

Contents of iPRECIO® Installation CD

All iPRECIO® support materials are provided in the installation CD. It includes an electronic version of the printed copy of the User's Manual and FAQ. Additional documents include Technical Notes and Surgical Video. It also includes documents for returns. **Refer to the User's Manual for Installation Procedure.**

Folders in the CD:

Name	Date modified	Type	Size
1 User Manual - FAQ - Workflow	5/31/2016 5:56 PM	File folder	
2 Programming Examples (step by step guide)	5/31/2016 5:23 PM	File folder	
3 Technical Notes (surgical)	5/31/2016 5:23 PM	File folder	
4 Surgery Videos	5/31/2016 5:37 PM	File folder	
5 Technical Notes	5/31/2016 5:23 PM	File folder	
6 Returns Documents	5/31/2016 5:23 PM	File folder	
7 Troubleshooting	5/31/2016 6:45 PM	File folder	
20160304 IMS-300 Application Software Release Notes (v3 3 7)	3/4/2016 2:10 PM	Adobe Acrobat D...	181 KB
iPrecioMouseSoftware	11/25/2015 6:31 PM	Windows Installer ...	1,185 KB
setup	11/25/2015 6:31 PM	Application	411 KB

1 User Manual – FAQ - Workflow

1. 20160802 iPRECIO SMP-300 User Manual v2.2.4.pdf
2. 20150710 SMP-300 Workflow for Programing_SMP-300.pdf
3. 20150804 Dual Antennae Assembly and recommended orientation of UCD-300 and Pumps.pdf
4. 20150806 SMP-300 Compatibility.pdf
5. 20150806 Refilling FAQ.pdf
6. 20160802 SMP-300 FAQ.pdf
7. Dead Volume Calculation.xls
8. Sample Log Data.xls

2 Programming Examples (step by step guide)

1. 20150806 Step by Step Programming Guides (6 examples).xls

Worksheet Examples in Excel File

1. One step protocol
2. Two step repeating protocol
3. KVO using excel sheet
4. KVO using application software
5. Circadian Profile
6. How to Re-Program

3 Technical Notes (surgical)

1. 20141112 SMP-300 Intravenous Administration.pdf
2. 20150625 SMP-300 Intracerebral Administration.pdf
3. 20150625 SMP-300 Subcutaneous Administration.pdf
4. 20150728 SMP-300 Intraperitoneal Administration.pdf



4 Surgery Videos

1. 20160531 Rat and Mouse surgery Links.pdf
2. SMP300_IP_v1.0en
3. SMP300_IV_v1.0en_iphone
4. SMP300_SC_v1.0en

5 Technical Notes

1. 20141110 SMP-300 Accuracy Evaluation.pdf
2. 20150625 SMP-300 Angiotensin II Infusion with Blood Pressure.pdf
3. 20150728 SMP-300 Body Weight and Strain Information.pdf
4. 20150730 SMP-300 SOP Flow Validation Summary.pdf

6 Returns Documents

1. IPRED070101-iPRECIO-ReturnEquipmentDeclaration.pdf
2. IPRSI070101-iPRECIO-Return_Shipping_Instructions.pdf

7 Troubleshooting

1. 20160801 SMP-300 Trouble Shooting - Cannot Detect An Activated Pump.pdf
2. 20160531 Faraday Cage to try to see if interference is the issue to date.pdf

Note:

One (1) SMP-300 Pump Sample included with IMS-300 system

- For IMS-300 system set-up and verification
- For set-up and training purposes only. Not for in-vivo use!!
- After set-up and training purposes with pump, it is recommended to <Delete> this pump from UCD-300 memory. See pages 47 to 48 of User Manual <How to Re-Program a Pump>. It explains how to use Utility Pump Database Manager and also Utility Pump BaseStation Manager for re-programming and also for excluding pumps.
- If the old pumps' IDs are left in UCD-300, communication time will be assigned for all the pumps in memory. Therefore more time will be required for programing, log collection etc. Remove pumps by deleting as required.



