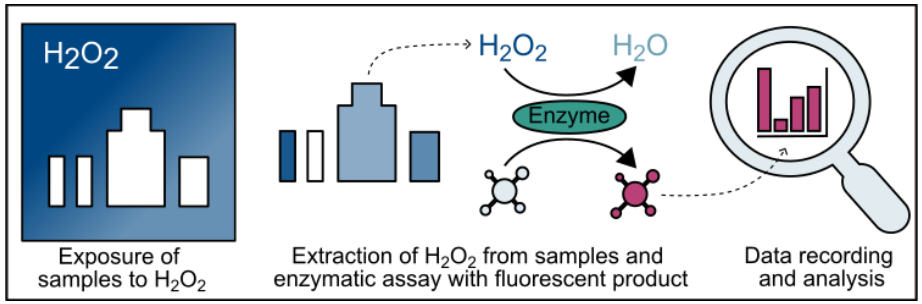
- Standardized measurement setups
- Screening packaging permeability
- Uptake of H_2O_2 by packaging materials or construction materials
- Outgassing kinetics



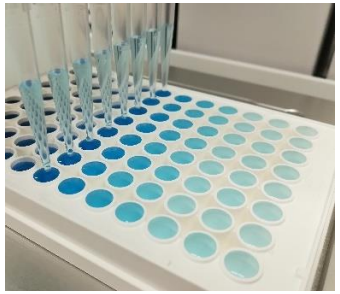
Hydrogen peroxide trace analysis

Contact of H_2O_2 with filled drug product can be detrimental to product quality or the validity of sterility testing.

It is important to understand the amount of H_2O_2 that can be taken up during the decontamination or filling process.



- Dedicated test systems
- Exposure to decontamination cycles
- Generation of stable low H_2O_2 levels
- Quantification of H_2O_2 ingress
- Precise spiking studies for sensitive products
- Influence of H_2O_2 ingress on sterility testing

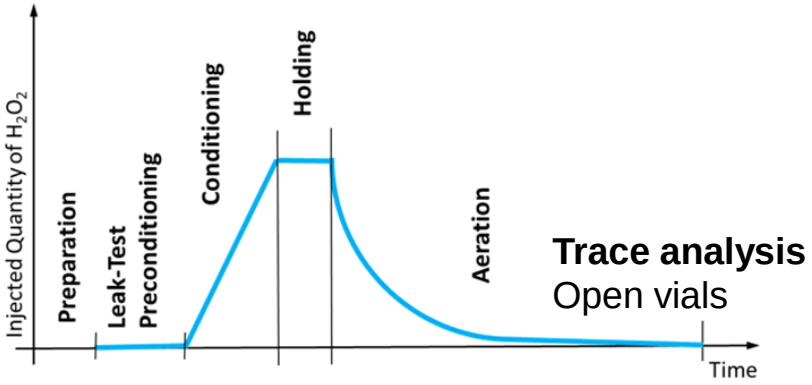


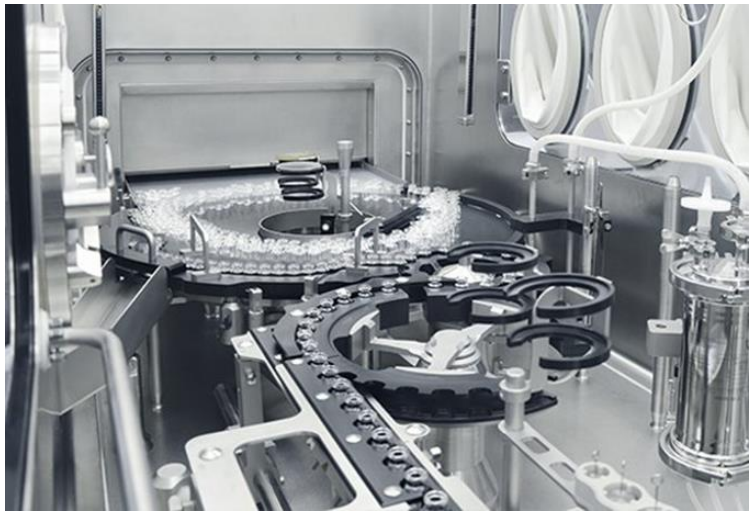
Case Study – Filling in Isolator

- Sensitive product that is filled in isolator
- Worst-case residual H_2O_2 present in atmosphere

- H_2O_2 ingress over time
  1. How much H_2O_2 could open vials accumulate during production?
  2. In case of delays, how long can product still be used?

