

Cleaning of Semi-Solid Products

Gordon Scott

Process Engineering Lead
Global Manufacturing & Supply
GSK

26th January 2017

Definition of Clean

Pharmaceutical Industry



1. Visually clean

- Free from product / contamination
- Determined by staff responsible for equipment cleaning
- Verified after every clean

2. Chemically clean – free of API (or selected chemical marker)

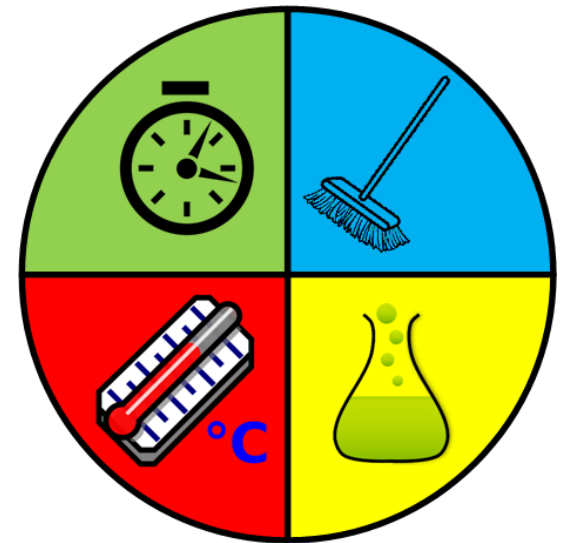
- Determined by the lab through swabbing
- Proven during validation. Periodically re-confirmed as part of validation maintenance

Cleaning is therefore the actions required to return a piece of process equipment back to a clean state after manufacture

HoW are you cleaning?



- Effective cleaning is the result of cleaning for the right length of **Time** at the right **Temperature** using the right **Detergent** (chemistry) and the right level of **Energy** (mechanical)
- Having this balance wrong will lead to ineffective cleaning cycles or extended cleaning times
- The balance of these four factors will be product dependant, hence no one standard cleaning cycle on the manufacturing vessels or washers for all products



Product Overview



Dermatological / Skin Health Products

Creams

- O/W emulsion
- Dissolved / dispersed drug active
- Medium viscosity

Lotions

- O/W emulsion
- Dissolved / dispersed drug active
- Low viscosity

Ointments

- Single phase
- Petrolatum based
- Dissolved / dispersed drug active
- High viscosity

Gels

- Single phase
- Aqueous based
- Dissolved / dispersed drug active
- Medium - high viscosity

Pharmaceutical products

- Smaller range of excipients
- Drug actives

Cosmetic / Consumer products

- Wide range of excipients

Viscosity

Really interested in rheology

- Shear thinning?
- Yield?
- Etc

-
- Manual cleaning
 - Wash bays
 - Manual preparation for automated cleaning
 - Dismantling / initial bulk product removal
 - Cleaning-In-Place
 - Integral part of equipment
 - Dedicated CIP skid
 - House CIP skid
 - Cleaning-Out-Of place
 - Parts Washers
 - Typically, cleaning operations are more manual than they are automated
 - Supporting operators with basic training on the importance of cleaning
 - Increasing application of manual inspection of components post cleaning → visually clean
 - Initial “3-batch” validation followed by periodic revalidation → chemically clean
 - Cleaning being viewed as another processing step by the regulators. Expecting good understanding of critical cleaning processes
 - **Process understanding work with University of Leeds**
 - **Pulling together chemical and mechanical aspects of cleaning**
-

What are you cleaning?