Frequently Asked Questions

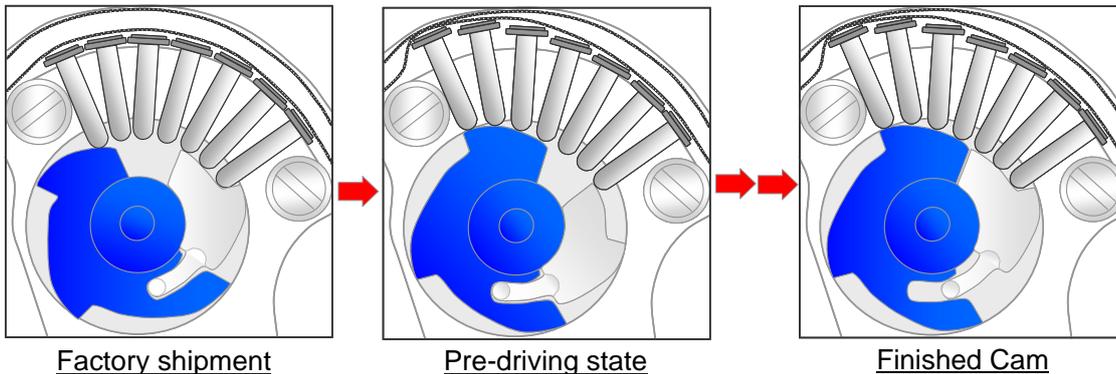
Q1) I am not sure I have switched on and activated the pump. How can I check?

There are 4 options.

1. If you have correctly switched on and activated the pump, you should be able to confirm that the pump's CAM and pin are either in the pre-driving state or the infusing state. Refer to page 25, process of activation figures. Figures and details are reproduced below.
2. You can also press on the reservoir to see if the solution in the reservoir is pushed out of the catheter. If this happens, it means that the pump did not activate correctly. You need to do so gently or you will lose a lot of drug solution. Also make sure that the solution does not spray out and injure your colleagues or yourself.
3. If you can <Detect> the pump (see page 26 of user manual), means the pump has been switched on and activated.
4. As a final option, you may also try to switch on the pump again. Take care not to damage silicon coating on pump. Use forceps to press firmly down the black power button switch. Down movement of switch can be felt/heard. After 1 minute 30s, try points 1 or 2 or 3 above again. See also page 25 of User Manual.

The Process of Activation

The cam of the pump driver consists of two parts, shown in blue and white in the diagram on the right. The white part is in a fixed position prior to use. This prevents the finger pins from compressing the tube, leaving it in an "open-tube state". Upon activation, the blue part begins to turn clockwise, pushing a single finger pin against the tube, creating a "closed-tube state". This cycle takes about 120sec. This process is called the pre-driving state. The pump remains in this state until the pre-set dosage start time, at which point, clockwise rotation of the blue part resumes until the white and blue parts connect, creating a cam with four equal centurms, which move the seven finger pins in the driving state.



During the activation procedure, a small volume of liquid may be pushed out of the catheter (infused out). If necessary, remove or wipe away the solution before implanting.

Q2) I am sure that I have switched on and activated the pump(s) and I have checked (see Q1) but I still cannot detect all of the pumps.

You need to check various points.

1. Has the pump antenna been damaged or cut?
2. Is the pump antenna as straight as possible? If not straighten slowly and carefully. Do not pull and handle with care.
3. Move the pump(s) closer to the UCD-300. As close as 20-30 cm from the UCD-300. They should be within 1-3 meters of the UCD-300. The closer the better.
4. Allow sufficient time for all pumps to be detected.

Q3) I accidentally introduced bubbles into the reservoir and catheter. How do I remove the bubbles and what precautions should I take next time?

If you have not activated the pump, you will have the option of trying to extract the bubble out again via the septum port or trying to flush out the bubble by filling with more solution.

