Dissolution Cleaning and Care

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Agenda

- Paddle, Basket Shaft, and Basket Care
- Vessel Care
- Cleaning the Dissolution Unit
- Routine Maintenance
- Cleaning Autosamplers
Dissolution Cleaning - General

- Cleaning should be done as soon as possible after a run has been completed
- No abrasives should be used on any dissolution item
- No bleach should be used on the dissolution unit
- Appropriate cleaning solvents should be determined on a formulation by formulation basis
Clean as soon as possible after a run

- Evaporation happens
- Acids become much more concentrated
- Salts and excipients precipitate out
Paddles/Basket Shafts/Baskets

- Fabricated from type 316 stainless steel
- Passivated with nitric acid for greater protection against acids
- If cleaned properly, they will last years before replacement needed
- Dull finish and signs of rust indicate a change is needed
Stainless Steel Paddles – Minor Rusting
Stainless Steel Paddles – Advanced Corrosion
PTFE-coated shafts

- PTFE (commonly called Teflon) shafts are acid resistant, but are more fragile than stainless steel shafts
- Care must be taken to prevent abrasion against other surfaces
- Properly store when not used
- Abrasion of surfaces leads to larger surface areas leading to:
  - Greater mixing
  - More variability
  - Cross-contamination
Teflon Paddles – Good, Okay, and Terrible
Shaft Cleaning/Care

- For most products, cleaning can be done in place with squirt bottle of soapy water and gentle cleaning with a soft cloth or wet paper towel followed by a DI Water rinse
- Some sticky excipients may require more aggressive cleaning – if residue remains, acid attack will continue and become more concentrated
- When shafts are not on instrument, store carefully on racks or wrapped appropriately
Basket Clips

- Prongs should hold tightly to basket and not spin
- O-ring attachment is not USP/FDA/ASTM compliant
Dissolution Baskets

- Most fragile item
- Always handle by top ring only
- Rinse gently in water
- Follow with sonication in alcohol
- Return to safe storage container
Baskets – From New to Dead
Basket – Bad Example

- Residue traps in where mesh meets itself and upper and lower rings
- Seam is split
- Gray, dull appearance
- Denting/High Wobble
Paddle and Basket Depth – Setting Heights
Dissolution Vessels

- Generally made of glass
- Do not use abrasives (be careful of some lab brushes)
- Soap and Water usually all that is needed
- Use appropriate height setting tools to prevent scratching
Vessel Residues

Vessel Residue most persistent on bottom of the vessel and on the top level of the media

Look at vessels when dry

In extreme cases, dilute nitric acid can “deglaze” vessels
Vessel Cleaning

- Dishwashers safe with most vessels
- If vessel has plastic element, generally should not exceed 50C
- When not in use, store in safe environment
Apparatus Cleaning Sequence

- Remove Baskets
- Clean Shafts
- Clean vessels (back first, then front)
- Clean sampling lines if applicable
Water Bath Care

- Maintain Proper Visibility
- Use Bath Clear or other approved algaeicide
- Clean as needed
- **NO BLEACH**
Other Condition Checks

Centering Rings:

- All teeth in place
- O-Rings present, hold well onto plate
- No rings w/ removable pegs
Waterbath Maintenance

Acrylic water baths should be maintenance free, except for routine cleaning.

Do not use cleaning compounds containing ammonia; these can cause deterioration of the plastic. Use only cleaners approved for plastic materials. These can be found in the catalogs of most scientific supply houses.

Do not use abrasive cleaners that will scratch the plastic. Besides the unsightliness of the scratches, they also provide active sites for the propagation of algae.
What Not To Clean With
Waterbath Maintenance

A water bath algaecide or clear bath product is recommended.

Ensure it is compatible with Acrylic and vinyl plastics.

The flow paths in most heater/circulators are primarily stainless steel and should tolerate most clear bath formulations. Check with the manufacturer of the circulator to be sure.

Care must be taken when removing dissolution vessels so they do not drip circulator water into clean vessels.

Clean and replace the back vessels before cleaning the front vessels.
Algaecide Options

Typical:

- Clear Bath Algaecide (good for 3-6 weeks on average)

Long-term, but hazardous:

- Bronopol
- Sodium Azide
Vessel Plate

The vessel plate is steel as well, and should be kept clean to prevent rusting.

Rust will swell, and can push vessels out of alignment.
Preventative Maintenance Plan

• Recommend PM every 6-12 months depending on use, age of equipment, and treatment
• Check Belt
• Lubricate Appropriate Components
• Check Electrical Components
• Temperature Verification
• Clean waterbath as needed
Cleaning Autosamplers
Autosampler Cleaning

- Cleaning should be done as soon after run as possible
- Cleaning method should be set-up which cleans all portions exposed to media
- Media(s) used should be checked to ensure they properly remove residues
Cleaning Validation

• Perform Dissolution Run
• Perform System Clean
• Sample Dissolution Media after clean
• <1% response of standard in the blank is typically acceptable
• If carryover is at or near 1%, modify cleaning method
Cleaning Methods – VK8000

• Always use “Clean System” or equivalent

• For cleaning out buffers, salts, sugars, etc. use DI Water (up to 60C)

• For cleaning out sticky/filmy/gummy residues use alcohol

• For more automated cleaning, a sample method can be created with multiple timepoints with max prime/purge values
One Cleaning Method not fit for all

Cleaning methods should be validated for each dissolution method

What works for one, won’t necessarily work for the next
Cleaning Extended Release Products

Extended Release Products tend to have both water soluble elements and non-water soluble elements, so you must clean for both:

- Clean system 1x HOT DI Water
- Clean system 1 or more times w/ MeOH or EtOH
- Clean system 1x with DI Water
Keeping Systems Clean

Tubing tends to be very inert, but needs to be replaced from time to time:

• Teflon tubing – every 1-2 years
• Peristaltic tubing – every 6-12 months

If there is persistent carryover, replace peristaltic tubing first and try a different chemistry tubing
Cannula Cleaning and Care

• Clean like you clean the shafts – soap and water
• Occasionally, plastic tubing on tip should be replaced as it will shrink with age, and filters will fall off (4005-0061)
What Water for What?

Tap water should only be used for peristaltic pump automatic calibration

Any other time – DI Water

Tap water varies in quality and can leave poorly soluble residues and damage components
Sampling Replacement Items

Valves and Needles will need replacement on occasion, the better the cleaning – the less often

- Needles – Look out for rust/discoloration on the needle, as well as non-centered hits on HPLC vials with septa
- Valves – Look for corrosion around the valve indicating blockage
- Floor of the 8000 head also a good indicator if clogging has occurred.
Automated cleaning and media replacement is standard on all 850-DS sampling stations.

An automated cleaning cycle can be added to the end of any method to keep the system operating properly and extend the life of internal components.
850-DS Cleaning

- Cleaning done from a rinse bottle connected to sampler – not connected to cannulas
- Can be autocleaned once sample method is complete
- Can have limited cleaning between timepoints
Dissolution Exchange

http://dissolution.chem.agilent.com/

New Dissolution Focuses website which is a one-stop location for information

• Online course on dissolution fundamentals
• FAQs
• Dissolution Hotline
• Dissolution Discussion Group
• Previously recorded webinars on various topics including MQ
Questions?

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