PRODUCT PERFORMANCE REPORT

SUMMARY OF DATA FROM THE MEDTRONIC POST-MARKET REGISTRY

2024

v.1.0 15APR2025

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3 Targeted Drug Delivery Systems

3.1 Study Participants

3.1.1 Centers

The Targeted Drug Delivery (TDD) tables and graphs were generated based on data collected between August 7, 2003, and the report cut-off date of October 31, 2024. Seventy-seven centers spanning 13 countries/territories in North America, Europe and South America, enrolled patients and contributed patient data to the targeted drug delivery systems section of this report. Figure 3.1 shows a World Map, in which the countries that enrolled TDD patients are highlighted.

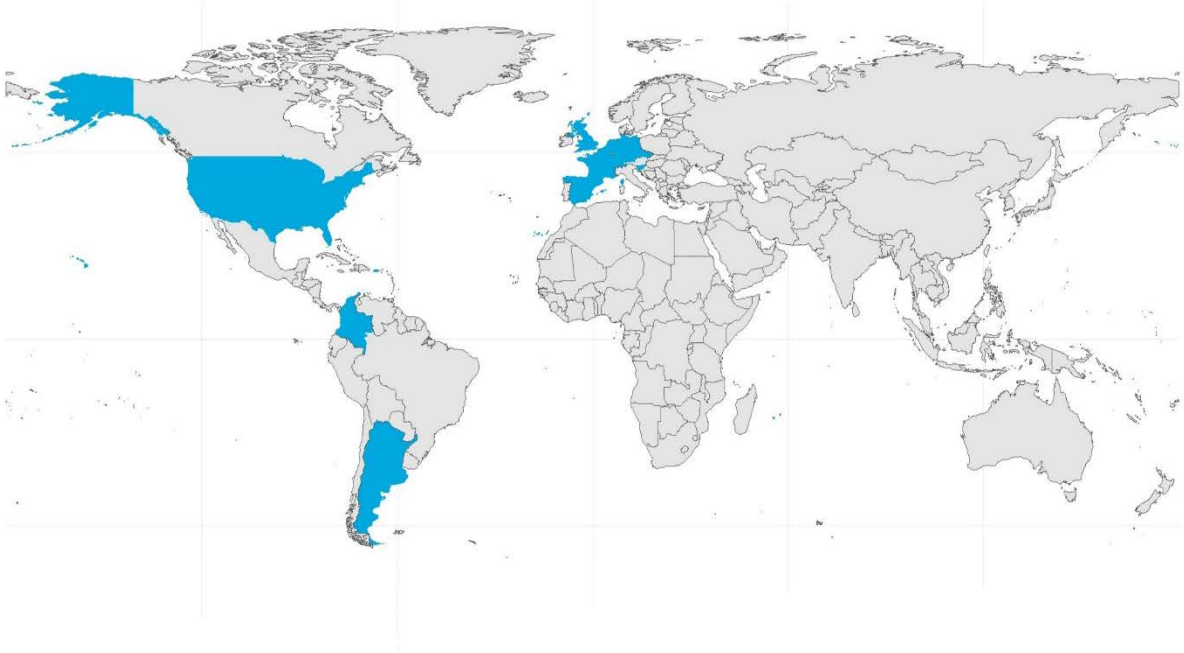


Figure 3.1: Countries with Targeted Drug Delivery Therapy Patients in Registry (Highlighted)

3.1.2 Patients

There were 10,793 total targeted drug delivery system patients enrolled through October 31, 2024. In Table 3.1 and Figure 3.2, 59.5% of patients were implanted with a targeted drug delivery system for treatment of non-malignant pain (pain not related to cancer and its treatment), followed by 21.2% for treatment of spasticity, and 17.0% for treatment of malignant pain (pain related to cancer). Primary treatment indication is provided by the physician. The sites of pain

for the malignant pain patients are presented in Table 3.2, while the sub-indications for the non-malignant pain and the spasticity patients are presented in Table 3.3 and Table 3.4, respectively.