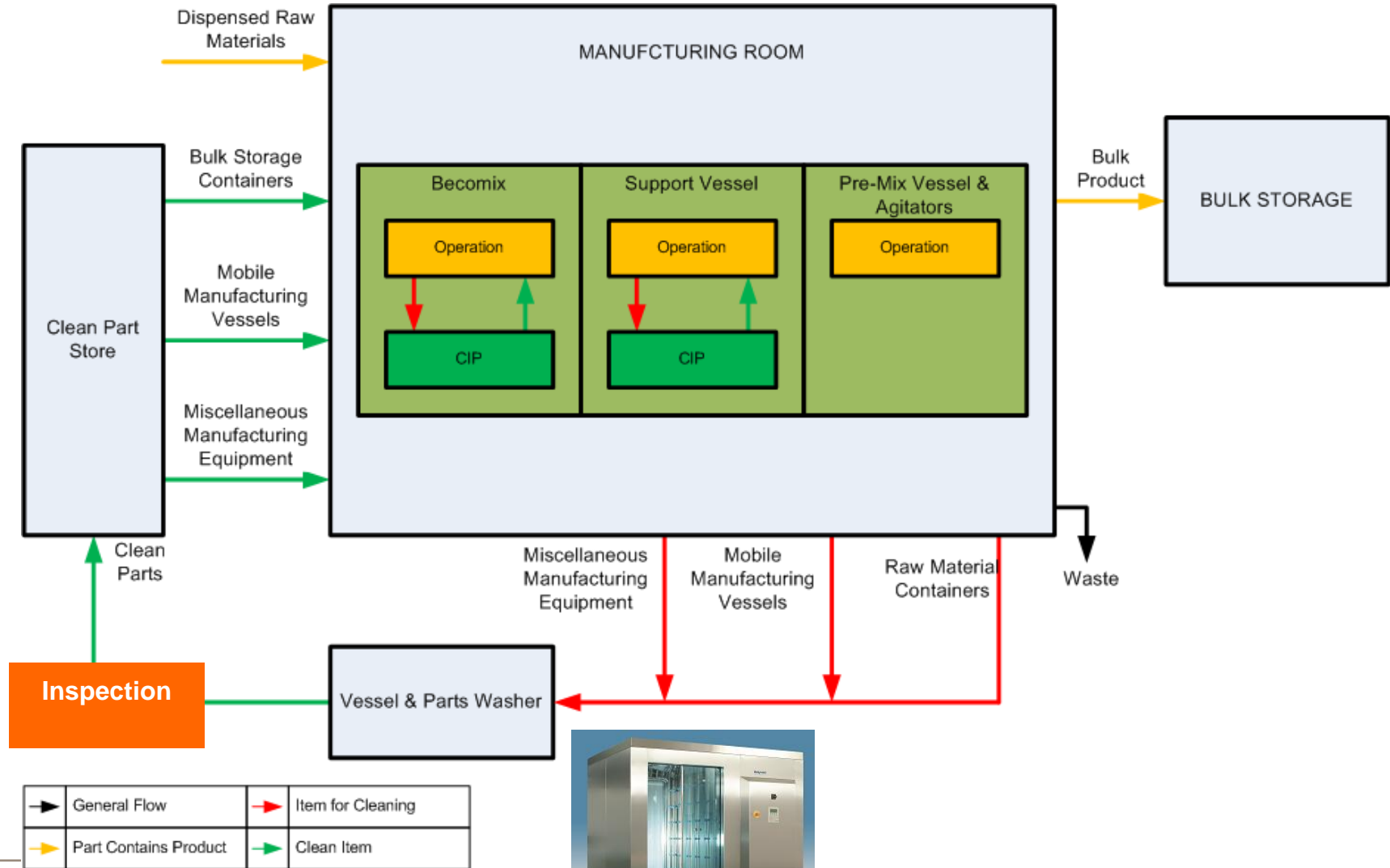
- All equipment used in the manufacture and filling of product
 - Dispensing, bulk manufacture & filling
- Focus here is on product contact parts – critical cleaning
- Equipment used to clean equipment
 - Parts washers, CIP systems



