# Accuracy of the Prometra® Programmable Pump System in a Prospective, Non-Randomized Clinical Trial

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## INTRODUCTION

A primary goal of advancing medical technology is to increase the benefit of a given component in a therapeutic treatment modality. In turn, that benefit should translate into an improved ability to manage patient care. Pumps currently market-approved are labeled for accuracy of ± 14.5%. A number of design elements of the Prometra Pump are expected to improve accuracy, including:

- Non-compliant dosing chamber that provides meticulous measurements (no rollers)
- Precise, controlled drug flow with electronic dual gated system
- A reservoir that acts as a volume-control regulator in micro increments
- An isolated valve system robust to temperature & pressure changes
- Ability to completely shut down (zero flow)

Accuracy of drug delivery is an important therapeutic component when treating pain patients. This is especially important when infusing drugs with low therapeutic indices.

In a prospective, multi-center, FDA-approved clinical study (Prometra's Utilization in Mitigating Pain, or PUMP), accuracy of the Prometra Programmable Pump was evaluated.

## METHODS

### *Device Description*

The Prometra Programmable Pump, developed by InSet Technologies Incorporated (Mt. Olive, NJ), is a pressure-driven pump. This type of design is expected to provide a number of improvements over older generations of pumps. In addition to improved accuracy, it is expected to have micro-volume delivery capability, a long device life (due to few moving parts and energy-efficient design), relative light weight, and the ability to deliver advanced compounds, such as large proteins.


The Prometra Programmable Pump contains a metal bellows drug reservoir with a capacity of 20 mL. The reservoir propellant is stored within the rigid housing surrounding the bellows and provides the driving pressure for the pump. The driving pressure on the reservoir forces drug through an outlet filter and into an electronically controlled flow-metering valve-accumulator subsystem. The drug passes from the flow-metering subsystem into the catheter access port, then into the catheter for delivery to the intrathecal space. The teardrop shape of the pump is designed to help the clinician differentiate the catheter access port from the central access port after the pump is implanted. The drug chamber is refillable and is percutaneously accessed via the centrally located access port using a 22-gauge non-coring needle. The catheter access port is located on the periphery of the pump to allow for direct access to the catheter without interfering with the drug reservoir. The catheter access port can be used to evaluate catheter patency and placement.

### *Protocol*

The PUMP Study was a prospective open-label evaluation of the Prometra Programmable Pump System to treat chronic pain with morphine sulfate ($MSO_4$). After IRB approval was obtained at seven clinical sites, 110 patients (age: 56 ± 13, gender: 51F) were enrolled after giving informed consent. Data was collected in three phases: baseline (pre-implant), monthly follow-up for the first 6-months post-implant and then every three months. Refill accuracy was calculated by dividing the total measured delivered volume by the total volume programmed for delivery. Data were tabulated by an independent third party (inVentiv Clinical Solutions, The Woodlands, TX).

## METHODS

**Table 1: Enrollment by Clinical Site**

| Clinical Site | Location | Primary Investigator | Number of Subjects |
|---|---|---|---|
| Center for Interventional Pain Management | St. Louis, MO | Gurpreet Padda | 31 |
| Pain Institute of Tampa | Tampa, FL | John Barsa | 20 |
| Fox Chase Pain Management Associates | Jenkintown, PA | Steven Rosen | 17 |
| Center for Clinical Research | Winston-Salem, NC | Richard Rauck | 16 |
| The Center for Pain Relief | Charleston, WV | Timothy Deer | 16 |
| Pain Control Network | Louisville, KY | Elmer Dunbar | 7 |
| Lowell General Hospital | Lowell, MA | Gopala Dwarakanath | 3 |
| | | | **Total 110** |

## RESULTS

One-hundred-ten patients were enrolled. Of those, accuracy data was collected on 107 patients; three patients required explants prior to the Month 1 visit due to infections. Demographics of the study population are described in Table 2; pain history data is provided in Table 3.

**Table 2: Demographics**

| Demographic | Total (*N*=107) |
|---|---|
| Gender – *N* (%) | |
| Male | 56 (52) |
| Female | 51 (48) |
| Age at Implant | |
| Mean ± SD | 56 ± 13 years |
| Range | 28-84 years |
| Patients with Spinal Cord Stimulators | 21 (19) |
| Patients having Previous Pump System Replaced with Prometra System | 19 (17) |

**Table 3: Pain History**

| Pain History Variable | Total (*N*=107) |
|---|---|
| Duration of Pain (mean ± SD) | 12.6 ± 9.7 years |
| Pain Category – *N* (%) | |
| Neuropathic | 63 (59) |
| Nociceptive | 12 (11) |
| Both | 32 (30) |
| Causes of Pain[1] – *N* (%) | |
| Post Lumbar Spine Surgery with Pain | 58 (54) |
| Intractable Back Pain | 56 (52) |
| Arachnoiditis | 25 (23) |
| Chronic Regional Pain Syndrome | 24 (22) |
| Post Cervical Spine Surgery with Pain | 13 (12) |
| Vertebral Body Compression Fractures | 6 (6) |
| Post Thoracotomy Pain Syndrome | 3 (3) |
| Cancer Pain | 3 (3) |
| Other | 70 (65) |

[1]Percentages add up to greater than 100% because patients may be counted in more than one category.

