rev. 3.10e

Technical Note

Micro SMP-200

Materials Compatibility Kit for iPRECIO® Pump

Standard Operating Procedure (SOP) for evaluating the compatibility of vehicle/solvents and agents to iPRECIO® is described in this technical note along with details of the available kits.

The SMP200-Materials Compatibility Kit, part number SMP200-MC KIT, consists of the 4 materials which are in the fluidic path of the iPRECIO® pump and described in detail in Table 1:-

1. Septum
2. Connectors
3. Tubing
4. Reservoir

	Part / Material	Number of units	Total Weight (approximately in milligrams)
A	Septum / Isoprene Rubber	1	20
B	Connector / PP	1	30
C	Catheter tubing / SEBS	1	30
D	Reservoir / SIBS	10	10

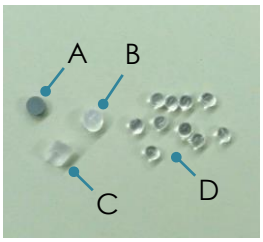

Table 1: Material contents of each set.

Each kit comprises of 5 sets of the 4 materials described in Table 1. The kit will be used to evaluate compatibility to vehicle/solvent and also agent to iPRECIO® pumps. Compatibility to vehicle/solvent is evaluated by weight loss/gain of the 4 materials when stored with vehicle/solvent at physiological temperature for the appropriate duration. For the agent, it's concentration is monitored at physiological temperatures for the appropriate duration. Discoloration and clarity of the vehicle/solvent agent solution is monitored in the presence of a set of the 4 materials. If the concentration is significantly reduced, it could be due to adsorption into one or several materials and/or degradation of the agent caused by one or several materials.

SMP200-MC Kit (5 sets)

SD-SMP-200 and SD-SMP-310R are also available. These devices consist of the reservoir and fluidic components (tubing, connectors) used to manufacture the iPRECIO® SMP-200 pump and SMP-310R pumps which come into contact with the drug formulation or vehicle. The device should be filled with vehicle/solvent with/without agent as appropriate and incubated at 38°C for as long as the planned duration of the study or the expected duration before extraction and re-fill of the reservoir to refresh the solution. This kit is most appropriate for monitoring concentration changes of the agent at physiological temperatures.

Note.
If loss of concentration of agent is mainly due to absorption to reservoir, tubing and connectors, a 24-48 hour conditioning period with the agent is recommended at physiological temperatures.

WARNING：iPRECIO® Micro – Infusion Pump is not intended for human use.

REQUIREMENTS

- SMP200-Materials Compatibility Kit (Part No. SMP200-MC)
- 20 ml screw cap glass vials (used with headspace autosamplers with Teflon coated seal septum) or appropriate test tubes and caps.
- Analytical Balance of 0.01mg resolution. (e.g. A&D GH 202 Analytical Balance)
- Appropriate size pipettes for preparing solutions
- Incubator for evaluation at physiological temperatures
- Vehicle/solvents and agent as required
- Safety equipment and appropriate MSDS documentation

METHODS

1. Method for testing compatibility of solvent/vehicle to pump materials

One vial per vehicle is required for testing solvent/vehicle compatibility.

1. Weigh the contents of each bag of materials to at least 0.01 mg decimal point. This will be the initial weight for each of the 4 materials [initial Weight]
2. Contents of each of the 4 materials are then placed in the 20 ml glass vial.
3. Pipette or measure out between 5 and 10 ml of the appropriate solvent(s) and place into the 20 ml glass vial containing the 4 materials.
4. Screw cap on tightly
5. Incubate at 38°C for the appropriate duration. Appropriate duration would be at least the same length as the planned study or the duration before extraction and re-fill to refresh the solution in the reservoir.
6. Once the appropriate duration is reached, the materials should be removed and allowed to dry on absorbent tissue. If necessary, blot dry.
7. Separate the 4 materials and then weigh them like in (1). [This will be the intermediate/next weight or final weight] See Table 2. If this is an intermediate time point, return the materials to the 20ml vial and screw cap on tightly.
8. Values measured in (1) and (7) will be used to calculate % of weight change of the 4 difference materials.
9. **$\%\Delta^{weight}$** materials should not exceed ± 7% of initial weight.
10. Repeat the process 6-9 as appropriate.

