

## **Urgent Field Safety Notice**

### **SynchroMed® II Implantable Infusion Pump - Models 8637-20, 8637-40**

---

#### **SynchroMed® II Missing Propellant - Physician Letter Important Patient Management Recommendations**

Dear Healthcare Professional,

This letter provides important safety information and patient management recommendations related to a small number of SynchroMed II pumps that may have been manufactured without propellant. Medtronic is notifying all physicians who have implanted or are managing a patient with a pump that falls within the parameters of the suspect population.

Medtronic is retrieving potentially affected pumps that **have not** been implanted. Identification and management of implanted pumps affected by the missing propellant condition is described below.

#### **Nature of the device issue:**

To date, eight SynchroMed II pumps have been returned to Medtronic and confirmed to be missing propellant. The pump propellant provides positive pressure to the reservoir from which drug is dispensed. Pumps without propellant cannot be fully aspirated. Due to this, the full volume of drug cannot be loaded into the device, and the drug will be diluted by the remaining sterile water that is contained in the reservoir of all new pumps. Additionally, an implanted pump without propellant can initially infuse, and then stop infusing without warning or alarm.

The missing propellant condition can cause drug dilution in the pump reservoir, leading to unknown drug concentration, and inconsistent or variable therapy results.

The clinical manifestations of a pump that is missing propellant may include:

- Inconsistent or variable therapy results
- A clinically significant drug underdose
- A return of underlying symptoms and/or withdrawal symptoms
- Lack of therapeutic effect
- A clinically significant drug overdose

Note: for a detailed description of the effect of the missing propellant condition on device functionality, along with underdose and overdose scenarios, refer to the enclosed "*Effects of Missing Propellant on the SynchroMed Pump*" enclosure.

For underdose and overdose signs and symptoms, please refer to the relevant drug labeling.

## SynchroMed II Missing Propellant - Physician Letter

### Potential severity of the issue:

No death or permanent patient injury has been reported due to this issue. The patient symptoms reported due to this issue are a return of underlying symptoms and/or withdrawal symptoms. Patients receiving intrathecal baclofen therapy (e.g. Lioresal® Intrathecal) are at higher risk for adverse events as baclofen withdrawal can lead to a life threatening condition if not treated promptly and effectively<sup>1</sup>.

### Scope and likelihood of the issue:

Medtronic has identified the suspect population as all pumps manufactured prior to the manufacturing process change that was implemented in April 2007 to correct the issue. Pumps manufactured after April 2007 are not affected.

To date, eight (8) SynchroMed II pumps from the suspect population have been returned to Medtronic and confirmed to be missing propellant. Based on conservative estimates from occurrence modeling, Medtronic estimates that fewer than 21 additional pumps (0.16%) out of 12,976 devices distributed worldwide (1,481 distributed in Europe) from the suspect population may be affected by the missing propellant condition.

The enclosed list of pump serial numbers will help you to identify your patients who are currently implanted with a pump from the suspect population.

**The inclusion of a pump in the suspect population does not mean that the pump was manufactured without propellant.** Additionally, it is important to note that pumps manufactured with propellant **do not** lose their propellant over time and are expected to function normally.

### How to Identify Pumps Without Propellant:

Pumps without propellant can be identified prior to or after implant. This can be accomplished prior to implant through careful adherence to pre-implant pump preparation instructions as set forth in the labeling, along with awareness of the expected aspiration and fill volumes for each pump. Prior to or after implant, pumps without propellant will present with an inability to fully aspirate the reservoir contents along with an inability to fill the pump to capacity. Please refer to the enclosed "*How to Identify Pumps Without Propellant*" document for details regarding the identification process.

If you **are** able to aspirate all expected fluid from the reservoir, and **can** fill the reservoir to the labeled capacity of the pump model (i.e., 20 ml or 40 ml), your pump **is not** affected by the missing propellant condition. As noted above, pumps manufactured with propellant **do not** lose their propellant over time and are expected to function normally.