- If the bubble is close to the septum port, you can try to extract out the bubble by withdrawing solution and bubble too.
 - It is also possible to orientate the bubble towards the septum port by orientating the pump and tapping it gently.
- Alternatively, try to orientate the bubble towards the catheter exit point from the reservoir and continue to fill the reservoir. Remember to collect solution which will be pushed out the end of the catheter when you do this.
- If the air gap or bubble is in the catheter you will be able to push out the bubble by filling until the bubble is washed out.

If the pump has been activated, you can extract out all of the solution from the reservoir and refill.

- Extract the solution out slowly and when empty, you should pull a slight vacuum. (air gap created in syringe barrel of not more than 0.5cm).
- Block the plunger with your finger to maintain slight vacuum and pull out syringe from septum port. The bubble should be pulled out too.
- The reservoir will be completely empty and compressed.
- Refill the reservoir without too much delay (not more than 10 minutes) slowly with new solution.
- Alternatively, it is also possible to orientate the pump in such to move the bubble towards the septum port. It is then possible to extract out the bubble without extracting all of the solution in the reservoir.

If the air gap or bubble is in the catheter (after activation), you can only flush it out once the pump is operating. It will depend on flow-rate pump and location of bubble in the catheter.

Precautions to prevent air bubbles in catheter and reservoir.

1. Use pre-warmed solution (38°C) and take care not create bubbles by moving the solution too much.
2. Ensure that the outlet tube is cut to allow air to escape when filling. Catheter is sealed at factory to prevent contamination.
3. Fill syringe slowly. (filling too fast will create micro bubbles and this will become a bubble in the pump.)
4. After filling syringe, ensure that there are no bubbles in syringe barrel or near the needle entry and plunger end.
5. Injecting /filling the pump reservoir too fast will also create bubbles. Fill slowly.
6. Ensure that you fill the pump slowly and oriented the pump to allow any bubbles/air to escape via the reservoir catheter exit point and fill until it all the bubbles are washed out of the end of the catheter.

Q4) What is the length, ID and OD of the SEBS catheter of the iPRECIO pump?

Length of catheter of iPRECIO pump is approximately 135mm, ID is 0.55mm and OD 1.20mm. It is between 3.5Fr and 4Fr.

A 3Fr and 3.5Fr catheter maybe added easily with the use of a coupler.

Q5) Why do I need to fill the estimated maximum weight and minimum weight in the Group Profile (Group ID) Window? (Page 31 in manual)

Estimated Max/Min Animal weight is especially important when using dose infusion programming. By filling the correct values for Max/Min Animal weight, you can be sure that if you work within the limits as indicated by the iPRECIO® Management software, it will be possible to have exactly the same infusion protocol for all the individual animals even though there is a weight difference between them. The software dose limits take into account the min/max infusion pump infusion flow-rate. See also Q6.



Q6) I would like to program in dose and maximize infusion duration for the group. What is best practice?

If you wish to have only constant dose for all animals at the start of drug administration, you should start programming your infusion protocol with the highest initial weight animal. The iPRECIO Management software would allow you know the maximum duration for that particular protocol based on the largest animal. This is especially important if you wish to get maximum battery life out of your iPRECIO pumps. See Pg. 31 of Users Manual.

Q7) Why is iPRECIO® pumps only for one time use?

There are two main reasons:-

- 1) It is not possible to re-sterilize the reservoir and attached pump catheter.
- 2) Once the pump has been activated, the finger pin mechanism would always be compressing the soft catheter tubing as the CAM rotates to create the peristalsis action. If the pump stops infusing, these pins would stop and continue to exert pressure on exactly the same location on the tubing for the duration the pump is off or stopped. See figure in Question 1. (Factory shipment and finished CAM)

Primetech has not characterized the effect of compression of tubing for long periods of time on accuracy and reliability. The pumps are delivered with all the fingerpins down or open. (No compression of tubing and easy to fill pump)

Lastly, the battery cannot be replaced in the sealed iPRECIO® pump enclosure.

