Rouge Control Options for Stainless Steel Bio-Pharmaceutical Process Equipment

Part 1 of 4

Diruneutra pH neutral derouging
ASME BPE identifies three types of rouge:

• Type I red-brown mobile rouge Hematite

• Type II red-brown Hematite that forms on equipment surfaces and can become source for Type I

• Type III blue-black Magnetite high temp >90C (typical in clean steam system)
Fe$^2$O$^3$ Hematite Type I Rouge

Type I Rouge can be wiped off and can move throughout a system. The rouge layer consists of heavy-metal-oxides, preferably Fe-Oxides. The rouge-layer consists of particles of heavy-metal-oxides which can leave the surface based on stream conditions.

Wipe test of a production vessel

Wipe test of a WFI pipe
Fe$^2$O$^3$ Hematite Type II Rouge

Typical Type I & II rouge is caused by hot purified water or clean steam exposure.
Fe$^3$O$^4$ Magnetite or Type III Rouge

Believed to have been caused in WFI system running 90°C water. Not removed during typical de-rouging procedure.
Rouge Control Options

• There are four Rouge Control Methods that offer varying degrees of performance;

• Conventional Chemical de-rouging using hazardous acids

• **NEW**: pH neutral de-rouging with nonhazardous chemistry

• Electrochemical Cleaning (ECC)™ de-rouging

• Electropolishing to remove minimum .0005” to control rouging
Conventional Acid De-Rouging and Passivation

- DI Water Flush
- Derouging with Organic Acid Intensifiers and Reducing Agents to remove rouge (iron by products)
- High Purity Water Rinse
- Citric/Chelant or 20% Solution Nitric Acid to remove free iron (alloy surface)
- High Purity Water rinse
- Neutralization (often introduced into system to adjust pH)
- High Purity Water Rinse
- Oxidizer or Sanitization with Peroxides (Citric process only)
- Final High Purity Water Rinse

Approximately 24 Hour process time
This product comes in 3 component “kit” form, premeasured to treat a specific number of liters of 60-80°C water.

This product is “non-hazardous” and can be shipped and disposed of as same.
Diruneura pH Neutral
De-Rouging and Passivation

• Mix 80C High Purity Water with two premeasured Diruneutra “kit” parts (LIQ, P)
• Maintain 60-80C for up to four hours with complete exposure.
• Add part N to solution and let stand for one additional hour
• Drain & Rinse
• Hydrogen peroxide 1.5-3% <30C one hour
• High Purity Water Rinse
• **Approximately 6-8 Hour process time**
First Article by UltraClean
Derouging chemicals [1]

- **Strong acid** derouging solutions can contain the following chemicals:
  - Phosphoric acid
  - Sulfuric acid
  - Oxalic acid
  - Citric acid
  - Nitric acid
  - Hydrofluoric acid!!!
    - Good derouging effect
    - Caution: fast surface attack with sustainable destruction of stainless steel
  - Salts containing fluorides (Sodium fluoride, Ammonium bifluoride, etc.)
  - Chelates (EDTA, NTA, etc.)
  - Surfactants
Derouging chemicals [2]

- **Soft acid** derouging solutions can contain the following chemicals:
  - Citric acid
  - Oxalic acid
  - Salts (Phosphates, Oxalates, etc.)
  - Chelates (Phosphonates, EDTA, NTA, etc.)
  - Surfactants

- **pH-neutral** derouging solutions can contain the following chemicals:
  - Salts (Phosphates, Oxalates, etc.)
  - Chelates (Phosphonates, EDTA, NTA, etc.)
  - Reducing agents
  - Surfactants
<table>
<thead>
<tr>
<th></th>
<th>Strong acid chemicals</th>
<th>Soft acid chemicals</th>
<th>pH-neutral chemicals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pro</strong></td>
<td>residue-free rinsable unless neutralization performed in system sprayable</td>
<td>residue-free rinsable sprayable</td>
<td>residue-free rinsable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>low acidity</td>
<td>short derouging time (1 – 4 hours)</td>
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<tr>
<td></td>
<td></td>
<td>selective for iron oxide/hydroxide</td>
<td>selective for iron oxide/hydroxide</td>
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<tr>
<td></td>
<td></td>
<td>normally no chemical attack on the metal surface</td>
<td>wide range of efficacy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>lower costs for waste disposal</td>
<td>standardized processes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>lower risk in case of a damage</td>
<td>neutral = pH 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>no risk of chemical attack</td>
</tr>
<tr>
<td><strong>Con</strong></td>
<td>High acid concentrations (15 – 40%)</td>
<td>high application temperature (&gt; 50°C)</td>
<td>high application temperature (≥ 50°C)</td>
</tr>
<tr>
<td></td>
<td>mostly high application temperature (&gt; 50°C)</td>
<td>high chemical concentration (&gt; 10%)</td>
<td>partially not sprayable, oxygen</td>
</tr>
<tr>
<td></td>
<td>not selective for iron oxide/ hydroxide</td>
<td>long derouging time (often more than 10 hours)</td>
<td>sensitive if applied by spray balls</td>
</tr>
<tr>
<td></td>
<td>dissolves also Cr and Ni from the metal surface</td>
<td>very small range of efficacy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mostly long derouging time (often more than 10 hours)</td>
<td>□ pretests are necessary for chemical concentration adjustment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>small range of efficacy</td>
<td>neutralization of rinse water which may still be hazardous waste</td>
<td></td>
</tr>
<tr>
<td></td>
<td>□ pretests are necessary</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>High risk of damage to equipment and surrounding environment</td>
<td></td>
<td></td>
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</table>
## Diruneutra vs. Phosphoric Acid