---

<sup>1</sup> For complete product information refer to the Lioresal® Intrathecal (baclofen injection) Package Insert.

**SynchroMed II Missing Propellant - Physician Letter****Patient Management Recommendations:****For Patients with Pumps from the Suspect Population:**

At the next refill appointment, discuss this important information with your patients and their caregivers who have been implanted with pumps in the affected population. Explain the need to review the functioning of the pump related to the missing propellant issue.

**For Pumps Positively Identified as Lacking Propellant:**

If a pump is identified as lacking propellant, Medtronic recommends the healthcare professional consider immediate pump replacement because proper drug delivery cannot be ensured, and because patient injury may result from drug dilution, underdose, overdose, or abrupt delivery cessation.

**For All Pump Patients:**

Continue to educate patients and caregivers about the signs and symptoms of drug underdose, overdose, and withdrawal. Instruct patients to seek immediate medical assistance in the event that signs or symptoms of drug underdose, overdose, or withdrawal appear.

Please return any explanted SynchroMed II pump to Medtronic. Contact your Medtronic field representative to facilitate the device return procedure.

**Additional Resources:**

For additional information and/or updates, please contact your Medtronic field representative or your appropriate Medtronic Technical Services contact [countries to edit].

Enclosed is a listing of your SynchroMed II pumps within the suspect population for the missing propellant issue. Additionally, the following website can be used to identify (based on pump serial number) whether a specific SynchroMed II pump is potentially affected by the Missing Propellant condition:

<http://synchroMed2propellant.medtronic.com>.

The Competent Authority of your country has been notified of this action.

Patient safety is Medtronic's highest priority. We are committed to answering your questions and keeping you informed. We appreciate your assistance with this matter and regret any inconvenience this may have caused you or your patients.

Sincerely,

Enclosures: - Effects of Missing Propellant on the SynchroMed Pump  
- How to Identify Pumps Without Propellant  
- Device Serial Numbers Affected By This Action

*Lioresal® is a registered trademark of Novartis Corp.*

**SynchroMed® II Implantable Infusion Pump (Models 8637-20 and 8637-40)  
Missing Propellant Physician Letter – Enclosure**

**How to Identify Pumps Without Propellant**

---

**How to Identify Non-Implanted Pumps Without Propellant:**

Medtronic recommends careful adherence to pre-implant pump preparation instructions set forth in the labeling. If a discrepancy is noted when aspirating the pump, followed by the inability to fill the pump to capacity, the device should not be used, and should be returned to Medtronic for analysis.

Expected Aspiration Volume: (Note: this volume is variable based on the product shelf life because the pump continually dispenses 0.006ml/day from the date of manufacture)

- 20 ml pump, at least 16.1 +/- 0.5 ml (less 0.18 ml for each month beyond manufactured date)
- 40 ml pump, at least 36.1 +/- 0.5 ml (less 0.18 ml for each month beyond manufactured date)

Expected Fill Volume (completely full)

- 20 ml pump, at least 18 ml
- 40 ml pump, at least 36 ml

**How to Identify Implanted Pumps Without Propellant:**

Pumps without propellant may be identified during clinical follow up by reviewing the patient's clinical history and evaluating the reservoir volume. Physicians should use their medical judgment in considering prioritization of patient follow-up based on therapy and associated withdrawal risks. The patient's clinical history should be reviewed for the following conditions:

**Implanted Pump Identification Conditions**

▪ When programmer reservoir volume is less than 25% of actual reservoir volume.
▪ Inability to aspirate the expected reservoir volume when removing all fluid from the reservoir.
▪ Subsequent to complete reservoir volume aspiration, full pump reservoir capacity cannot be filled. <ul style="list-style-type: none"><li>○ 20 ml pump, inability to fill &gt; 18 ml</li><li>○ 40 ml pump, inability to fill &gt; 36 ml</li></ul>

If **all** of the conditions identified above are identified during the review of the patient history, Medtronic recommends performing the following troubleshooting procedures immediately.

