

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:

-  1 User Manual - FAQ
-  2 Programming Examples (step by step guide)
-  3 Technical Notes (surgical)
-  4 Surgery Videos
-  5 Videos and Photos - ON - OFF SMP-310R
-  6 Returns Documents
-  7 Troubleshooting
-  20200130 IMS-310R Application Software Release Notes (v1.0.4.0) 0-10
-  iPRECIO_IMS-310R
-  setup

User Manual - FAQ

1. iPRECIO SMP-310R User Manual ver1.0.3.e
2. Recommended orientation of UCD-X10R and SMP-310R pumps
3. Refilling FAQ.pdf
4. Sample Log Data.xls
5. 310R FAQ v1.0.3.e
6. SMP-310R and SMP-300 Compatibility
7. **SMP-310R handling precautions (Magnetic Fields)**

2 Programming Examples (step by step guide)

Step by Step Programming Guides (4 examples) IMS-310R v1.0.0.e

Worksheet Examples in Excel File (4 examples)

1. 1 Group ID (One(1) Group ID)
2. 3 Group ID with ADD PUMPS (Three(3) Group ID with ADD PUMPS)
3. Abort and Reprogram
4. Scheduled Activation

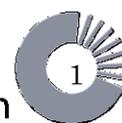
3 Technical Notes (surgical)

1. SMP-310R Intravenous Administration.pdf
2. SMP-310R Intracerebral Administration.pdf
3. SMP-310R Subcutaneous Administration.pdf
4. SMP-310R Intraperitoneal Administration.pdf

4 Surgery Videos for 300

(310R surgeries will be exactly the same as the 300 but without external antenna)

1. Rat and Mouse surgery Links.pdf (for 310R too)
2. SMP300_IP_v1.0en (for 310R too)
3. SMP300_IV_v1.0en_iphone (for 310R too)
4. SMP300_SC_v1.0en (for 310R too)



5 iPRECIO Magnet Switch ON/OFF videos and photos

1. Switching OFF 310R - 5s on magnetic switch - remove vertically
2. Switching ON 310R - 5s on magnetic switch - remove vertically
3. Switching ON 310R - 5s on magnetic switch - remove vertically 2
4. SMP-310R Blister Pack - ON-OFF location with iPRECIO Magnet 1
5. SMP-310R Blister Pack - ON-OFF location with iPRECIO Magnet 2
6. More photos
7. iPRECIO 310R switch ON device with LED Monitor

6 Returns Documents

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

7 Troubleshooting

1. Cannot Detect a SMP-310R pump which has been switched ON with an iPRECIO ON-OFF Magnet v1.0.1.e
2. Cage to try to see if interference is the issue to date

Testing may be done after installation IMS-310R Application software which is outlined in User Manual

Note: See FAQ Q1.

Review User Manual and install IMS-310R system with UCD-X10R to make sure working correctly prior to switching ON any pump.

If any purchased pumps are used for testing and training, remember to switch OFF. After using for test, remember to switch OFF Pump or all battery will be depleted. Switch Procedure of pump MUST be followed exactly. For easy reference, relevant procedures from User Manual.

- For IMS-310R system set-up and verification
- After set-up and training purposes with pump, it is recommended to <Delete> this pump from UCD-X10R memory. See pages 52-54 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-X10R, 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.

iPRECIO® SMP/IMS-310R User's Manual ver 1.0.1.e

Switching ON pump with magnet –outside blister pack

It is important to make sure that IMS-310R and UCD-X10R connected and working together prior to switching ON the SMP-310R pumps. IMS-310R Application should already be in <Detecting> mode.

Power On Pump is switched ON magnetically. (S Pole -ON & N Pole - OFF) magnetic strength > 100mT. **5 seconds directly** above the Magnetic Switch location as shown below to switch ON or OFF. **Remove the magnet perpendicularly away from the top of the pump.** After switching ON, wait at least 10 seconds before switching OFF. If there is any doubt, repeat procedure to switch ON or switch OFF with the exact procedure.