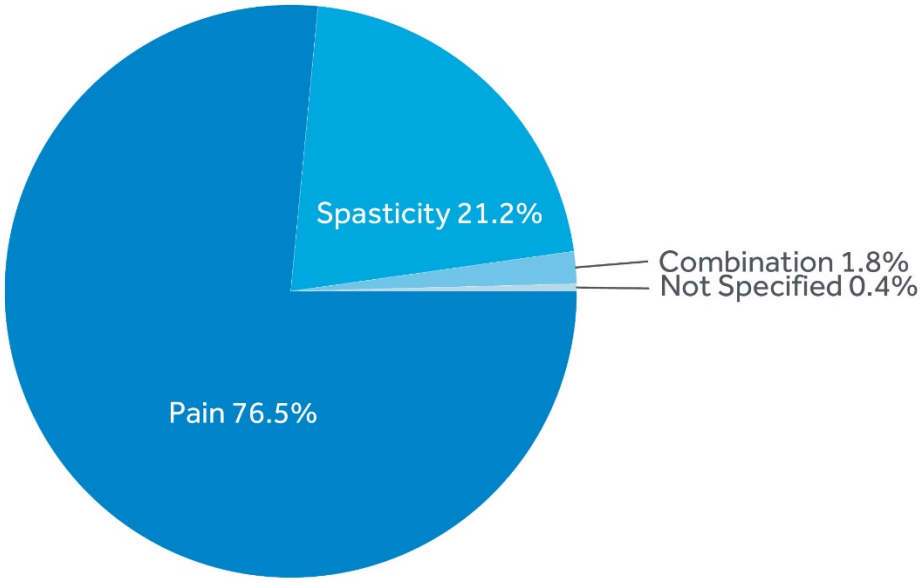


Figure 3.2: Targeted Drug Delivery Primary Treatment Indications

Table 3.1: Targeted Drug Delivery Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Pain	**8259 (76.5%)**
Non-malignant pain	6419 (59.5%)
Malignant pain	1839 (17.0%)
Pain not specified	1 (<0.1%)
Spasticity	**2293 (21.2%)**
Combination	**196 (1.8%)**
Non-malignant pain & Spasticity	193 (1.8%)
Malignant pain & Chemotherapy	1 (<0.1%)
Malignant pain & Spasticity	1 (<0.1%)
Non-malignant pain & Chemotherapy	1 (<0.1%)
Not Specified[b]	**45 (0.4%)**

Primary Treatment Indication[a]	Enrolled Patients (%)
Total Patients	**10793**

[a] For approved indications refer to product labeling for your geography.
[b] Includes incomplete data forms at the time of the data snapshot and exited patients where indication was never provided.

Table 3.2: Targeted Drug Delivery Malignant Pain: Site of Pain

Malignant Pain: Site of Pain	N (%)
Spine/Back	761 (41.3%)
Abdominal/Visceral	451 (24.5%)
Extremity	341 (18.5%)
Pelvic	251 (13.6%)
Thoracic	206 (11.2%)
Head/Neck	128 (7.0%)
Other	207 (11.2%)
Not Specified	439 (23.8%)
Total Patients[a]	**1841**

[a] 2784 sites of pain in 1,841 patients with indications of malignant pain, malignant pain &chemotherapy, and malignant pain &spasticity. Total number of patients is not equal to number of reported sites of pain as patients may have multiple sites of pain.

Table 3.3: Targeted Drug Delivery Non-Malignant Pain: Sub-Indications

Non-Malignant Pain: Sub-Indications	Enrolled Patients (%)
Back Pain with Leg Pain	2352 (35.6%)
Back Pain without Leg Pain	1715 (25.9%)
General Neuropathic Condition	251 (3.8%)
CRPS I[a]	205 (3.1%)
Peripheral Neuropathy	85 (1.3%)
Joint Pain/Arthritis	74 (1.1%)
General Nociceptive Condition	59 (0.9%)

Non-Malignant Pain: Sub-Indications	Enrolled Patients (%)
CRPS II[a]	39 (0.6%)
Osteoporosis	20 (0.3%)
Abdominal pain	13 (0.2%)
Pelvic pain	9 (0.1%)
Other	836 (12.6%)
Not Specified	955 (14.4%)
Total Patients[b]	**6613**

[a] CRPS is complex regional pain syndrome.

[b] Includes patients with indications of non-malignant pain, non-malignant pain & spasticity, and non-malignant pain & chemotherapy.

