

Technical Note

Micro SMP-200

SOPs for flow validation of iPRECIO® pumps

Standard Operating Procedure (SOP) for verifying flow infusion accuracy by residual/remaining solution in iPRECIO® pump reservoir. For first use (or first fill), the following procedure must be used to ensure that accurate volumes estimates are obtained.

We also recommend you refer to the following pages in the iPRECIO® Users Manual Ver. 5.0.8.e in before following this SOP.

Page 43 for detailed description of “Initial filling of the reservoir.”

Page 44 for detailed description of “Activating the pump.”

Page 65 for detailed description of “Refill.”

Page 67 for detailed description of “Replacing the reservoir solution in post recovery infusion mode.”

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

REQUIREMENTS

- iPRECIO® pumps
- 1ml (1000 μ l) syringe - smaller than 27G needle - or ideally use a PG25-500 Huber point needle (supplied by Access Technologies)
 - a. This syringe size is required to generate sufficient suction to remove solution from reservoir and to avoid putting undue negative pressure on pump reservoir.
- Sterile solutions to be infused (e.g. saline or medical solution, >1000 μ l)
- Analytical Balance of 0.01mg resolution. (e.g. A&D GH 202 Analytical Balance)

METHODS

For first use (or first fill), the following procedure must be followed to ensure maximum accuracy:-

1. After programming the pump, fill iPRECIO® pump with solution to be infused to the tip of the outlet tube or catheter (if attached)
2. Activate pump, so that the fingerpin mechanism blocks the tubing.
 - b. Remove solution with 1 ml syringe to remove/extract all.
3. Accurately fill syringe with 900 μ l of solution into syringe. By following **<Reservoir filling SOP>** on pg. 2.
4. The iPRECIO® pump had been accurately filled and is now ready for implantation.
 - a. The volume remaining in the iPRECIO® pump can now be used as an accurate measure of performance.
 - b. Each re-fill must also be filled accurately with the same protocol as in step 3 **<Reservoir filling SOP>** on pg. 2.
5. After a fixed duration of infusion, at refill schedules or when replacing the reservoir solution in post recovery infusion mode, follow the **<Reservoir Extracting SOP>**. Sequence of events should be:-
 - a. First, follow the **<Reservoir Extracting SOP>** to remove solution in iPRECIO® pump to obtain accurately and reproducibly the remaining amount of solution in iPRECIO®

- pump.
- b. Secondly, follow the **<Reservoir Filling SOP>** to accurately refill reservoir with a known amount of solution.

iPRECIO® management software would allow the user to calculate total programmed infusion volume. Actual total volume infused can be calculated from Initial volume and residual/remaining solution when verification is made.

- a. Total volume remaining = Total volume filled – Total volume infused based on programmed method and elapsed time (infusion flow (µl/hour) x duration (hours))
- b. Total volume infused = Total volume filled – Total volume remaining
- c. Actual infusion rate is then calculated by dividing the total volume infused (µl) by duration (hours)
- d. Flow infusion accuracy can then be compared between actual and programmed.

See figure 1 on pg. 3 for brief illustration of SOP.

Notes.

1. It is recommended to practice extraction of solution for point (3) to get good experience of the procedure before implantation. Extraction of 900µl (< ±5%) should be possible if the procedures were followed carefully. For extraction of lower volumes than 900µl, errors will be between ±5% to ±10%.
2. It is actually possible to fill/re-fill the reservoir (flexible material) to more than 900µl. Therefore the syringe must be used to measure the volume precisely and 900µl maximum volume must not be exceeded.
3. It is recommended that during the refilling and/or extracting solution procedure from the implanted pump, the animal is lightly anesthetized (for example with isoflurane or ether).
4. **It may be useful to confirm the expected remaining volume in the pump using iPRECIO® Management software prior to extracting. This value should be a guide on what to expect but <Extracting SOP> will allow maximum accuracy to be obtained.**

<Reservoir filling SOP>

1. Accurately weigh filled syringe on analytical balance.
 - a. Allow reading to stabilize and zero balance
2. Inject the 900µl (or amount needed for refill) into filling septum port to fill the reservoir.
3. Weigh empty syringe. The weight difference between filled syringe and empty syringe will give precise weight/volume of solution filled into reservoir of iPRECIO® pump.
4. Record this weight difference. This is the exact amount filled into reservoir

<Reservoir Extracting SOP>

1. Weigh empty syringe on Analytical Balance.
 - a. Allow to stabilize then zero balance.
2. Find septum on implanted iPRECIO® pump and insert needle through septum.
3. Gently pull plunger of syringe to withdraw solution with reservoir to limit + a little more. (You will be able to see air in the syringe as there is no more liquid to “extract”)
4. Re-inject some of liquid in syringe back into reservoir and perform (3) again.
5. Repeat (4) for another 1 to 2 times. (By repeating this procedure several times, you will have an indication/experience of pressure to pull the plunger and resistance of the pull will indicate if extra solution remains in the reservoir. This procedure ensures that solution in the reservoir can be extracted in a repeatable and reproducible manner)
- On the final time, pull the plunger until 0.5 cm air gap (vacuum) can be seen in the barrel of the syringe,
 - Block the plunger with your finger to maintain the slight vacuum and pull out the syringe quickly from the septum port.
 - Do not leave the reservoir compressed for more than 10 minutes or it may be permanently damaged.
- Weigh filled syringe on Analytical balance which was zero-ed (when syringe was empty).
 - Allow to stabilize and read weight of liquid in syringe.
 - Record weight. This is the exact amount remaining in reservoir.