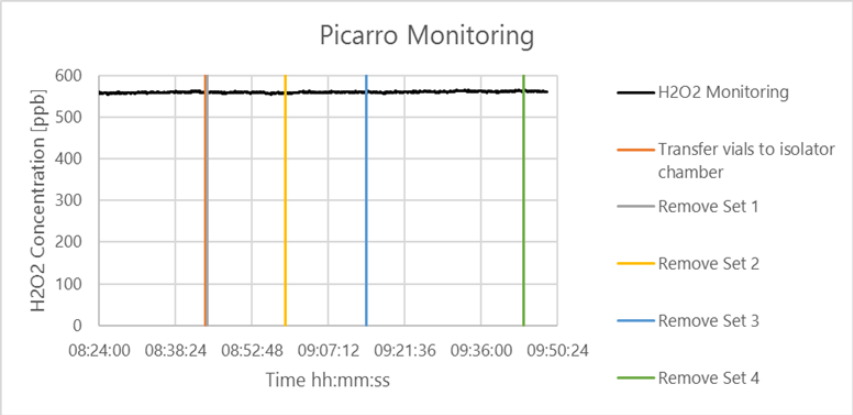
- H_2O_2 ingress depending on
  - Packaging
  - Vial material and shape
  - Filling volume
  - Residual H_2O_2 in the atmosphere

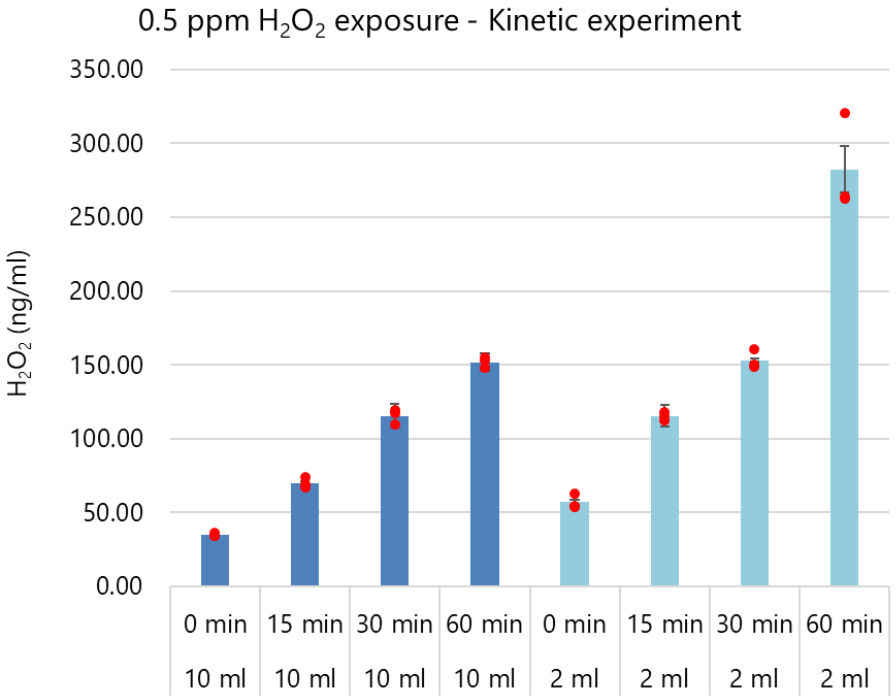




Trace analysis – H2O2 uptake during production

- Open vials
  - Present during production
  - Two different sizes
- Exposure at 0.5 ppm
  - Worst-case based on set aeration level



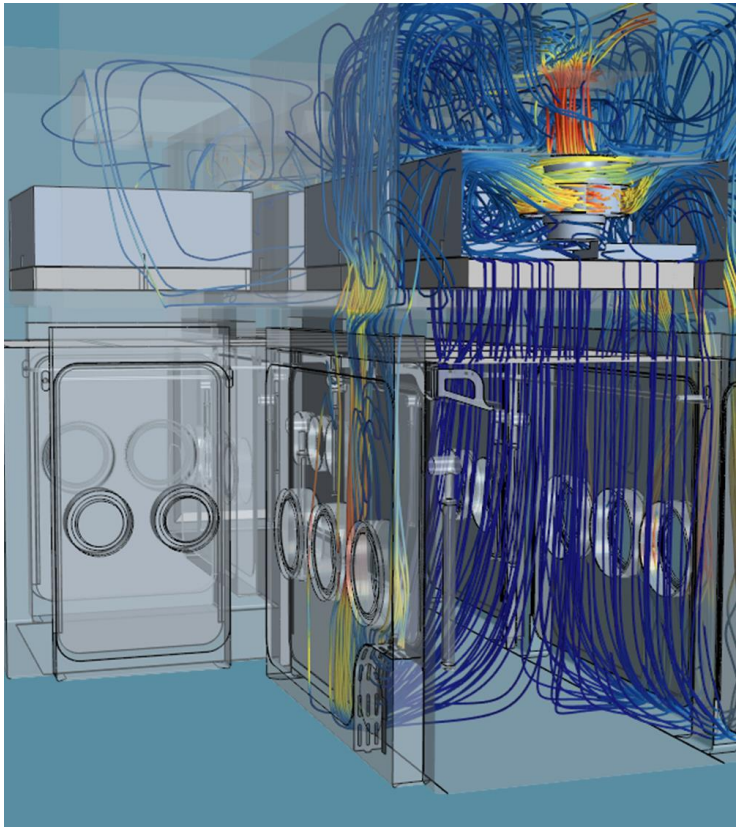


CFD simulation

Supply of grade A air and the principle of first-air are critical for aseptic processing. Simulation of the airflow can help evaluate the design of equipment and processes.