Q8) How can I ensure long term reliable implantation of iPRECIO® Pumps?

Good fixation of iPRECIO® pump and catheter at the infusion site, inclusion of stress loop and considerations to prevent kinking will ensure that reliable infusion is achieved.

Migration of the iPRECIO® pump from the ideal fixed position will significantly increase the risk of kinking. The use of sutures and Vetbond™ will provide additional support, natural healing and tissue growth to ensure a reliable fixing of the infusion tube position and iPRECIO® pump.

Q9) Can I log an extraction from the reservoir?

Yes, iPRECIO® Management Software Ver 3.3.5 allows you to log an extraction by using the minus sign. Only whole numbers may be used and you may not extract remaining volume below 0µl in the software.

If the reservoir is emptied by extraction, it is recommended to log the estimated remaining volume and note the difference. Differences are usually due to ±5% pump accuracy plus experimental errors related to filling/extracting.

Q10) Are there any workflow examples for iPRECIO® Management System and pumps?

Yes, workflow examples are provided separately. A printed version is included with the Management system and an electronic version of the printed one is also included in the install CD. Note that the workflow guide does not replace the User Manual. Primetech strongly recommends to use the User Manual.

Q11) Would iPRECIO® be affected by the use of an MRI Scan?

iPRECIO® cannot be used with a MRI due to strong magnetic fields that will likely damage the pump or the electronic components of the device. Weak magnetic fields like the magnet used to turn on and off the DSI telemetry transmitters will not affect the iPRECIO® pump.

Q12) I am using a high viscosity vehicle/solvent. Is this a problem for iPRECIO® pumps?

iPRECIO® fingerpin technology is not influenced by viscosity of vehicle/solvent. $\pm 5\%$ accuracy of infusion flow-rate will be obtained. Primetech has evaluated vehicles up to 20 cp. Higher viscosity solvents were not tested due to the use of 27G needles. It is very difficult to aspirate higher viscosity vehicle/solvents with a 27G needle.

Q13) I have to use a quite a high concentration of agent/drug with iPRECIO®. What would be the recommended way to test for precipitation potential?

It is very important that agent/drug does not precipitate out of solution at the administration site as the formulation infuses into the body for both welfare and reliability/reproducibility reasons. If the precipitation occludes/blocks the iPRECIO® pump catheter, infusion will fail and eventually the pump will also fail.

One easy way to test this is by filling an iPRECIO® pump with the formulation and infusing it into an appropriate media which is representative at the administration site. For example, infusing the drug formulation into Sorenson buffer (for blood) for IV administrations.

2 different techniques have also been described by Li et al. in "Developing early formulations: Practice and perspective" Li P., and Zhao L. (2007). Intl. Journal of Pharmaceutics 341, 1 – 19.

<http://www.sciencedirect.com/science/article/pii/S0378517307004553>

Q14) I have difficulties to locate the refilling port and inserting the syringe into the port.

See details here after. See also refilling FAQ <20150806 Refilling FAQ> which includes video link.