- Perform a complete aspiration of the pump reservoir
- Perform a complete fill of the pump reservoir

If the expected amount (20ml in the 8637-20 or 40ml in the Model 8637-40) of drug cannot be injected into the pump, this pump may not contain propellant. Medtronic Technical Services should be contacted for additional troubleshooting support.

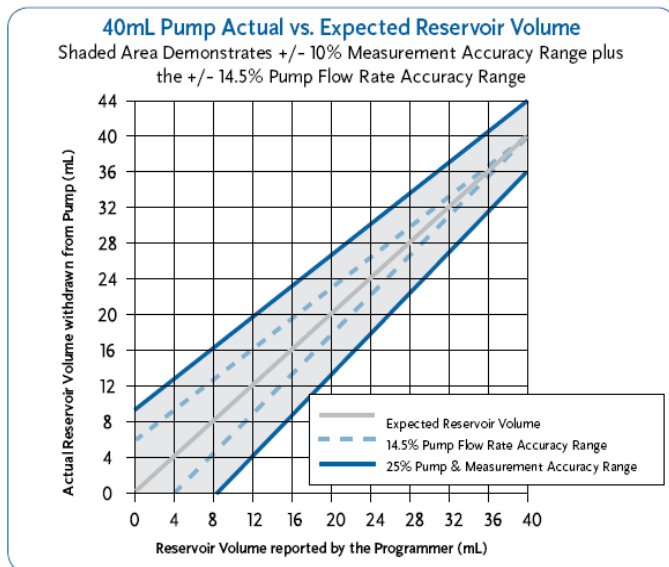
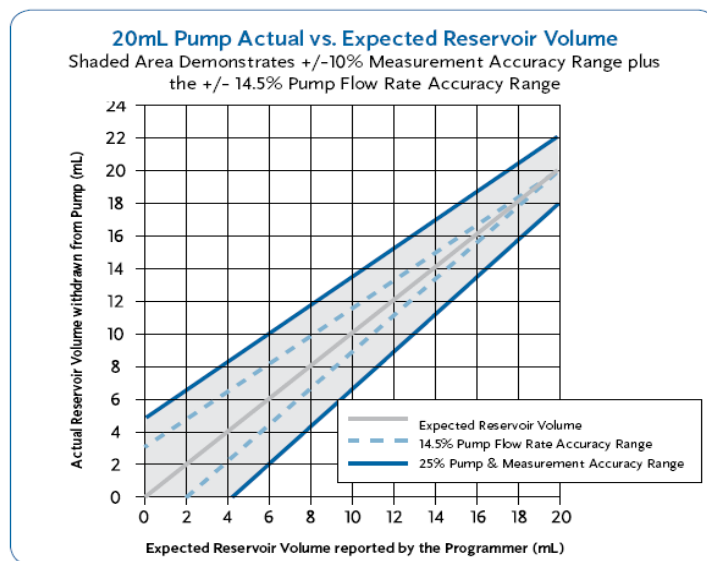
### Reservoir volume percent error calculations:

The following describes the calculations used for performing pump reservoir volume percent error calculations, along with error measurement guidelines.

Compare the actual residual volume with the expected residual volume (reservoir volume reading from the initial interrogation).

$$\% \text{ Error} = \frac{(\text{Expected Residual Volume in mL} - \text{Actual Residual Volume in mL})}{(\text{Previous Refill Volume} - \text{Expected Residual Volume})} \times 100$$

If necessary, use the Flow Rate Accuracy Charts below to help determine if a residual volume is within the error measurement guidelines.