By combination with physical models, more advanced simulations can be performed to optimize contamination control strategies, risk assessments, cleaning procedures

- Flowfield
- Particle tracking
- Aerosolization



clean

Improve your cleaning assessment workflow

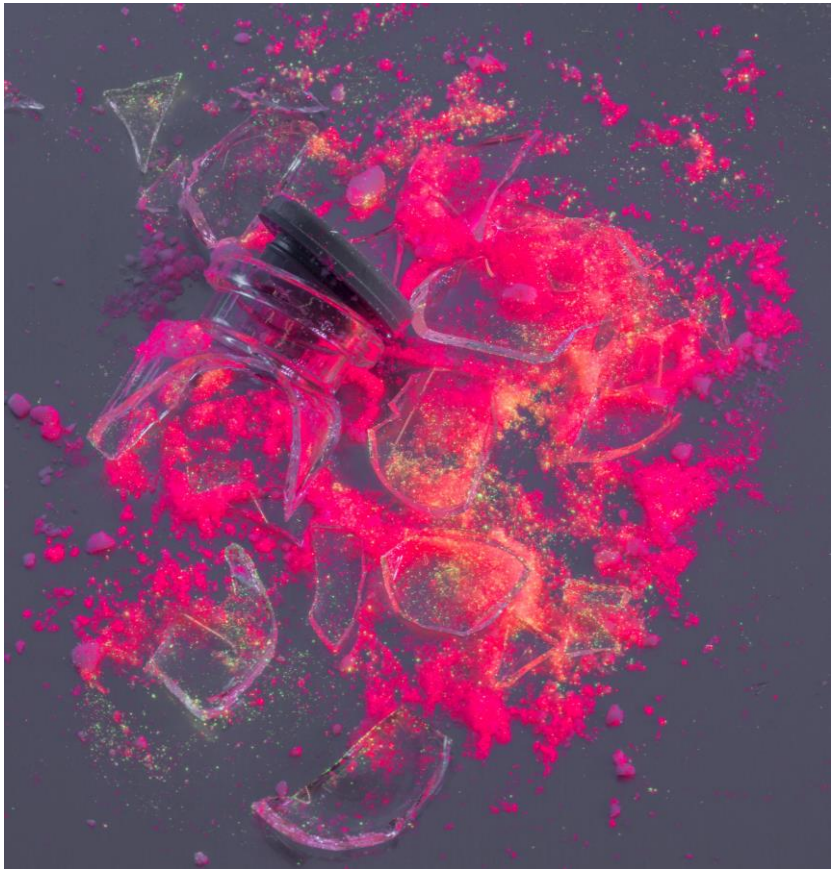
- Identify with a traceable substance (i.e. fluorescence) the source and contaminated areas in the filling line during production & failure mode
- Characterize the distribution patterns
- Choose the surrogate substance
- Determine the more adequate sampling method (swab or rinse sampling) - based on reproducibility and sensitivity requirements by the PDE
- Set up tailor-made MOC coupon spiking studies to achieve more realistic recovery factors estimation
- Force contaminate the filling line, test the efficacy of the cleaning SOPs and check for possible airborne residues
- Test the effectiveness of the containment equipment during challenging operations by measuring airborne emissions and surface contamination

clean Mapping

Understanding the distribution of potential soils is the first step in designing appropriate cleaning measures.

By visualizing different failure modes, critical areas can be defined as well as identifying hard to reach areas

- Qualitative assessment
- Visualization of soils and process characterization
  - Simulation of different modes/failures
  - Evaluation of cleaning procedures
- Worst-case positions
- Risk assessment