Equipment Flow & Cleaning



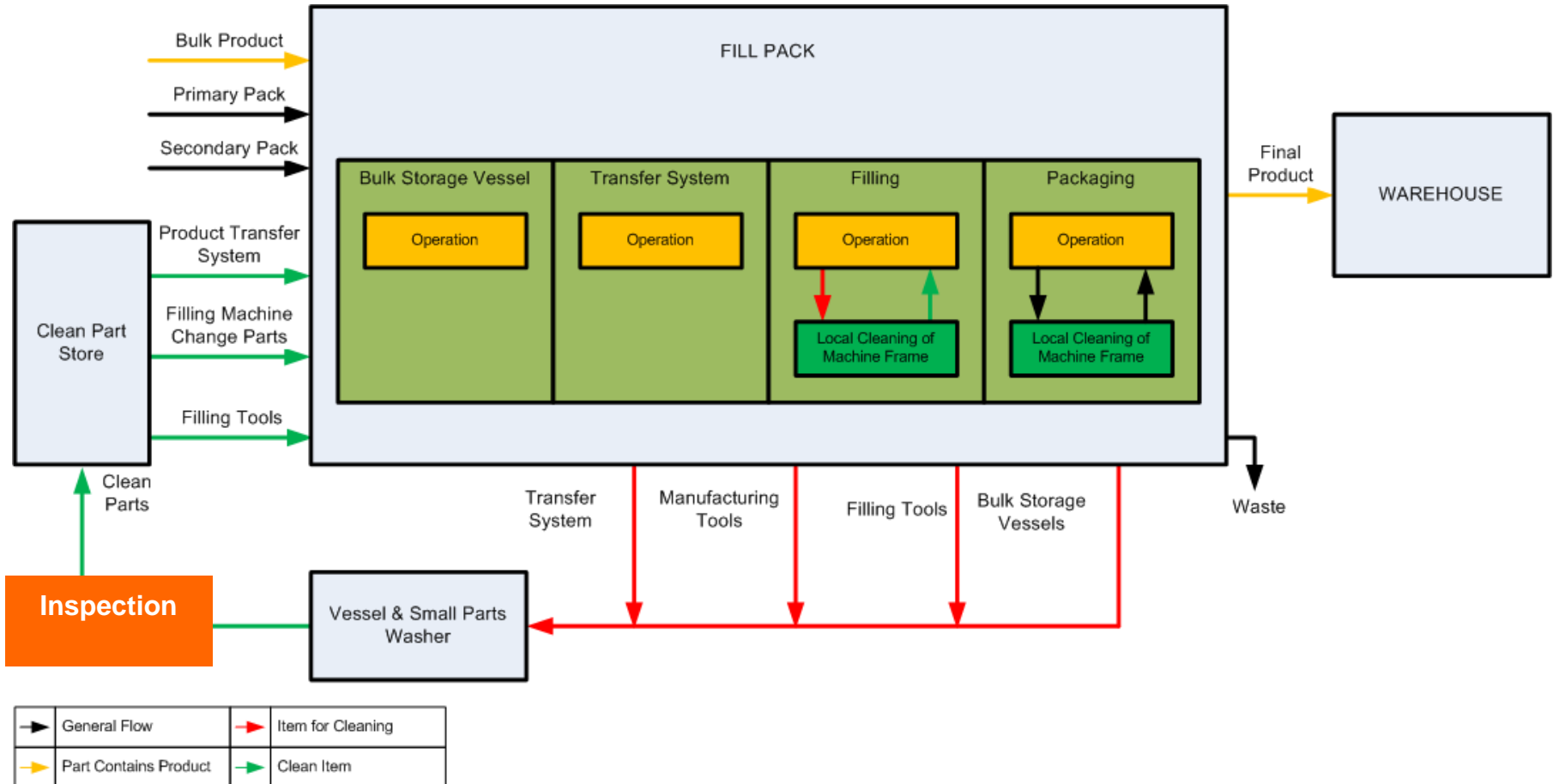
Bulk Manufacture



Equipment Flow & Cleaning



Filling



Typical Failure Modes



- Equipment not visually clean at end of validated wash cycle
 - Both CIP and COP
 - Failures associated with residues of final product and components within product (e.g. API enriched in heavy components of white soft paraffin and part hydrated Carbomer gel)
 - View is that the CIP and COP equipment delivers a repeatable cleaning cycle, though there may be subtle differences that could be driving cleaning failures
 - Human activities are controlled by procedures (e.g. stacking of wash racks) though there are probably degrees of freedom that have not been tied down sufficiently leading to variability in the input to the cleaning process. This is particularly true for COP
-

-
- Automated cleaning
 - Minimised / optimised manual intervention
 - Manual → COP
 - COP → CIP
 - Automated inspection and release
 - Fully validated
 - Optimised cleaning cycles
 - Detergents / water / heat etc
 - Underpinned by sound product & process understanding
-

Areas of Interest



Must Drive Understanding and Productivity

- **Mapping** of removal mechanisms
 - The role that flow, temperature and detergent action have on the removal of products from surfaces)
 - E.g. removal of hydrophobic materials (e.g. pigments and sunscreens) or polymer-thickened products (e.g. Carbomer gels)
 - **Modelling** the cleaning of complex geometries
 - e.g. sprays & jets used in CIP and COP systems
 - **Optimising** cleaning regimes in CIP and COP systems (e.g. parts washers)
 - **Detection** methods of visual and chemical contamination on surfaces that can be integrated into CIP and COP systems
 - **Assessment** of current cleaning technologies
 - E.g. sprayball / jet technology → selection guides?
 - **Novel** cleaning technologies (e.g. ice-pigging, ultrasonics)
-