Table 3.4: Targeted Drug Delivery Spasticity: Sub-Indications

Spasticity: Sub-Indications	Pediatrics (%) (<18 years)	Adults (%) (>=18 years)	All Patients (%)
Cerebral Palsy	388 (77.1%)	287 (14.5%)	675 (27.1%)
Multiple Sclerosis	0 (0.0%)	597 (30.1%)	597 (24.0%)
Spinal Cord Injury	9 (1.8%)	394 (19.9%)	403 (16.2%)
Brain Injury	39 (7.8%)	130 (6.6%)	169 (6.8%)
Stroke	1 (0.2%)	103 (5.2%)	104 (4.2%)
Other	22 (4.4%)	243 (12.2%)	265 (10.7%)
Not Specified	44 (8.7%)	230 (11.6%)	274 (11.0%)
Total Patients[a]	**503**	**1984**	**2487**

[a] Includes patients with indications of spasticity, non-malignant pain & spasticity, and malignant pain & spasticity.

It is recognized that health care providers prescribe therapies to meet specific patient needs; however, Medtronic only directs the use of its products based on approved labeling. Product labeling varies by geography. Contact a local Medtronic representative for region-specific product labeling - https://www.medtronic.com/us-en/our-company/locations.html .

3.2 Event Summary

Events are reported via database by physicians trained in the PSR. Events are reviewed internally and coded as either a product performance event (e.g. catheter kink, motor stall) or a non-product performance event (e.g. adverse drug reaction and incision site swelling). There were 2,632 product performance events reported between August 7, 2003 and October 31, 2024, in 1,691 patients with targeted drug delivery systems. These events represent 13.1% (2632/20,034) of the total reported events and are presented graphically within this report (e.g. events per patient years as well as survival curves). As an ongoing registry, events not coded at the time of the data snapshot (waiting for further information) will be included in future reports (n=884).

All registry devices that are returned to Medtronic are analyzed via a Returned Product Analysis (RPA) process. If available, RPA findings assist in the classification of the events. Within this report, Table 3.5 and the event tables in the pump and catheter sections differentiate the events by those determined by the RPA process versus those determined by the physician. Please refer to the Methodology section for more information.

There were 2,933 deaths reported in patients with targeted drug delivery systems (see Table 3.12). None of these deaths were reported as a direct result of a product performance event. Early versions of the protocol required events to be reported only when the event required a surgical intervention, resulted in therapy abandonment, or resulted in death. The required event reporting definition was expanded in April 2010 to include all adverse events related to the device, implant procedure, and/or therapy. Table 3.5 includes combined data from these versions of the protocol.

3.2.1 Product Performance Events

Table 3.5: Targeted Drug Delivery System Product Performance Events

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=10793[b]
RPA Determination	**359**	**0.9**	**327 (3.0%)**
Pump Motor Stall	197	0.5	190 (1.8%)
Laboratory Overinfusion Finding[d]	40	0.1	39 (0.4%)
Corrosion And/Or Gear Wear	29	0.1	29 (0.3%)
Battery High Resistance	12	<0.1	12 (0.1%)
Confirmed overinfusion[e]	11	<0.1	5 (<0.1%)
No Anomaly Found By RPA[l]	11	<0.1	10 (0.1%)
Reduced Battery Performance	10	<0.1	10 (0.1%)

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=10793[b]
Deformed Pump Tube	9	<0.1	8 (0.1%)
Reservoir Access Issues Due To Residue	9	<0.1	8 (0.1%)
Motor Feedthrough Anomaly	8	<0.1	8 (0.1%)
Alarm And/Or Resonator Anomaly	2	<0.1	2 (<0.1%)
Concave Pump Shield	2	<0.1	2 (<0.1%)
Hole In Pump Tube	2	<0.1	1 (<0.1%)
Other[f]	17	<0.1	17 (0.2%)
Physician's Determination	**2,273**	**5.6**	**1509 (14.0%)**
Catheter Occlusion	539	1.3	471 (4.4%)
Catheter Dislodgement	431	1.0	346 (3.2%)
Catheter Kink	281	0.7	240 (2.2%)
Catheter Break/Cut	273	0.7	244 (2.3%)
Device Malfunction[g]	127	0.3	109 (1.0%)
Pump Motor Stall[h]	97	0.2	79 (0.7%)
Catheter Leakage	89	0.2	82 (0.8%)
Catheter Disconnection At Pump	54	0.1	52 (0.5%)
Pump Reservoir Volume Discrepancy	49	0.1	38 (0.4%)
Pump Unable To Enter/Withdraw From Catheter Access Port	49	0.1	42 (0.4%)
Catheter Dysfunction	48	0.1	43 (0.4%)
Device Difficult To Use	27	0.1	26 (0.2%)
Pump Underinfusion	23	0.1	19 (0.2%)
Catheter Related Complication	22	<0.1	21 (0.2%)
Device Component Migration	21	<0.1	21 (0.2%)
Pump Connector Break/Cut	19	<0.1	18 (0.2%)
Catheter Damage	17	<0.1	17 (0.2%)
Device Issue[i]	15	<0.1	15 (0.1%)