Switching ON pumps which are outside the blister pack are shown below.



Magnet should be sterilized prior to use. Alternatively, use a sterile surgical drape or sterile plastic wrap around magnet to keep the pump sterile. Switch ON pumps sequentially, 5s per pump directly above magnetic switch. **Remove the magnet perpendicularly away from the top of the pump.** Keep the pumps in switching ON order by the UCD-X10R. As the pumps are switched ON, they will

start to communicate with UCD-X10R.

Important Notes.

Switching ON pump with magnet –inside blister pack Scheduled Programmed Activation Time. (not default setting)

When activation time of pump is programmed, switch ON, detecting and programming may be completed with the pump in the blister pack. Important to make sure to <Add Catheter Connection and Pump filling> before programmed scheduled activation time.

In their blister packs, pumps are switched ON by aligning the ON side of the magnet towards blister pack as shown. The magnet should be left in place for 5s to be sure to switch ON the pumps. Ideally only switch ON when everything is ready. **To switch OFF, this is also very important to follow the procedure to be sure that they are OFF.** 5s OFF side of the magnet facing the blister pack/pump. **Remove the magnet perpendicularly away from the top of the pump/Blister Pack.**



Frequently Asked Questions

Q1) I am not sure I have switched ON the pump(s) correctly with the iPRECIO SMP-310R magnet as I cannot detect the pump(s). What should I do?

Best to start just with one pump to make sure everything is working correctly before switching ON multiple pumps.

The best option is to switch OFF all pump(s) until after installation and checking that IMS-310R Application software working correctly. See User Manual pg. 35 and switching OFF video on iPRECIO installation CD. It is important to follow exact procedure to make sure pumps have been switched OFF.

Then review and follow the "Trouble Shooting for SMP-310R – Cannot Detect a SMP-310R pump has been switched ON with an iPRECIO Magnet".

Always follow switch ON and switch OFF procedure exactly to be sure pump(s) are OFF.

When not using a pump, always remember to switch OFF the pump. If not, the battery will be depleted and pump lost.

Q2) After checking that everything was working with one pump, I am sure that I have switched ON all the new pumps but I still cannot detect all of the pumps.

You need to check various points. Make sure IMS-310R Application Software is still in detect mode.

1. Move the pump(s) closer to the UCD-X10R and are placed according to recommended orientation. Move pumps as close as 10-50 cm from the UCD-X10R.
2. Allow sufficient time for all pumps to be detected.
3. Open Utility Pump Database Manager2 and make sure that the pump (SN) condition is set to STATE_NEW and Showing Status as STATE_IDLE. See page 52 of User Manual. **If pump (SN) is not shown, nothing needs to be changed.**
4. Find the pump (SN) which has not been detected yet and switch ON using iPRECIO Magnet according to procedure in User Manual page 35 and wait 3 minutes to see if pump(s) are detected. If not, switch OFF magnetically, wait 10-15s and then switch ON again. Pump should be detected within 1-3 minutes.

Q3) I am sure that I have switched on and detected a new pump with SN and Cal Factor but after a very long time, the pump has not been programmed. What should I do?

You need to check various points.

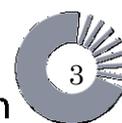
1. Move the pump(s) closer to the UCD-X10R and are placed according to recommended orientation. Move pumps as close as 10-50 cm from the UCD-X10R. Alternatively, if already as per recommended orientation, then change position with a pump which has been programmed.
2. Double check that sufficient time for all pumps to be programmed. Sometimes a pump may take a little longer.
3. Find the pump (SN) which has not been detected yet and switch ON using iPRECIO Magnet according to procedure in User Manual page 35. IMS-310R Application software must be in programming mode and usually, the algorithm prioritizes pumps which have not been programmed.
 - If not, switch OFF magnetically, wait 10-15s and then switch ON again. Pump should be already in UCD-X10R memory and programming will continue.

Always follow switch ON and switch OFF procedure exactly to be sure pump(s) are off when not in use.

Q4) How can I check that the pumps have been correctly activated?

There are 2 options.

