

Contents of iPRECIO® Installation CD

All iPRECIO® support material are provided in the installation CD. It includes an electronic version of the printed copy of the User Manual and FAQ. Additional documents include Technical Notes, Workflow and example ipf files. It also includes documents for returns.

Refer to the User's Manual for Installation Procedure.

Folders in the CD:

Name	Date modified	Type	Size
 Readme (for Serial Number information)	10/10/2012 10:35 ...	Text Document	1 KB
 FirstStep	9/25/2012 8:48 AM	Application	788 KB
 AUTORUN	6/16/2007 2:24 PM	Setup Information	1 KB
 User Manual - FAQ	10/26/2012 4:28 PM	File folder	
 Technical Notes	10/26/2012 4:28 PM	File folder	
 iPRECIO Workflow Examples	10/26/2012 4:28 PM	File folder	
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 DISK2	10/26/2012 4:28 PM	File folder	
 DISK1	10/26/2012 4:28 PM	File folder	

Technical Notes

1. iPRECIO_Performance_rev100e
2. SOPflowValidation_summary_rev400e
3. MaterialsCompatibilityKit_rev300e
4. SCrecomendation_rev300e
5. IPrecomendation_rev300e
6. IVrecomendation_rev300e
7. ICVrecomendation_rev300e
8. Intrathecal_rev300e

iPRECIO® Workflow Examples

These workflows and examples should only be with the User's Manual.

1. iPRECIO_WorkFlow_Instant-Constant_rev07
2. iPRECIO_WorkFlow_RCV-Variable _rev07
3. Instant Constant Workflow.ipf
4. RCV Variable Workflow.ipf



Frequently Asked Questions

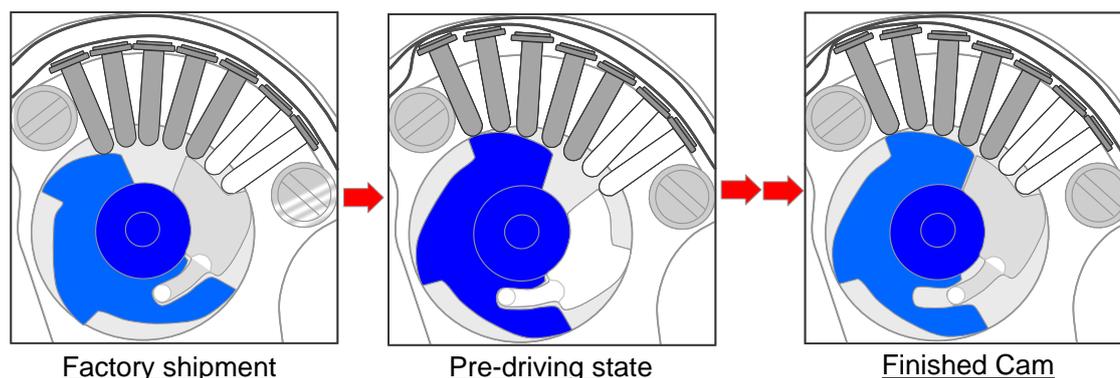
Q1) I am not sure I have activated the pump. How can I check?

There are 3 options.

1. If you have correctly activated the pump, you should be able to confirm that the pump's CAM and pin are either in the pre-drive state or the infusing state. Refer to page 46, 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. You may also try to re-activate the pump using software activation. The software is able to give more details on the status of the pump.

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 have downloaded to the pump but I cannot activate my pump. What should I do?

You need to check various points.

1. Did I activate the pump in the correct time window? You need to activate between 3 minutes and 3 hours before start of administration for instant mode or start of RCV period for RCV mode. If you have missed the activation time window, you will need to re-program your pump.
2. Check that you are trying to activate a pump which has been programmed. Infusion program downloaded. You may have mixed up pumps from other group which has not been downloaded.
3. Check your infusion protocol and make sure there is no mistake for the start administration or RCV mode.
4. If (1), (2) and (3) was not the issue, try to Detect the pump again, download with protocol (if still valid) and try to activate.