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=10793[b]
Catheter Disconnection Between Catheter Segments	13	<0.1	12 (0.1%)
Device Connection Issue	10	<0.1	10 (0.1%)
Device Damage	10	<0.1	8 (0.1%)
Catheter Access Port Issue	6	<0.1	6 (0.1%)
Device Breakage	6	<0.1	6 (0.1%)
Device Charging Issue	5	<0.1	5 (<0.1%)
Device Displays Incorrect Message	4	<0.1	4 (<0.1%)
Device Reset Issue	3	<0.1	3 (<0.1%)
Medical Device Complication[j]	3	<0.1	3 (<0.1%)
Pump Not Infusing	3	<0.1	3 (<0.1%)
Catheter Disconnection Issue	2	<0.1	2 (<0.1%)
Device Infusion Issue	2	<0.1	2 (<0.1%)
Device Kink	2	<0.1	2 (<0.1%)
Device Material Corroded	2	<0.1	1 (<0.1%)
Physician reported overinfusion[k]	2	<0.1	2 (<0.1%)
Pump Infusion Issue	2	<0.1	1 (<0.1%)
Pump Inversion	2	<0.1	2 (<0.1%)
Other[f]	15	<0.1	14 (0.1%)
Total	**2,632**	**6.4**	**1691 (15.7%)**

[a] Medical Dictionary for Regulatory Activities (MedDRA) Lower-Level Term or Medtronic's coding system term for events that do not exist in the MedDRA dictionary.

[b] The total number of patients with events may not represent the sum of all rows, as a patient may have experienced more than one type of event.

[c] Of the 197 RPA-determined motor stalls, 196 had a pump etiology and 1 had other etiology. Motor stall count does not include temporary motor stalls that may be expected (e.g. due to MRI) and recovered within a 24-hour period. The SynchroMed II and Synchromed III pumps are designed to temporarily stop the rotor of the pump motor and suspend drug infusion for the duration of the MRI exposure for patient safety.

[d] Includes pumps that had a laboratory finding but the patient did not have clinical signs or symptoms consistent with pump overinfusion.

[e] Patient had clinical signs and symptoms consistent with pump overinfusion, pump returned and positive laboratory test.

[f] Composed of event codes with 1 event each.

[g] The majority of these events were attributed to the Patient Therapy Manager (PTM).

[h] Of the 97 physician-determined motor stalls, 88 had a pump etiology and 9 had an MRI etiology. Of the 9 physician-determined motor stalls with an MRI etiology, 3 pumps were reprogrammed and 6 had no action taken. Motor stall count does not include temporary motor stalls that may be expected (e.g. due to MRI) and recovered within a 24-hour period. The SynchroMed II and Synchromed III pumps are designed to temporarily stop the rotor of the pump motor and suspend drug infusion for the duration of the MRI exposure for patient safety.

[i] Of the 16 device issues, 12 have an etiology of catheter or other component. The 16 device issues include 8 unable to aspirate catheter, 4 PTM Error Codes, 2 pump alarms, and 1 pump in safe state.

[j] Includes1 where metal clips on connector appear bent, 1 pump beeping, and 1 roller arm seized to ball bearing.

[k] Patient had clinical signs and symptoms of overinfusion, but pump not returned and analyzed.

[l] Return Product Analysis (RPA) found no anomaly with the pump but physician initially reported an issue with the device. Events remain reported as PPE for transparency.