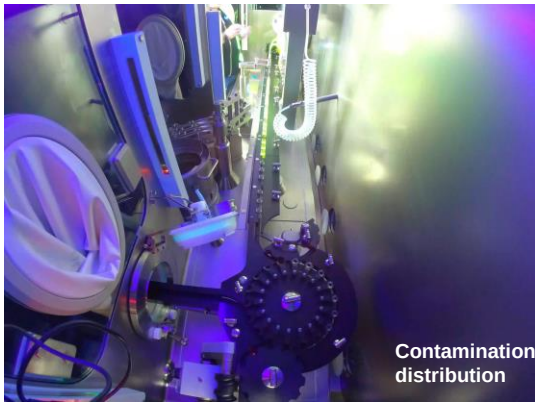
clean Mapping

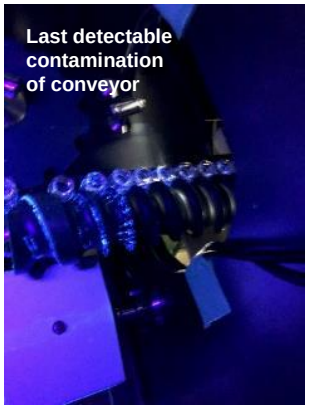
Filling simulation

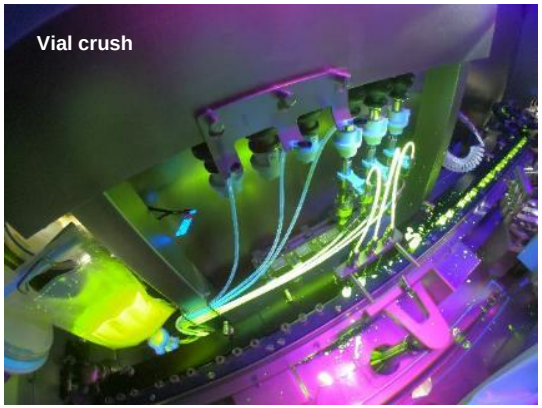
Mechanical transfer

Vial breakage

clean Contamination Mapping



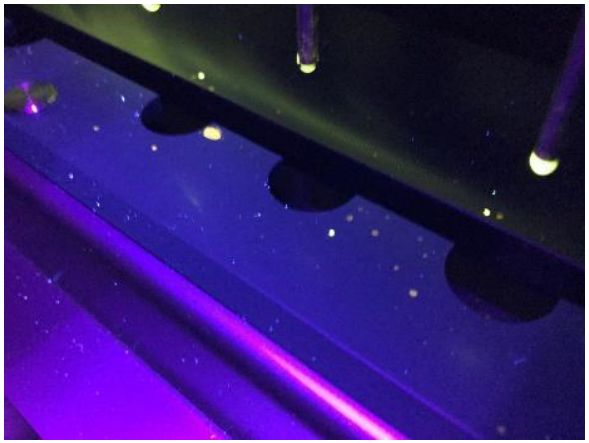




- Simulation of filling with worst case parameters (highest speed and volume)
- Simulation of worst case scenarios – vial break, contamination distribution, spillage in FIPA, splashes on RTP ports, etc.
- Delineation of practical contamination level risk sub-areas
- Characterization of distributions patterns

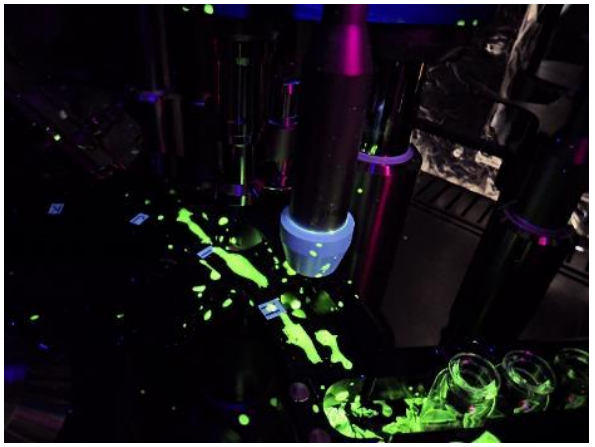
Typical contamination locations in fill & finish processes

Contamination spread



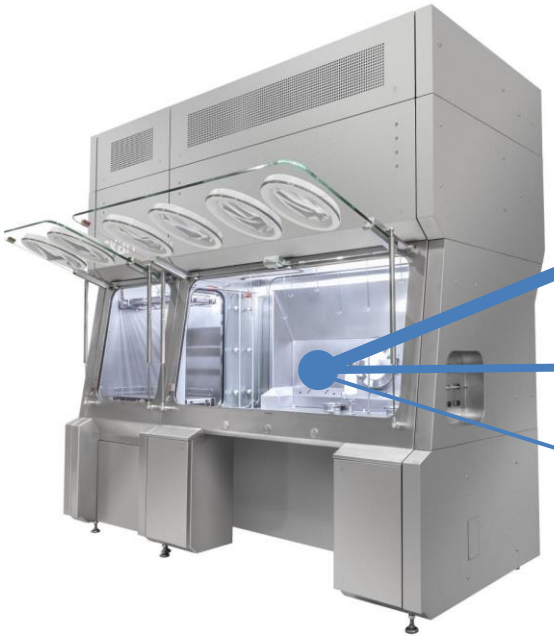
Filling

Mechanical transfer



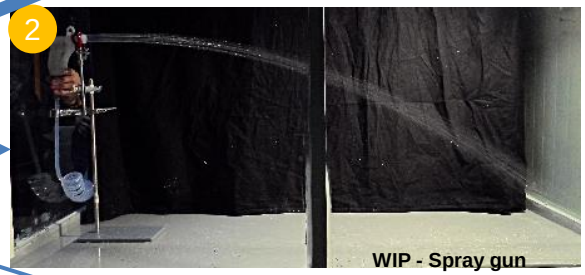
Vials crush

clean – Cleaning methodologies



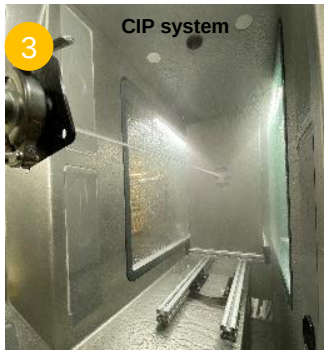
1 Manual cleaning/wiping

2



WIP - Spray gun

3 CIP system



clean
Isolator & Material

High levels of cleanliness of equipment must be documented to ensure personnel safety as well as preventing risks of cross-contamination.

Verification of effectiveness of cleaning procedures in lab-scale experiments and conducted directly in the isolator.