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.

Related topic: Low Flow Infusion SOP, manual page 41.

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 Animal Group Settings 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.

If using variable mode with Dose Programming, the same recommendations apply.

Q7(a) I would like to program an infusion protocol with stop flow. Is this possible as it was not indicated in the manual?

It is possible to program 0µl/hour. It is however recommended that the stop time is minimized as stopping means that the fingerpin mechanism stops and continues to exert pressure on exactly the same location on the tubing. See Question 1, finished CAM figure where fingerpins are shown to push against tubing. If flow is stopped, fingerpins would remain in this condition until flow is started again.

3 hour stopping cycles have been tested. Accuracy and lifetime of pump was not reduced.

Longer stopping cycles of up 72 hours have also been tested by various users without any known issues. Primetech will continue evaluate stopping cycles to quantify effect on accuracy and lifetime.

Primetech also recommends that users consider using 0.2µl/hour and 0.5µl/hour instead of 0µl/hour to “simulate stopping the pump.” Flow infusion accuracies of ± 5% for these 2 flow-rates have not been fully validated but the fingerpin mechanism will continue to operate and therefore exert less stress on the tubing.

When using 0µl/hour, 0.2µl/hour and 0.5µl/hour, it is recommended that risk for thrombosis is minimized as stop flow and very low flow infusion rates are prone to blockage/thrombosis issues.

More recently, Primetech evaluated repeated stopping cycles to inject/infuse 15µl of water once a day using 4 different injection/infusion rates; 5µl/hr for 3 hours, 10µl/hr for 1.5 hours, 20µl/hr for 0.75 hours and 30µl/hr for 0.5 hours for 60 days. When pumps were not injecting/infusing, they were programmed to stop (0µl/hour). Total volume infused for the pumps over the 60 days (60 injecting/infusing cycles) were within ±5%. Three iPRECIO® pumps per injection/infusion rate were used. For more detailed information, contact Primetech or your authorized distributor.

Q7(b) Is it possible to use 0.2µl/hour and/or 0.5µl/hour infusion rates for ICV infusions where lower infusion rates are usually required?

Yes, you may program these flow-rates normally when using variable flow rate mode within any of one of the 10 steps but Primetech has not fully validated the accuracy in the same way as for flows between 1µl/hour and 30µl/hour.

Theoretically, ±5% accuracy should be possible. Semi-quantitative studies using real-time weight loss measurements using an analytical balance gave good results for 0µl/hour, 0.2µl/hour, 0.5µl/hour and 1µl/hour flow rates.

These flow rates cannot be programmed in RCV Flow-rate where only flows of 1µl/hour to 30µl/hour are possible. Also, they may not be programmed in constant flow rate mode where only flows of 1µl/hour to 30µl/hour are possible.

1. If you wish to have a recovery period using 0.2µl/hour or 0.5µl/hour, these should be programmed within instant/variable flow rate mode with saline filled in the reservoir initially. Exchange time will need to be calculated manually based on dead volumes and start administration time.
2. If only an instant/constant flow rate is required, you may program only 1 flow step in instant/variable flow mode using either of these flow rates.



Q8) 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.

See also Q7(a) of FAQ.

Q9) 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.

Q10) Can I log an extraction from the reservoir?

Yes, iPRECIO® Management Software Ver. 1.2 rev.528 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.

If you do not have iPRECIO Ver. 1.2 rev.528, please contact your local authorized distributor for update/upgrade details.

Q11) During RCV infusion duration in RCV mode, can I view remaining volume and next refill date?

In RCV infusion mode (prior to drug administration), remaining volume information is not available for viewing. The software automatically calculates refill date (if it is necessary) based on a remaining volume of 0 µl after an initial fill of 900µl volume and total volume infused. (RCV elapsed time multiplied programmed RCV infusion flow-rate). It is recommended to refill the pump 24 hours earlier taking into account ±5% infusion flow-rate accuracy and calculated remaining volume.

Software calculates automatically only one refill date for RCV mode.