1. If you have correctly switched on and activated the pump by <default activation> or <scheduled activation> (pg. 26, 34 & 35 of user manual), 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 41, process of activation figures. Figures and details are reproduced hereafter.

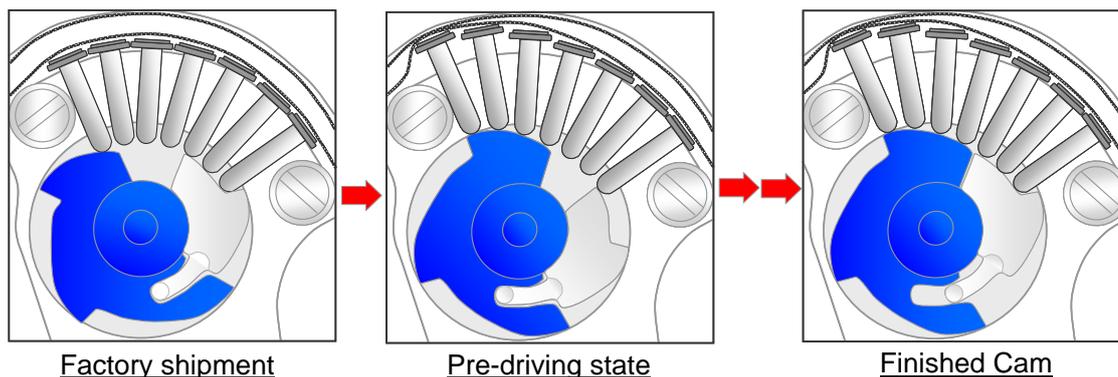


Frequently Asked Questions

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.

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.

Note that the activation process is non-reversible. Once pins have locked the tubing, this cannot be reversed. Additional activation basically rotates the CAM which infuses out formulation from the reservoir.

Q5) 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.

Q6) 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.

Q7) Why do I need to fill the estimated maximum weight and minimum weight in the Group Profile (Group ID) Window? (Page 27 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 Q8.

Q8) 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. 27 of Users Manual.

Q9) 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 4. (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.

Q10) 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.

Frequently Asked Questions

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.

Q11) Can I log an extraction from the reservoir?

Yes, the iPRECIO® IMS-310R Management Software 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 $\pm 5\%$ pump accuracy plus experimental errors related to filling/extracting.

Q12) Are there any workflow examples for iPRECIO® Management System and pumps?

Yes, see step by step guide in install CD and in User Manual.

Q13) 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.

Q14) 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.

Q15) 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>



Q16) I have difficulties to locate the refilling port and inserting the syringe into the port.

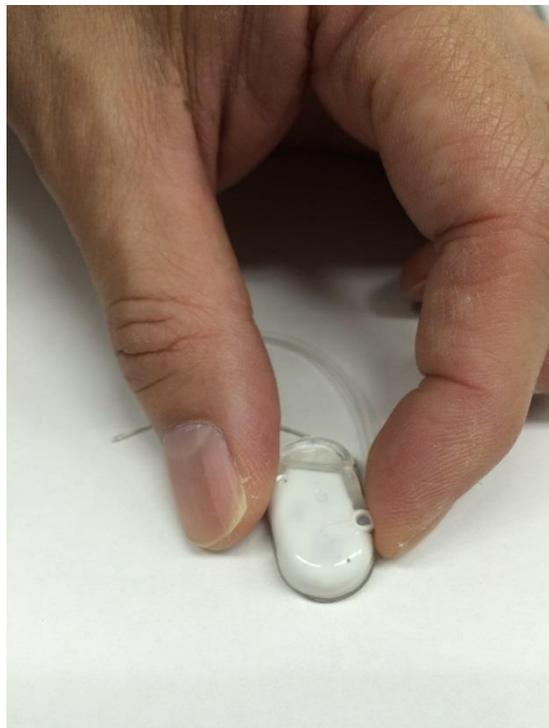
See details here after. See also refilling FAQ <Refilling FAQ> which includes video link.

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.

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