### Comparison in a laboratory test

<table>
<thead>
<tr>
<th>Derouging with DIRUNEUTRA</th>
<th>Derouging with acid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sample:</strong></td>
<td><strong>Sample:</strong></td>
</tr>
<tr>
<td>– A1</td>
<td>– B1</td>
</tr>
<tr>
<td><strong>Product:</strong> DIRUNEUTRA</td>
<td><strong>Product:</strong> Cleaning agent X with phosphoric acid</td>
</tr>
<tr>
<td><strong>Concentration:</strong></td>
<td><strong>Concentration:</strong></td>
</tr>
<tr>
<td>– 2.5% Diruneutra LIQ/P</td>
<td>– 30% X</td>
</tr>
<tr>
<td><strong>Temperature:</strong> 60 - 80°C</td>
<td><strong>Temperature:</strong> 70 – 80°C</td>
</tr>
<tr>
<td><strong>pH:</strong> 7</td>
<td><strong>pH:</strong> &lt; 1</td>
</tr>
<tr>
<td><strong>Time:</strong> 4 hours</td>
<td><strong>Time:</strong> 4 hours</td>
</tr>
</tbody>
</table>
Laboratory test pH-neutral Derouging

Comparison after 4 hours of treatment

« Diruneutra »

« Product X, acid »
Derouging with DIRUNEUTRA in production equipment

before Derouging

after Derouging
Derouging with DIRUNEUTRA

• Object: WFI Multiple-Effect Distillation unit
  – Columns: 5
  – Capacity: 1100 liters/hour (with 6 bar heating steam)
  – Filling volume: approx. 400 liters

• Derouging and Passivation procedure
  – Derouging with DIRUNEUTRA V10 at 80°C
  – Passivation with 3% Dirupass AP at 70°C for 1 hour
Derouging with DIRUNEUTRA

- Colorimetric iron content measurement (with HACH DR/890)
Derouging with DIRUNEUTRA

• Result:
  – Derouging process was finished after 2 hours process time
  – Iron concentration in the derouging solution: 60 mg/l
  – Amount of removed iron: 30 grams (equal to 43 grams Fe₂O₃)
Advantages of a neutral Derouging

• CAN BE PURCHASED IN PREMEASURED “KIT” FORM
• CAN SHIP AND BE STORED SAFELY UNTIL NEEDED.
• CAN BE USED BY PLANT PERSONNEL WITH THE ADVANTAGES OF;
  – Shorter process time
  – Low chemical concentration
  – Wide range of efficacy
  – Lower danger for the personnel
  – No risk to attack the material surface
  – Cost-saving waste disposal of the derouging solution
  – Not necessary to neutralize the rinse water
  – No damages in case of leakage
Diruneutra Practical Applications

• WFI and PW storage vessels (vertical and horizontal) as large as 18,000-gallon

• WFI and PW loops with pipe sizes ranging from ½” to 4” and volumes as high as 2000-liters

• MECO VC stills ranging from 400 GPH to 6,000-GPH

• MECO CS generators of all sizes

• Chromatography skids and UF skids of various configurations
<table>
<thead>
<tr>
<th>System Description</th>
<th>Working Volume (liters)</th>
<th>Process Time (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MECO 400 GPH VC Still</td>
<td>350</td>
<td>16 hours including set-up</td>
</tr>
<tr>
<td>MECO 6,000 GPH VC still</td>
<td>5,250</td>
<td>20 hours including set-up</td>
</tr>
<tr>
<td>10,000-gallon WFI tank</td>
<td>3,000</td>
<td>12 hours including set-up</td>
</tr>
<tr>
<td>Large WFI loop 1,000 FT of 4”</td>
<td>2,470</td>
<td>16 hours including set-up</td>
</tr>
<tr>
<td>UF or Chromatography skid</td>
<td>250</td>
<td>8 hours including set-up</td>
</tr>
</tbody>
</table>
Satisfied Diruneutra Customers

- Alcon US
- B. Braun, DE
- Baxter US
- Boehringer Ingelheim DE/US
- Cilag (J&J), CH
- Crucell, CH
- CSL Behring, CH + DE
- EGIS, HU
- Gedeon Richter, HU
- Genzyme, BE
- Lilly, FR/US
- Amgen US
- West Pharma US
- Lohmann & Rauscher, DE
- Lonza, CH
- MCL, NL
- Merck Serono, CH
- Novartis, CH + FR
- Roche Diagnostics, DE
- Roche, CH
- DSM US
- Solvay Pharma, NL
- Hospira US
- Grifols, NC
Conclusions

1. **Diruneutra** offers a **pH neutral, non-hazardous**, derouging alternative that can be used without risk to equipment, personnel, or the environment by equipment owners eliminating the need to hire contractors. Observation of treated systems over time has shown evidence this technology is retarding rouge reformation. (Part 1 of 3)