A total of 1,862 of the 2,632 product performance events were related to the catheter only. There were 541 events related to the pump only. There were 175 related to other components (e.g. PTM malfunction) and 54 (2.1%) related to other etiologies (e.g. bend in catheter anchor). Relatedness is reported by the physician.

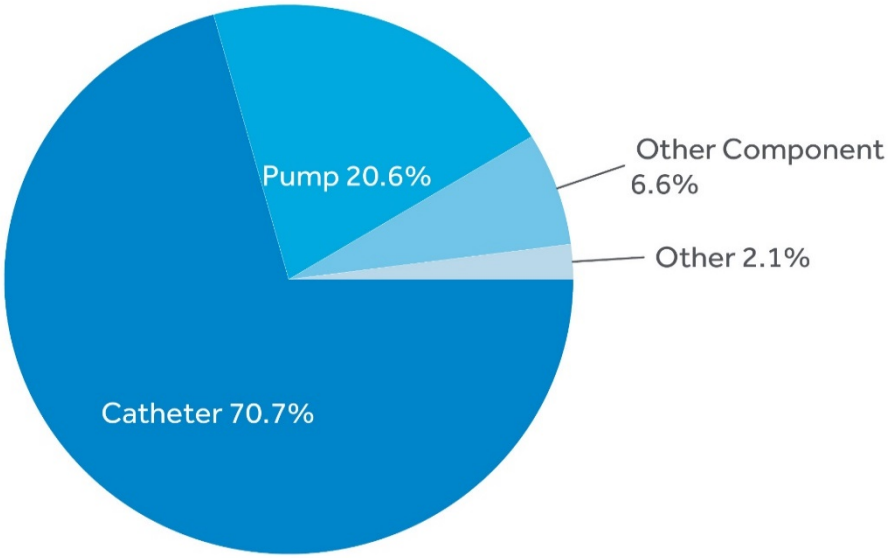


Figure 3.3: Targeted Drug Delivery System Product Performance Events by Relatedness

Table 3.6 describes the interventions completed for product performance events that required action from the health care provider and thereby may have resulted in an incremental impact to the patient. Survival estimates presented in previous product performance reports included events where no action was taken. To present survival estimates that may better correlate with patient impact, events where no action was taken have been removed from the

device survival estimates presented in this report. The far-left column lists the top five reported PPEs, and all other reported PPEs are listed under Other. The subsequent columns represent the actions taken by the reporting physician.

Table 3.6: TDD Product Performance Events by Intervention

Events by Intervention	Surgical Intervention	Reprogramming	Medical or Non-Surgical Intervention[a]	Therapy Suspension	No Action Taken	Total Events
Catheter Occlusion	494 (91.7%)	12 (2.2%)	17 (3.2%)	7 (1.3%)	9 (1.7%)	**539**
Catheter Dislodgement	380 (88.2%)	9 (2.1%)	8 (1.9%)	2 (0.5%)	32 (7.4%)	**431**
Catheter Kink	256 (91.1%)	6 (2.1%)	14 (5%)	1 (0.4%)	4 (1.4%)	**281**
Catheter Break/Cut	259 (94.9%)	1 (0.4%)	6 (2.2%)	1 (0.4%)	6 (2.2%)	**273**
Pump Motor Stall	167 (69%)	15 (6.2%)	4 (1.7%)	9 (3.7%)	47 (19.4%)	**242**
Other[b]	494 (63.3%)	31 (4.0%)	152 (19.5%)	5 (0.6%)	98 (12.6%)	**780**
Total	**2050 (80.5%)**	**74 (2.9%)**	**201 (7.9%)**	**25 (1.0%)**	**196 (7.7%)**	**2546[c]**

[a] Medical or Non-Surgical Therapy contains but is not limited to the following actions: medication adjustment based on disease symptoms, imaging (e.g. MRI or X-ray), other specialist referral.

[b] Other represents all reported PPEs that were not in the top five of occurrence.

[c] The total number of events in this table differs from the total number of PPEs overall due to 86 events with an unknown intervention, which are excluded.