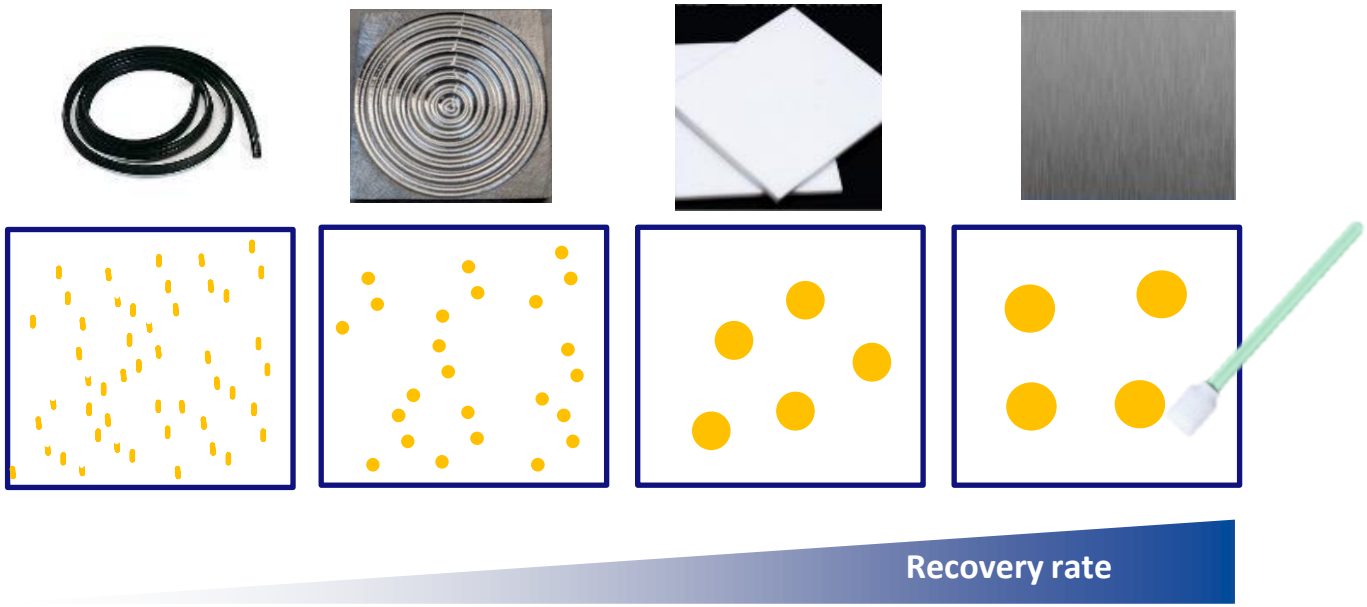
- Quantification of trace amounts of residuals
- Cleanability of materials
- Characterization of soil-material interaction
- Screening of different cleaning methods or detergents

clean - Contamination Characteristics

Coupons → Spike surrogate → Testing recovery technique → Sample preparation → Sample analysis → Recovery rate

Beside the chemistry of the soils, **recovery rates** are heavily **impacted** by the **type & geometry of the material,**

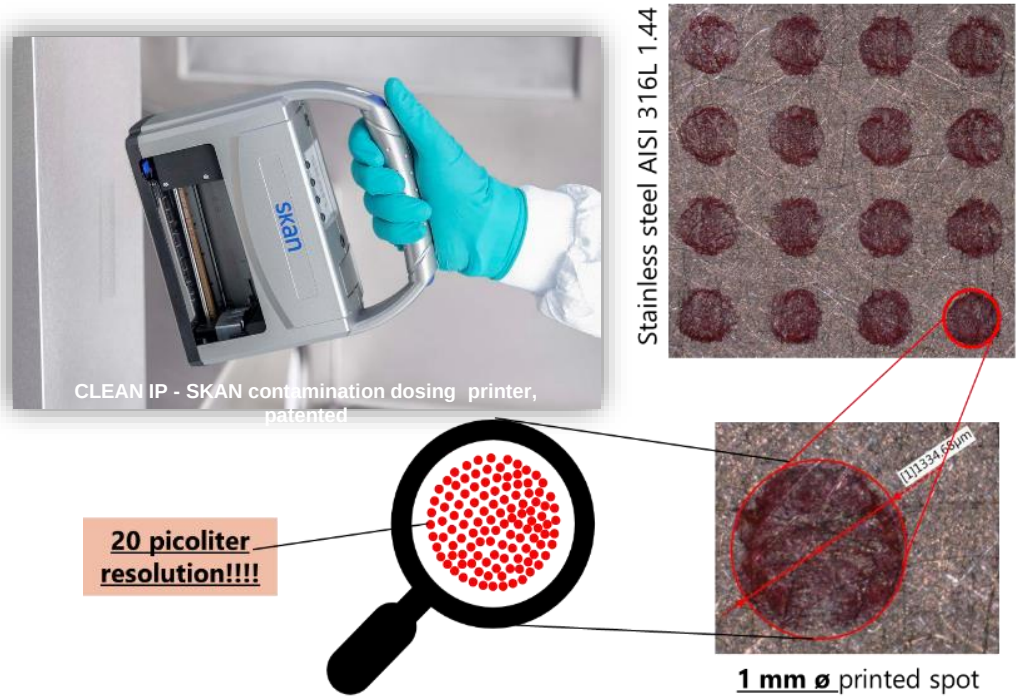
the **contamination distribution** and the type of **recovery tools** adopted in the cleaning studies



clean - Contamination Dosing

clean Indicators & Prints

- Produce chemical distributions at **predetermined doses**
- **Standardize contamination distribution** to reduce/eliminate variation in the recovery rates
- **Speedup recovery/cleaning studies**: no waiting times → immediately dry contaminated surface
- Generation of (custom) **cleaning performance indicators** (CPIs) to guide your bench and field studies

