Updated specifications for IND #79,005

<table>
<thead>
<tr>
<th>Test</th>
<th>Current Specifications</th>
<th>Original Filed Specifications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radiochemical Purity (TLC):</strong></td>
<td>$R_f &gt; 0.5$</td>
<td>$R_f &gt; 0.5$</td>
</tr>
<tr>
<td></td>
<td>Purity $\geq 95%$</td>
<td>Purity $\geq 95%$</td>
</tr>
<tr>
<td><strong>Residual Solvent Levels:</strong></td>
<td>Acetone $\leq 5000$ ppm</td>
<td>Acetone $&lt; 5000$ ppm</td>
</tr>
<tr>
<td></td>
<td>Acetonitrile $\leq 410$ ppm</td>
<td>Acetonitrile $&lt; 400$ ppm</td>
</tr>
<tr>
<td><strong>Radionuclidic Purity:</strong></td>
<td>Measured half-life 100 – 120 minutes</td>
<td>Measured half-life 100 – 120 minutes</td>
</tr>
<tr>
<td><strong>Bacterial Endotoxin Levels:</strong></td>
<td>$&lt; 175$ EU per dose</td>
<td>$&lt; 175$ EU per dose</td>
</tr>
<tr>
<td><strong>pH:</strong></td>
<td>4.5–8.0</td>
<td>6–8</td>
</tr>
<tr>
<td><strong>Sterility:</strong></td>
<td>Negative/no growth, must also pass filter integrity test</td>
<td>no growth observed in 14 days</td>
</tr>
<tr>
<td><strong>Residual Kryptofix® [2.2.2]:</strong></td>
<td>$&lt; 50$ µg/mL Kryptofix®</td>
<td>$&lt; 50$ µg/mL Kryptofix®</td>
</tr>
<tr>
<td><strong>Radiochemical Purity (HPLC):</strong></td>
<td>$\geq 95%$</td>
<td>$&gt; 95%$</td>
</tr>
<tr>
<td><strong>Chemical Purity (HPLC):</strong></td>
<td>FES $\leq 5$ µg/dose</td>
<td>FES $&lt; 5$ µg/dose</td>
</tr>
<tr>
<td></td>
<td>Other UV absorbing compounds $\leq 5$ µg/dose</td>
<td>other UV peaks $&gt; 3$ min $&lt; 5$ µg / dose</td>
</tr>
<tr>
<td><strong>Chemical Purity (particulates):</strong></td>
<td>Clear and Colorless</td>
<td>Clear and Colorless</td>
</tr>
</tbody>
</table>

The drug solution is stored at room temperature in a septum sealed, sterile, pyrogen-free glass vial with an expiration time of 8 hours.

The specifications that have been updated are for pH and acetonitrile. The purity specifications have been clarified to $\geq$ instead of $>$ to avoid ambiguity. These changes are not considered major and will not increase risk to the patient.
Justification for these changes is to align these specifications with similar FDA approved PET radiopharmaceuticals and ICH guidelines. Many sites are now preparing FES with pre-filled cassettes and automated synthesis instruments that were designed in compliance with these newer published limits.

1. Acetonitrile is listed in the Guidance for Industry, QC3 – Tables and List, Revision 2, February 2012 as a class 2 solvent with a concentration limit of 410 ppm. Acetone is a class 3 solvents and limited to 5000 ppm so no specification change is needed for them.

2. FDA approved labeling for two very similar radiopharmaceuticals, F-18 FDG and NaF F-18, has both drugs specified at pH 4.5-8. To be consistent with these drugs, we have changed the F-18 FES specification to 4.5-8. ¹

¹ FLT now has a monograph in the European Pharmacopeia with a pH specification of 4.5-8.5. There is no USP monograph