Part / Material	Number of units	Initial Weight mg	Next Weight (intermediate) mg	Final weight mg
Septum / Isoprene Rubber	1	Septum $^{initial\ weight}$	Septum $^{next\ weight}$	Septum $^{final\ weight}$
Connector / PP	1	Connector $^{initial\ weight}$	Connector $^{next\ weight}$	Connector $^{final\ weight}$
Catheter tubing / SEBS	1	Tubing $^{initial\ weight}$	Tubing $^{next\ weight}$	Tubing $^{final\ weight}$
Reservoir / SIBS	10	Reservoir $^{initial\ weight}$	Reservoir $^{next\ weight}$	Reservoir $^{final\ weight}$

Table 2: Weight information for the 4 materials

Percentage weight change, $\%\Delta^{weight}$ can be calculated by the following formula

$$\frac{[\text{Material A}^{\text{initial weight}} - \text{Material A}^{\text{final weight}}]}{\text{Material A}^{\text{initial weight}}} \times 100$$

Equation 1: Formula for calculating percentage weight change.

$\%\Delta^{weight}$ materials should not exceed ± 7% of initial weight.

1. **$\%\Delta^{weight}$** Septum
2. **$\%\Delta^{weight}$** Connector
3. **$\%\Delta^{weight}$** Tubing
4. **$\%\Delta^{weight}$** Reservoir

Notes.
For intermediate duration point, use weight measured at that point.

2. Method for testing compatibility of agent to pump materials

2 vials per concentration/vehicle/solvent is required, one as the control to evaluate stability of the agent at physiological temperatures and the second to evaluate absorption/reaction to the materials used in the iPRECIO® pump at the same temperatures.

1. Using a compatible solvent/vehicle, prepare at least 2-3 ml solution of the agent at the concentration which is intended for use in the iPRECIO® pump.
2. Place 1 ml of the solution in each of the 20ml screw cap vial. The color and clarity of the solution should be noted.
3. Place the contents of a set of the 4 materials into one of the 20ml screw cap vials. The other vial will act as a control as described before. Close both vials.
4. Incubate solutions at 38°C for the appropriate duration for your iPRECIO® study. Appropriate duration would be at least the same length as the planned study or the duration before extraction and re-fill to refresh the solution.
5. At the end of the incubation or at the appropriate duration, inspect the color and clarity of the solution in each 20ml vial. Determine the concentration of agent in each vial.
6. After incubation, the solution in each glass vial should have the same color and clarity as in step 2. If both solutions (test and control) changes color or becomes cloudy, the agent may be unstable at physiological temperatures. If the solution with the materials changes color or becomes cloudy and the control remains unchanged, the agent is unstable in the presence of the 4 materials. In this case, the agent, should not be used in the iPRECIO® pump or should be refreshed before the solution changes color or becomes cloudy.
7. The concentration of the agent in the 20ml vial with the 4 materials should be within 90% of the control value. If not, do not use with the pumps.

Notes:

- Sufficient solubility of the drug in the solvent should be assessed.
- It is important that the agent does not precipitate out of solvent/vehicle when it infuses out of the catheter to the appropriate administration site.

*Table 1 and associated figure from page 1 are reproduced hereafter to facilitate easy identification of the different materials. For additional clarity, material B (connector/PP) and material D are spherical. Material C (Catheter tubing/SEBS) is tubular.

Table 1: Material contents of each set.

	Part / Material	**Number of units**
A	Septum / Isoprene Rubber	1
B	Connector / PP	1
C	Catheter tubing / SEBS	1
D	Reservoir / SIBS	10