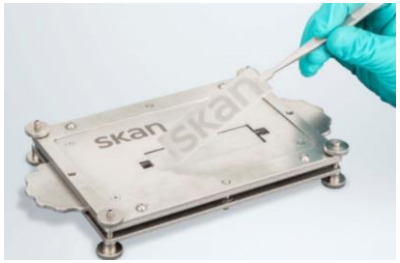


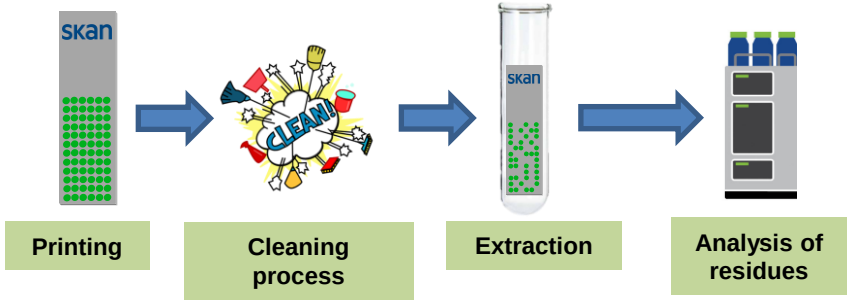
clean - Contamination Dosing

clean Performance Indicators

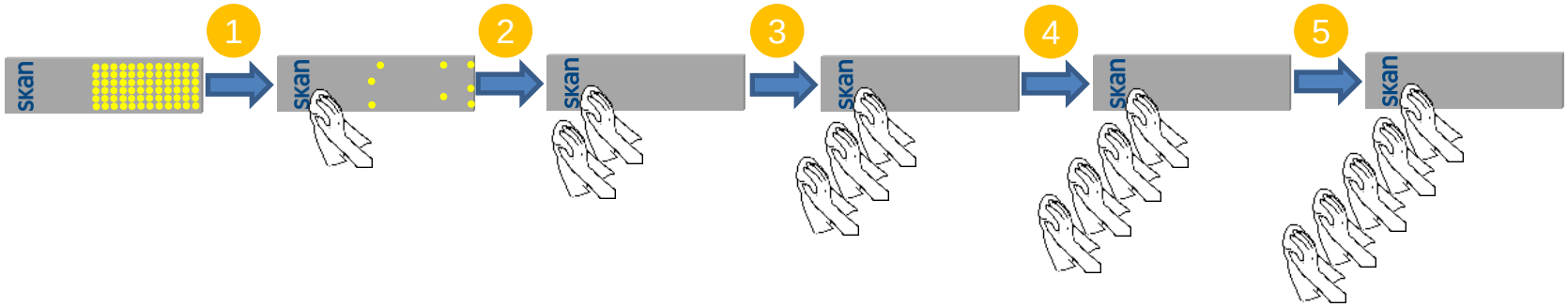
- **Standardize** your contamination:
- Level (ng-mg/dm^2)
- Distribution
- Surrogate
- Matrix / Additives
- Material surface

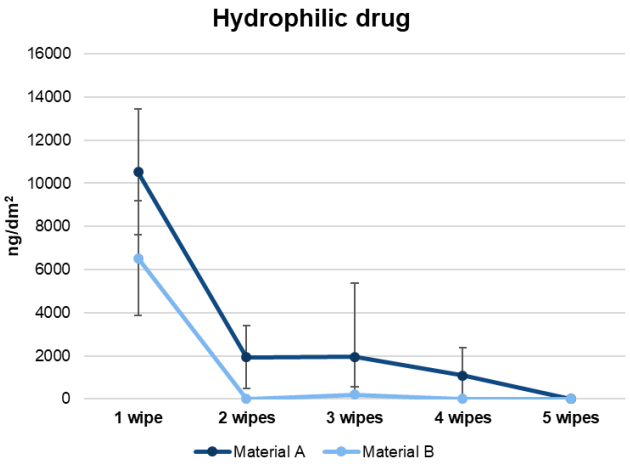
- No visual pass or fail inspection but based on **quantitative assessment** of the residuals
- **Swab-less assessment** based on direct surface extraction
- **Bench studies** and test/screen the efficacy of your **cleaning procedures**