Q12) I would like to save test agent and fill the minimum amount into the pump. What is the minimum fill/refill requirement for maximum accuracy/specifications?

The minimum amount to fill the pump is **<the amount to infuse + 100ul>**.
<The amount to infuse + 100ul> is the simplest rule to follow. Further refinement is possible. The iPRECIO® Management Software has a default alarm setting for refill of 100µl.

This requirement is because when the remaining volume in the reservoir is around 50ul, accuracy is reduced and the pump tends to infuse less than programmed as the remaining volume gets towards 50µl and lower. The other important characteristic is the pump's accuracy; ±5%. Therefore, if the pump is "fast", then the remaining volume will reach 50µl faster than anticipated.

The final point to consider is the total dead volume. This is the fundamental dead volume of the pump plus the dead volume of the catheter. It is recommended to fill to the distal end of the catheter with test agent for instant infusion. For example for SC administration, expected dead volume is 20.3µl (fundamental dead volume + 40mm of remaining catheter). This additional volume must be considered when filling. For RCV infusion, the same dead volume must be considered as the pump will flush the vehicle and prime the catheter with test agent. Remaining volume will decrease by the dead volume.

Notes

1. When filling test agent for instant infusion, it may be easier to fill the pump to 900µl + total dead volume to ensure that there are no bubbles in the reservoir. Then activate pump. Once pump is activated, withdraw excess test agent to reduce volume in reservoir.
2. When refilling with test agent in RCV infusion after saline/vehicle infusion, **<the amount to infuse + 100ul>** or <the amount to infuse + total dead volume> may be filled directly.

Q13) 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. ±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.

Q14) 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>



Q15) Are there any workflow examples for iPRECIO® Management System and pumps?

2 workflow examples and their Infusion Protocol Files (ipf) are included in the iPRECIO® Management Software Installation CD. The examples assume prior knowledge of iPRECIO® use and references the user manual.

1. Instant Constant Workflow
2. Recovery Variable Workflow

Q16) 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.



Q17) When I program in dose, why sometimes the programmed value does not correspond exactly with actual dose infused?

When programming in dose, iPRECIO® Management Software will need to convert/calculate it to a flow-rate. If the flow-rate cannot be programmed, it will be rounded up or down accordingly to fit the specifications of the iPRECIO® Pump. If the flow-rate can be programmed without rounding, then dose must be the same.

When programmed in Dose

Status Manager of Pump keeps the record in dose programmed (ug/kg/hr) and this may be printed out by using the print option in <File> Menu. **To have the actual dose (with valid flow-rate), use the export function in <File> Menu.** The file format is csv format file for Microsoft Excel®. File data not shown.

Record of programmed dose (µg/kg/hr)

Use <Print Function> Programmed dose **Calculated flow-rate (rounded up/down to fit pump specifications)**

Use <Export> in <File Menu> to have calculated dose based on exact flow-rate of iPRECIO® Pump. The file format is csv for Microsoft Excel®. File data not shown. Dose is re-calculated from actual flow-rate used.



Q18) I have difficulties to locate the refilling port and inserting the syringe into the port.

See details here after.

The 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 left and slightly further back towards the rear of the pump from the palpable reservoir.
- Once the exact location and size of refill port (septum) is located, center the needle to the middle of the septum port.
- 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.

Figure 1(a)-(c) and Figure 2(a)-(c) shows two different ways to triangulate over septum refilling port. Choose the most comfortable method for you to triangulate and “visualize” septum port.



iPRECIO SMP200 pump.