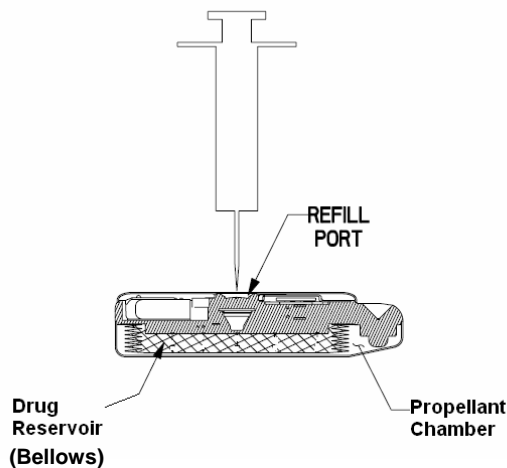
**NOTE:**

The manufacturing specifications of the SynchroMed II pump require the flow rate to be  $\pm 14.5\%$  of the programmed rate. However, clinical measurements can vary from the programmed rate due to errors in syringe measurement accuracy, human error, and the volume of prescribed fluid in the extension tubing and filter. Therefore,  $\pm 25\%$  flow rate error is the guideline for determining a significant discrepancy.

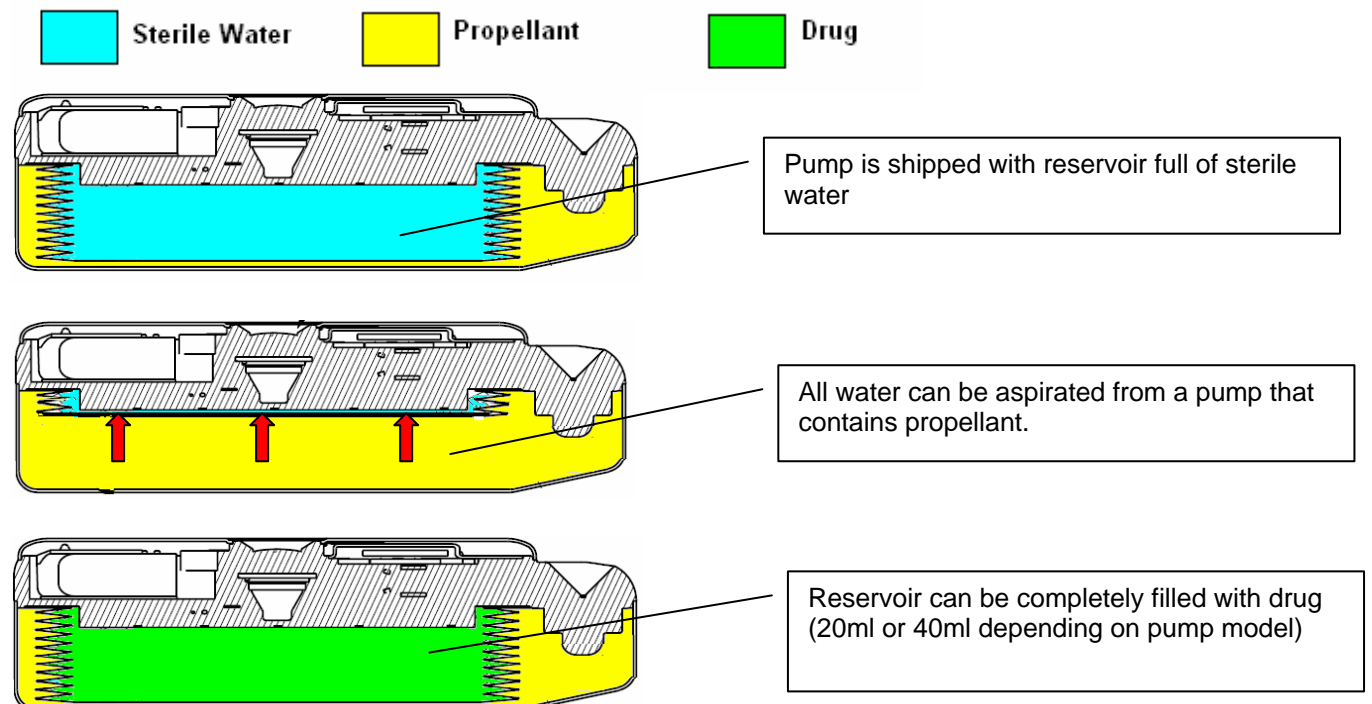
**SynchroMed® II Implantable Infusion Pump (Models 8637-20 and 8637-40)**  
**Missing Propellant Physician Letter – Enclosure**