Finding the septum

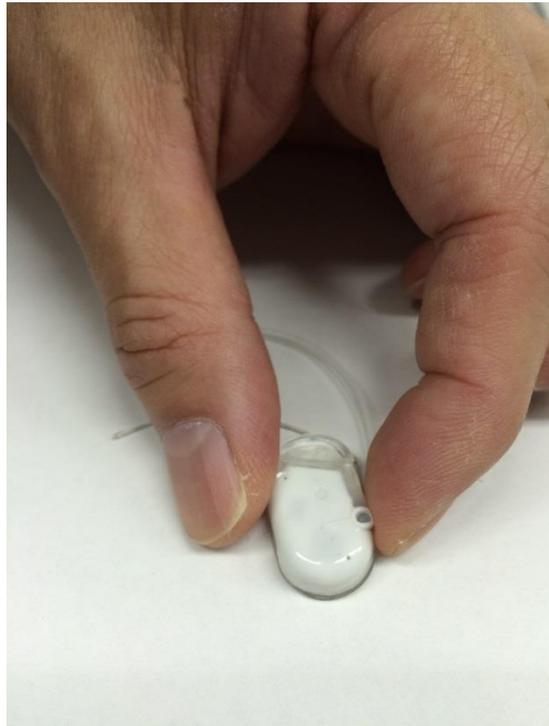
- Locate the pump and the palpable reservoir in the animal percutaneously. The palpable reservoir will be considered the front of the pump.
- The septum can be located more easily as you will be able to feel it to the left and slightly further back towards the rear of the pump from the palpable reservoir. It's exact position is more easily located from the side of the pump rather than the top. See pictures on next page.
- Once the exact location and size of refill port (septum) is located, center the needle to the middle of the septum port by aligning with the maximum point of the port (from the side) and aim 1 mm in from the maximum point. Take care not to injure yourself with the needle.
- Pierce the septum until the bottom of the port is reached.
- Once you have inserted the needle in through the septum, you may want to withdraw initially to ensure that you are in the refilling port. You will be able to withdraw and feel the reservoir reduce in size. For this to work, sufficient remaining volume in the reservoir is required. When you fill, the reservoir will increase in size.

We recommend you practice filling the pumps before implantation so that you will get good experience of the protocol. You will be able to feel the needle penetrating the septum and also when the needle comes to a rest at the bottom of the port. You will also be able to see the reservoir expanding and contracting with filling and extracting.

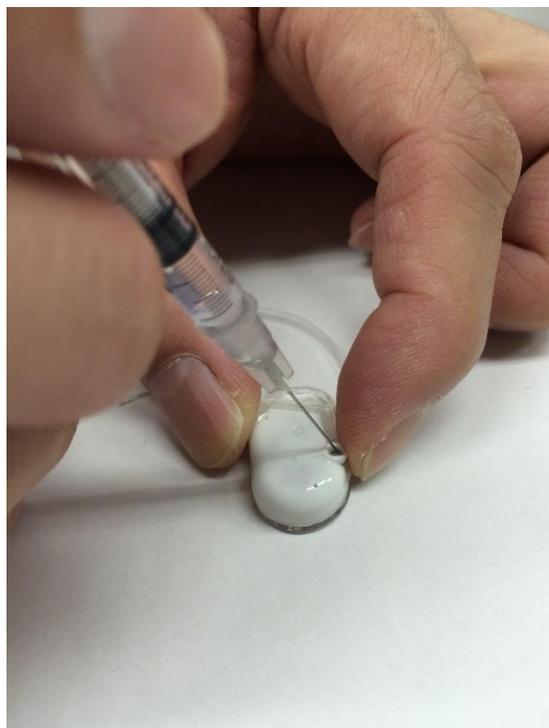


You may also want to cover the pump with several layers of tissue to simulate more closely the pump being