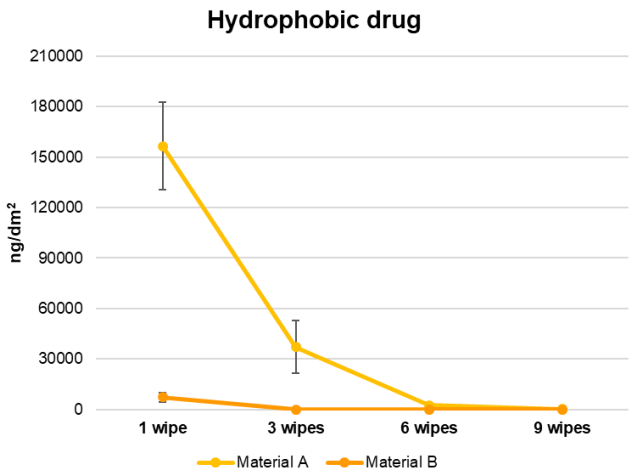




Manual wiping: Measure and quantify cleanness

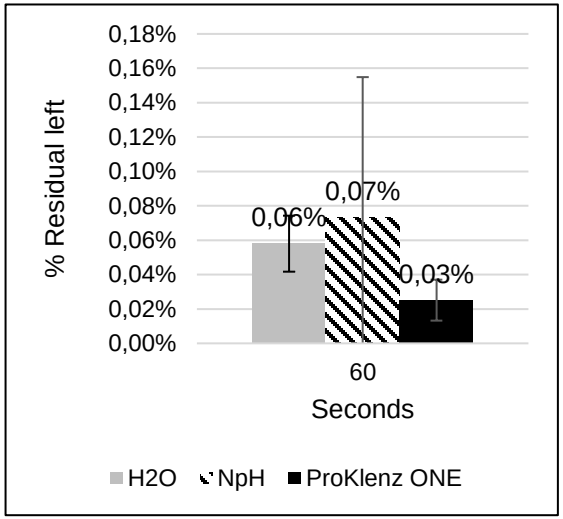




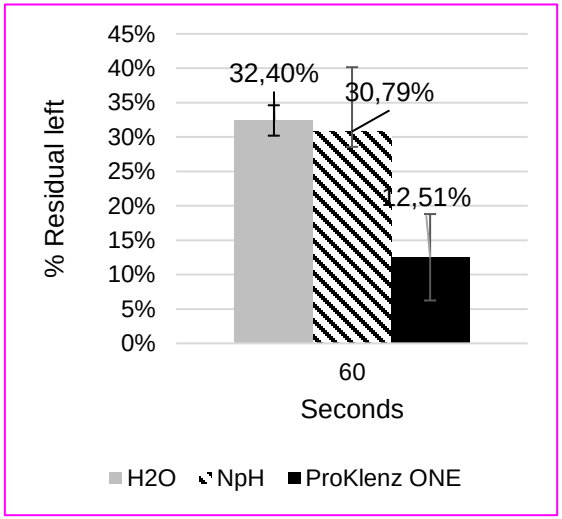


Understand and **quantify** the cleaning kinetic of **different materials** and **pharmaceutical soils**

Rinse Wash: Measure and quantify cleanness



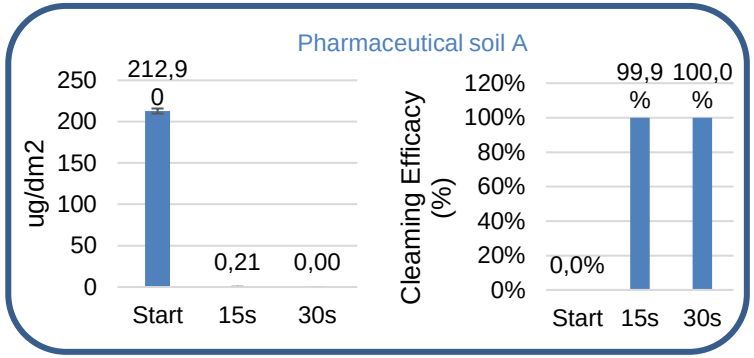
Hydrophilic drug

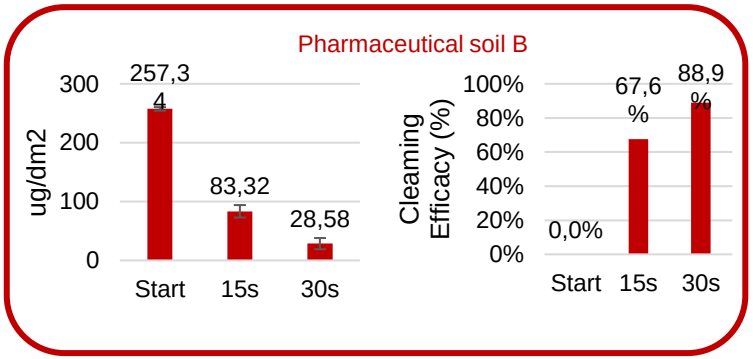


Hydrophobic drug

Understand and **quantify** the cleaning effect of **different detergents** and **pharmaceutical soils**

Rinse wash: Measure and quantify cleanness

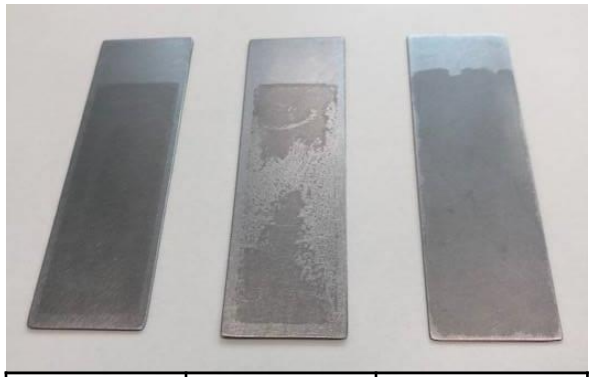




Understand and **quantify** the rinsability of **different materials** and **pharmaceutical soils**

clean-IP: Contamination Dosing – VRL case

- Different APIs ≠ VRL limits
- Different matrixes ≠ VRL limits
- Different materials ≠ VRL limits