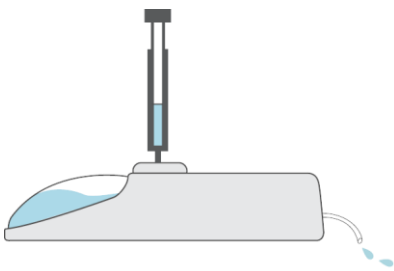
Caution:-

When filling and extracting viscous agents and vehicles, extra care must be taken. For example, it is necessary to hold the vacuum for up to several minutes to extract out the remaining volume accurately. It may also be necessary to create a stronger vacuum. It is strongly recommended to practice this procedure with a pump on the bench prior to in-vivo procedures.

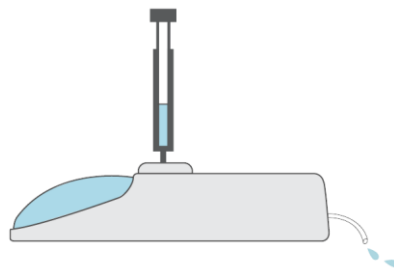
<Programmed Total Volume Infused>

From the printed “uploaded schedule list” or from the Offline Monitoring with Status Manager, all the programmed infusion protocol including Administration Information, Post Recovery Information and Refill information would be recorded. For refill information, accuracy calculated in the software would be dependent on the data entered by the user. With the following details (points 1 to 4 below) actual flow infusion accuracy can be calculated from fill, refilling volumes and remaining volume in reservoir at explantation or remaining volume extracted at exchange.:-

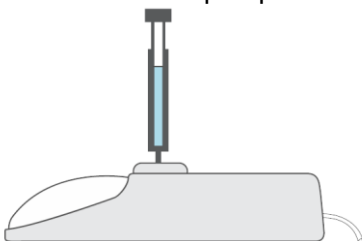
1. Programmed Total Volume Infused
2. Programmed Total Volume Post Recovery Infused
3. Actual Total Volume Infused
4. Actual Total Volume Post Recovery Infused



- Fill iPRECIO® pumps with solution.



- After filled, solution must reach the tip of the tube or catheter (if attached).
- Then activate pump.



- After activating pump, it takes about 120 seconds for the tube to be completely locked by the fingerpin mechanism. After this,
 - Extract solution with 1ml syringe until empty using **<Reservoir Extracting SOP>**. The reservoir in the diagram above is shown to be empty but not flat. In reality, the reservoir will become flat with the walls in contact with each other due to atmospheric pressure after removing solution.

- Measure accurately 900µl volume of solution and refill the empty reservoir using the **<Reservoir filling SOP>**
 - Ensure that there are no air bubbles when re-filling.
- Update information in iPRECIO® management software.
- After a fixed duration of infusion or during re-fill schedules, follow the **<Reservoir Extracting SOP>** and **<Reservoir Filling SOP>** to obtain further sampling times for total volume infused (time elapsed) for additional flow infusion validation points.

Figure 1: Brief description of SOP.

Minimum Operation for flow validation of iPRECIO® pumps.

Accurate initial weight, accurate remaining weight of solution at exchange, accurate re-fill weights (and therefore total volume infused) and accurate remaining volume in pump at explantation will be known. Minimum number of sampling points will be obtained.

1. At the beginning of the protocol, (fill to tip of catheter, activated and then withdraw solution)
2. Then refill precisely using syringe which has been weighed to have exact weight for empty syringe and filled syringe according to **<Reservoir filling SOP>**
3. Each time on re-fill (if extraction not required), weigh exactly empty syringe and filled syringe so that we have exact weight again according to **<Reservoir filling SOP>** .
 1. If exchange of solution is in recovery protocol, **<Reservoir Extracting SOP>** and **<Reservoir filling SOP>** should be used in sequence to obtained total volume infused (elapsed time) up to extraction and then iPRECIO® pumps filled accurately with drug solution.
4. Procedure 3 is repeated until explant where the remaining volume in pump is extracted according to **<Reservoir Extracting SOP>**. This procedure should be easier as the iPRECIO® pump would have been explanted.
 1. If not extracted immediately, then elapsed time should be recorded when extraction procedure actually occurs.
5. Therefore it is possible to calculate total volume infused as accurately as possible and calculate average flow infusion according to **<Total Volume Infused Calculations>**

Notes:-

1. With this method, only total volume infused flow accuracy is obtained and there is no intermediate information.
2. If **<Reservoir Extracting SOP>** and **<Reservoir filling SOP>** were carried out at exchange time, then another validation point would be available under this minimum operation for flow validation.