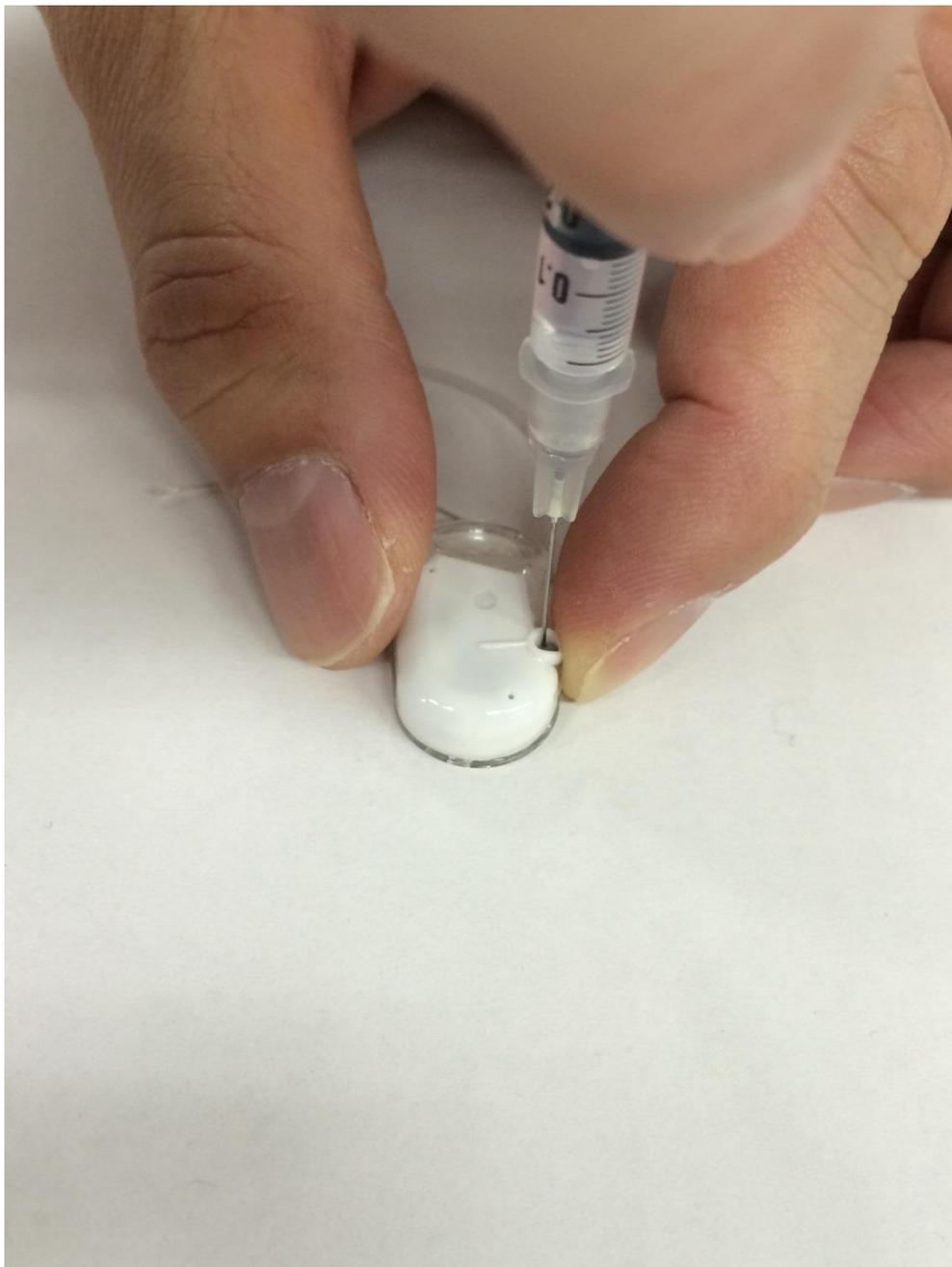
located percutaneously. With this in-vitro practice technique, you will have more confidence for the locating of septum port and refilling/extraction procedure.



Locating Septum Port: Find front of pump where reservoir is located then find septum port. Alignment with the septum port location with reference to it's design; port extending out beyond the pump body makes this easy.



Once the exact location and size of refill port (septum) is located, center the needle to the middle of the septum port by aligning with the maximum point of the port (from the side) and aim 1 mm in from the maximum point. Take care not to injure yourself with the needle. Try to **make the needle insertion perpendicular to the septum plane**. See picture on next page.



The 27 gauge needle is perpendicular to septum plane. Position of the fingers on syringe changed only to display clearly that the needle is straight and in the septum port. Hold the syringe comfortably so that it is possible to locate the middle of the septum as much as possible.

August 1, 2016



PRIMETECH CORP. Tokyo, Japan

▶ www.iprecio.com ▶ iprecio@primetech.co.jp