API	API + Component 1	API + Component 2

ug/dm²	API - 1	API - 2
313		
625		
1250		
2500		
5000		

clean IP

clean Indicators & Prints

Your challenge

Development and test of a suitable cleaning strategy

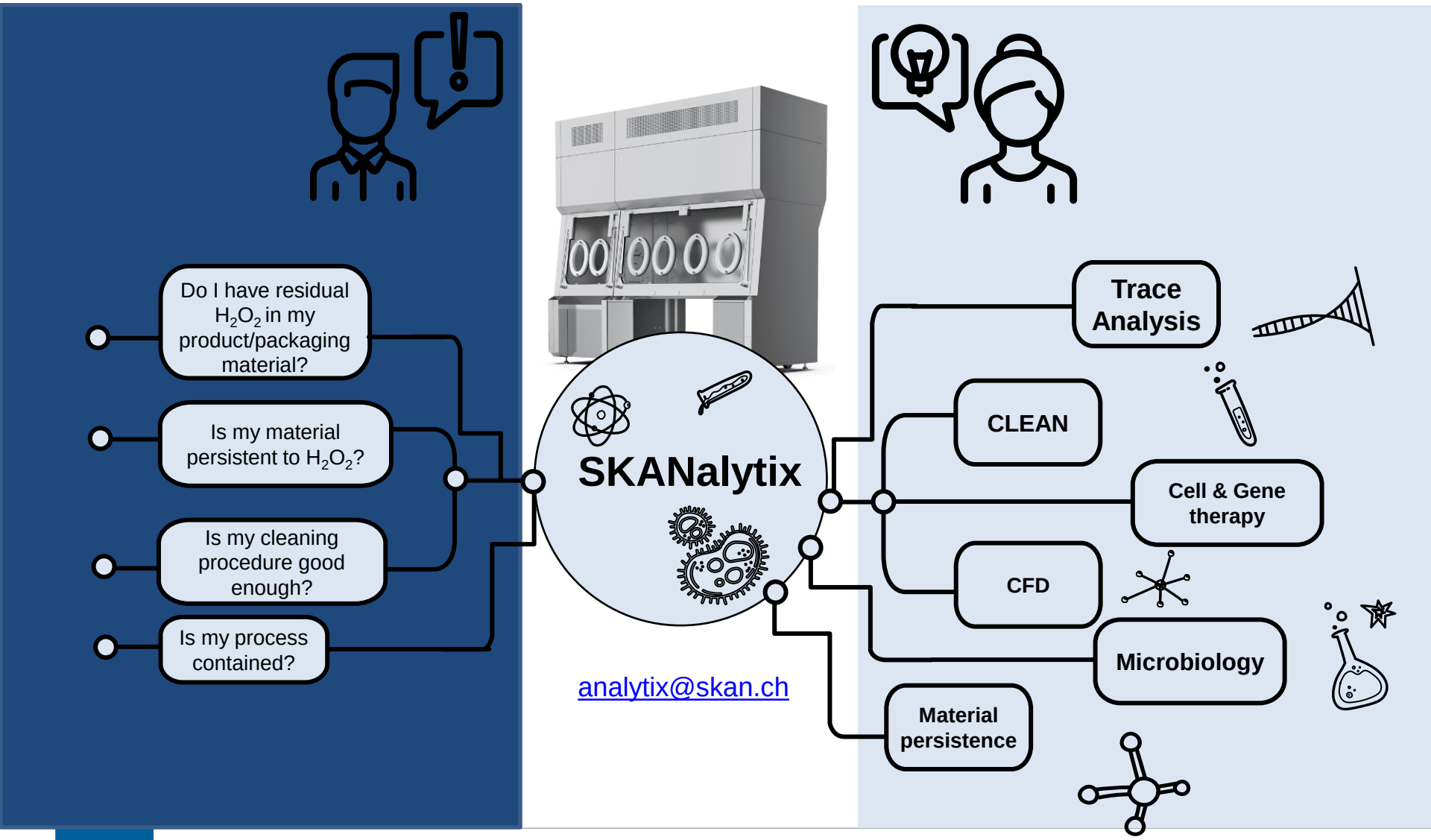
Identify for different materials the visual threshold when your API or residues becomes visible

Check residual contamination after the cleaning process

clean IP

CLEAN Indicators & Prints

- SKAN contamination dosing printer technology is designed to help our customer to establish suitable contamination control strategies
- No more random and uncontrolled spiking studies where the pattern distribution is left to chance
- By using our SKAN patented printing approach you will be able to reliably and accurately deposit contamination patterns on your manufacturing and surrogate materials


Do I have residual H_2O_2 in my product/packaging material?
Is my material persistent to H_2O_2?
Is my cleaning procedure good enough?
Is my process contained?
SKANalytix
analytix@skan.ch
Trace Analysis
CLEAN
Cell & Gene therapy
CFD
Microbiology
Material persistence

Thank you!

Questions?

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