**Effects of Missing Propellant on the SynchroMed Pump**

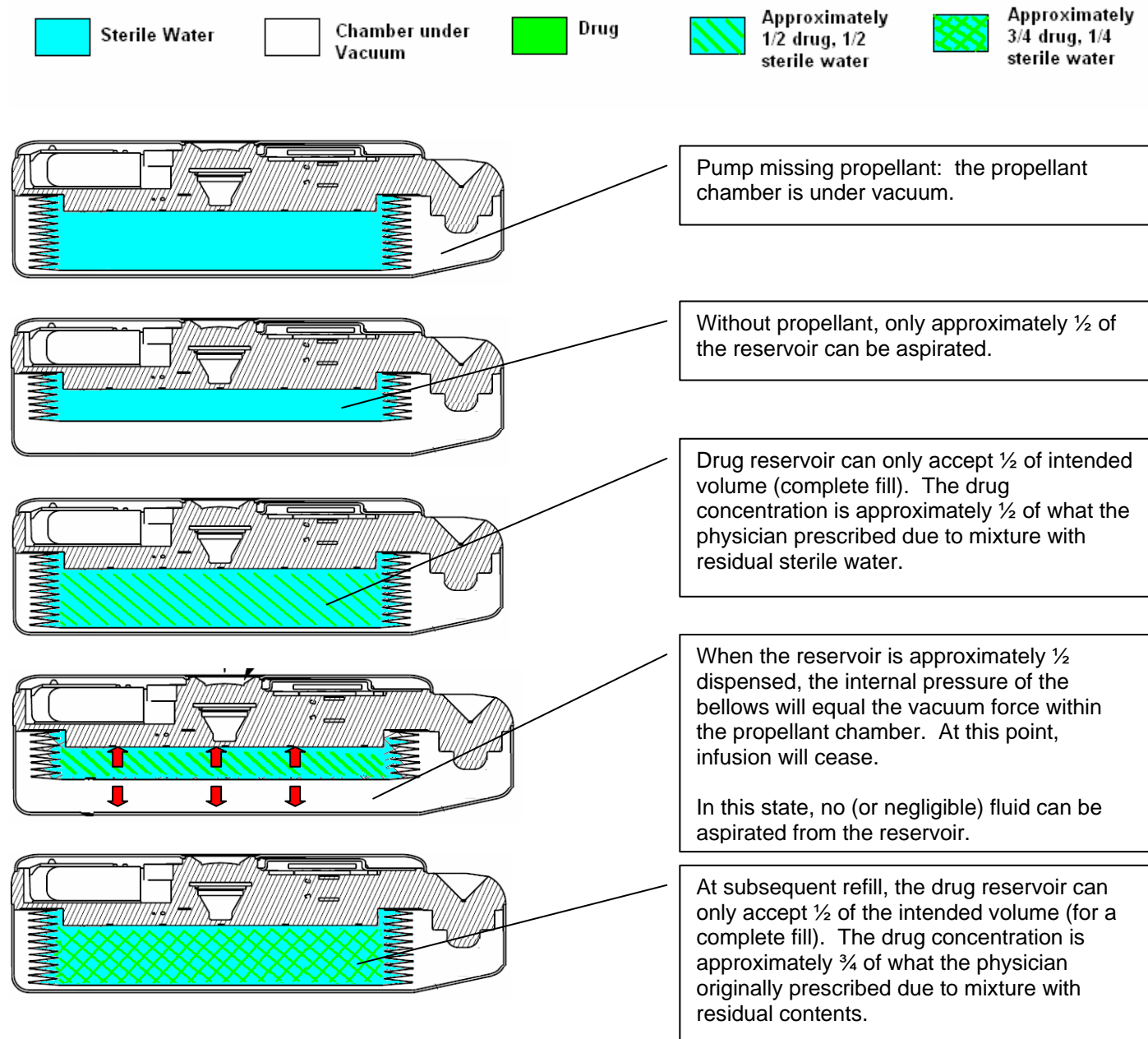
Drug is contained in an expandable reservoir, also referred to as a ‘bellows’. The device is shipped with the bellows full of sterile water. The bellows is enclosed within the propellant chamber which contains a specific volume of propellant (in the form of a gas) that exerts pressure on the reservoir. The gas pressure is the primary force which drives drug to the pump mechanism, which dispenses drug based on the programmed rate. If a pump is missing propellant, at the point at which approximately one-half of the reservoir contents are removed, there will be insufficient force in the system to drive the drug to the pump mechanism, resulting in zero output from the device regardless of the programmed dispensing rate.