## RESULTS

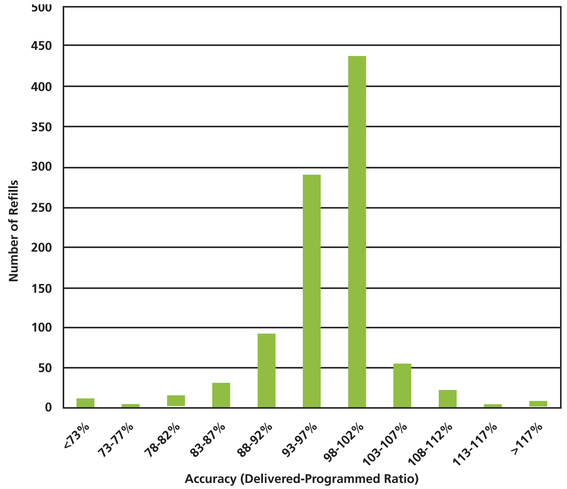
### *Overall Accuracy*

Based on 957 refill procedures completed in 107 patients as of November 1, 2008, the average accuracy of drug delivery was 97.3% ± 0.4%*. Accuracy is summarized in Table 4. Accuracy for 438 (46%) of the refills was measured to be between 98% and 102%, as presented in Figure 1.

**Table 4: Summary of Accuracy**

| Description | Results |
|---|---|
| Number of Patients | 107 |
| Number of Refills | 957 |
| Mean | 97.3% |
| Standard Error of the Mean | 0.4% |
| Median | 97.7% |
| ***90% Confidence Interval of Mean*** | ***96.6 – 97.9%*** |

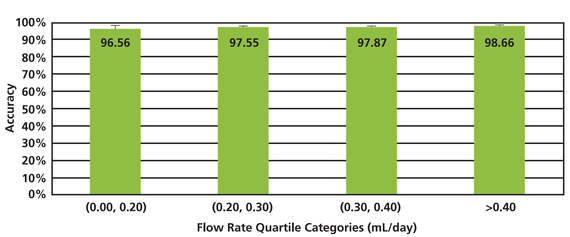
**Figure 1: Distribution of Refill Accuracy**




### *Accuracy by Flow Rate*

Programmed flow rates ranged from 0.0-1.5 mL/day. Programmed flow rates were divided into quartile categories in order to have similar numbers of measurements in each group. Results for accuracy by flow rate quartile categories are presented in Figure 2. There were no significant differences in accuracy among the quartile categories.

**Figure 2: Mean Accuracy by Flow Rate Quartile Categories**

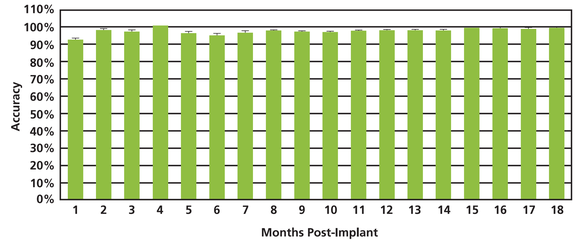



## RESULTS

### *Accuracy by Months Post-Implant*

Mean accuracy at the first visit (one-month post-implantation) was 93.1% ± 0.8%*, which was lower than the other months. This difference was statistically significant ($p<0.05$) when compared to Months 2-5 and 8-13. Statistically significant differences were also seen at Month 4 (mean accuracy 101.2% ± 3.3%*) when compared to Months 5 and 6. Differences in accuracy were not seen at any other visits.

**Figure 3: Accuracy by Months Post-Implant**




## DISCUSSION

Results show remarkable accuracy with the Prometra System.

Many of the refills in Figure 1 with accuracy results that are outside the range of 85-115% can be explained by very low flow rates. In these cases pumps were programmed to deliver as little as 0.5 mL over a one month period. When such small volumes are being delivered, any human error in measuring return volumes can have significant impact on the accuracy calculation. An error in reading the volume, even if only 0.2 mL, can impact the accuracy of such refills as much as 5-20%.

The accuracy results remain consistent when viewed over the range of flow rates programmed during the study. No statistically significant differences were observed, despite the few extreme cases discussed above.

The accuracy results are also consistent when viewed over the duration of the study with the exception of the Month 1 and Month 4 results. Month 1 had the lowest mean accuracy, and Month 4 had the highest mean accuracy. However, these mean accuracies were still well within the range that other market-approved pumps are labeled for. Both Months 1 and 4 included cases where pumps were programmed to deliver very small volumes, as described above. Some of these extreme cases contributed to the differences in mean accuracies for these months. There is also some speculation that Month 1 accuracy may be effected by the fact that pumps are initially filled in the operating room where medical personnel are often less experienced in doing so than personnel who fill them at follow-up visits. Less experienced personnel may have more variability in the total volume that is actually injected into the pump, and the amount injected may differ from the volume that is programmed into the pump via the programmer. Such discrepancies would be reflected at the Month 1 visit when the drug remaining in the pump reservoir is removed and measured.

## CONCLUSION

The Prometra pump demonstrated accuracy and consistency over time and over a wide range of flow rates. If the Prometra System is, in fact, proven to have superior accuracy and is approved for introduction to the market, its accuracy and consistency (in addition to other improvements noted earlier) have the potential to improve patient outcomes, both in efficacy and safety. This may be especially true if it is approved for use with drugs other than morphine that have low therapeutic indices.

*Data presented as mean ± standard error of the mean.

This study was sponsored and funded by InSet Technologies Incorporated.

CAUTION: Investigational Device.
Limited by Federal (or United States) Law to Investigational Use.