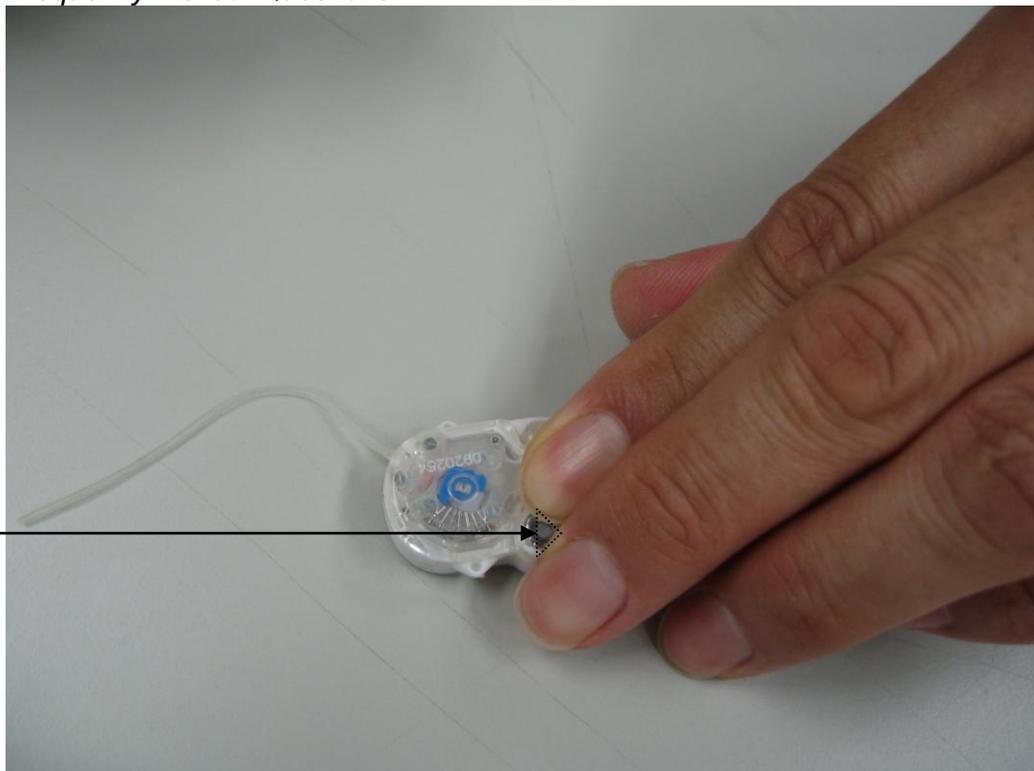


Figure 1(a): Locate refilling port: Locate the pump and the palpable reservoir in the animal percutaneously. The palpable reservoir will be considered the front of the pump. Triangulate over refilling port as shown in the photo above. Fingers will “protect” reservoir from damage.



Figure 1(b): After triangulation of refilling port, center syringe needle to center of triangle which should be the center of the septum.



Figure 1(c): Insert needle through septum and get a feeling of the needle piercing the septum and reaching the bottom of the septum port.