**Normal Pump**



## Pump Missing Propellant



## Detailed Description of Drug Underdose and Overdose Potential:

Drug underdose or overdose scenarios can only occur if the implanter or physician does not notice or disregards major volume discrepancies at the initial implant procedure or does not notice major Programmer versus Actual Residual volume discrepancies during serial refill sessions. Multiple events must occur for the missing-propellant anomaly to go unrecognized and cause an intrathecal drug underdose or overdose.

Due to the missing propellant condition:

- 1) The reservoir contents cannot be fully aspirated
- 2) The pump can only dispense approximately 1/2 of the full reservoir volume
- 3) The reservoir will only accept approximately 1/2 of the reservoir volume (due to residual volume)

**Drug Underdose** can occur at two different points in a patient's clinical course because of drug dilution and therapy cessation.

1. **Immediately after implant.** In this instance, because only one-half of the sterile water placed into the pump reservoir during the manufacturing process can be removed at implant, the concentration of drug in the reservoir will be approximately one-half of what was prescribed. If the affected pump is a replacement device which is programmed to deliver the same dose at the same rate as the previous device, the patient will receive approximately one-half of the expected dose, which may manifest clinically as return of symptoms or withdrawal.
2. **Between scheduled refill appointments.** The missing-propellant anomaly causes the pump to cease dispensing drug altogether when approximately one-half of the reservoir volume has been dispensed. Additionally the patient will have only received approximately one-half of the expected dose up until that point.

**Drug Overdose** can occur by three interrelated mechanisms if the missing-propellant anomaly goes unrecognized through serial refill appointments. The following list of mechanisms either independently or in combination could lead to overdose.

1. If the actual concentration of drug in the reservoir increases through serial pump refills because of a "serial concentration" (similar to the reverse of a "serial dilution") phenomenon.
2. The likelihood and/or magnitude of an intrathecal drug overdose caused by the "serial concentration" phenomenon hypothetically can be exacerbated if the physician escalates the programmed drug dosage (increases the pump flow rate) between or during pump refill appointments.

If scheduled pump refills proceed without regard for the **Programmer versus Actual** reservoir volume discrepancies, the drug contained in the reservoir will eventually approach what was originally prescribed or intended at the time of implant. However, because the patient may experience immediate post-implant underdose effects owing to drug dilution, and because the patient also may experience underdose effects due to cessation of drug delivery prior to scheduled refill – the physician may elect to program an escalation of the drug dosage (pump rate increase) between or at refill appointments. Programmed dosage escalations hypothetically can exacerbate the possibility of a drug overdose beyond what might be caused by the stepwise increments in drug concentration at serial refill sessions.

3. If the physician decided to increase the drug concentration at one or more serial refill sessions in addition to programmed dosage escalations.

These drug underdose or overdose scenarios can only occur if the implanter or physician does not notice or disregards major volume discrepancies at the initial implant procedure and/or during serial refill sessions. Significant volume discrepancies should always be investigated, as they may indicate a problem with the device or system that directly impacts patient therapy.