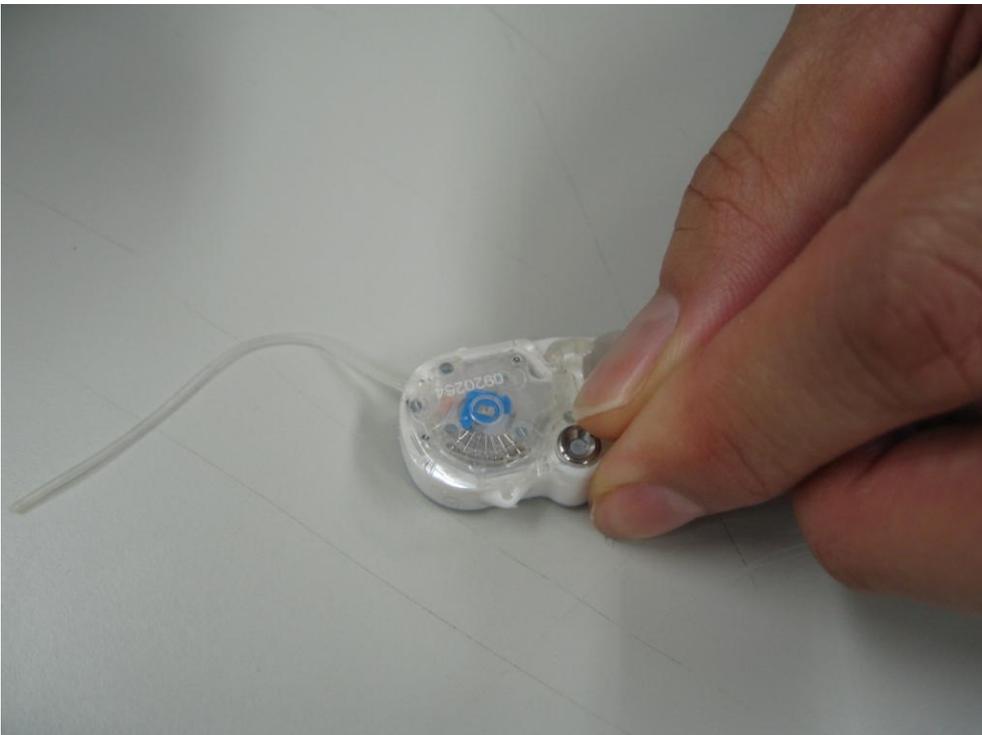


Figure 2(a): Locate refilling port : Locate the pump and the palpable reservoir in the animal percutaneously. The palpable reservoir will be considered the front of the pump. Triangulate over refilling port as shown in the photo above. Fingers will “protect” reservoir from damage.



Figure 2(b): After triangulation of refilling port, center syringe needle to center of triangle which should be the center of the septum.

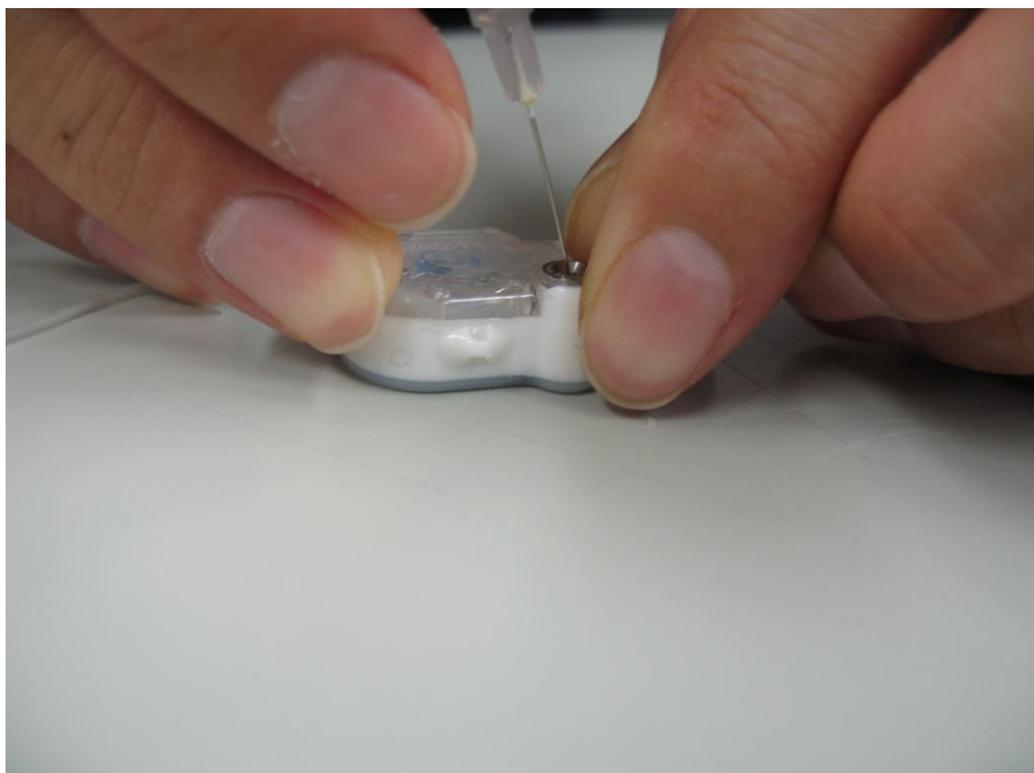


Figure 2(c): Insert needle through septum and get a feeling of the needle piercing the septum and reaching the bottom of the septum port.

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