3.2.2 Clinical Events Not Related ToProduct Performance

The clinical events not related to product performance are summarized if:

- The patient was enrolled in the PSR at the time in which the clinical event collection was initiated (n=4,217)
- Categorized as serious adverse events (SAEs, n=551)
- Occurred with a System Organ Class (SOC) threshold ≥1% of patients
- Other Considerations
  - Some events are described in high level group terms (HLGT) to provide more specificity, if needed

– Some therapies will provide therapy relevant events (e.g., Inflammatory Mass, Cerebrospinal Fluid Leaks)

Table 3.7: Targeted Drug Delivery Clinical Events Not Related To Product Performance

Event Type	Number of SAEs	Patients with SAE n (%) N=4,217	SAEs Per 100 Patient Months	Patients with SAE Requiring Surgical Intervention n (%) N=4,217
General disorders and administration site conditions	**238**	**212 (5.0%)**	**0.17**	**53 (1.3%)**
Therapeutic and nontherapeutic effects (excl toxicity)	174	156 (3.7%)	0.13	20 (0.5%)
Complications associated with device	42	41 (1.0%)	0.03	26 (0.6%)
General system disorders NEC[a]	12	12 (0.3%)	0.01	1 (<0.1%)
Administration site reactions	5	5 (0.1%)	<0.01	4 (0.1%)
Other[b]	5	5 (0.1%)	<0.01	4 (0.1%)
Infections and infestations	**116**	**108 (2.6%)**	**0.09**	**92 (2.2%)**
Infections - pathogen unspecified	95	90 (2.1%)	0.07	80 (1.9%)
Bacterial infectious disorders	20	19 (0.5%)	0.01	12 (0.3%)
Other[b]	1	1 (<0.1%)	<0.01	1 (<0.1%)
Injury, poisoning and procedural complications	**78**	**74 (1.8%)**	**0.06**	**20 (0.5%)**
Procedural related injuries and complications NEC[a]	38	37 (0.9%)	0.03	15 (0.4%)
Overdoses and underdoses NEC[a]	30	28 (0.7%)	0.02	2 (<0.1%)
Injuries NEC[a]	5	5 (0.1%)	<0.01	3 (0.1%)
Other[b]	5	5 (0.1%)	<0.01	0 (0.0%)

Event Type	Number of SAEs	Patients with SAE n (%) N=4,217	SAEs Per 100 Patient Months	Patients with SAE Requiring Surgical Intervention n (%) N=4,217
Nervous system disorders	**68**	**62 (1.5%)**	**0.05**	**29 (0.7%)**
Neurological disorders NEC[a]	31	29 (0.7%)	0.02	15 (0.4%)
Neuromuscular disorders	22	21 (0.5%)	0.02	10 (0.2%)
Other[b]	15	15 (0.4%)	0.01	6 (0.1%)
Other SOC Terms (<1.0% Threshold)	**51**	**49 (1.2%)**	**0.04**	**15 (0.4%)**
Total	**551**	**442 (10.5%)**	**0.40**	**189 (4.5%)**

[a] Not Elsewhere Classified.

[b] Composed of high level group term event codes with fewer than 5 events each.

3.2.3 Therapy Relevant Events

3.2.3.1 Cerebrospinal Fluid Leaks

Potential cerebrospinal fluid (CSF) leak events are identified and assessed by Medtronic personnel and the site physician for the case to ascertain the case definition using Table 3.8.

Table 3.8: Cerebrospinal Fluid Leak Event Definition

Case Definition	Ascertainment
Definitive CSF Leak	• Observation of clear fluid leaking from the wound, or • Contrast study demonstrates extravasation of dye outside dura, or • Patient with persistent post-operative ***positional*** headache, plus one of the following: – Blood patch or suturing relieves headaches, or – Subcutaneous ***persistent*** fluid collection on the catheter tract, or – Meningeal enhancement on MRI with contrast.
Probable CSF Leak	**Reproducible** post-operative **positional** headache for >14 days with or without report of subcutaneous fluid collection. No contrast study performed or contrast study result inconclusive.
Possible CSF Leak	**Intermittent** post-operative **positional** headache for >14 days without report of subcutaneous fluid collection. No contrast study performed or contrast study result inconclusive.

Not CSF Leak	Acute post-operative non-positional headache lasting less than 14 days.

The potential CSF leak status (N=520) at the time of this analysis is presented in Table 3.9 with a definitive and probable CSF leak rate of 1.5% (167/10,793). The causality of the CSF leak event is dependent on the individual case.

Table 3.9: Summary of Cerebrospinal Fluid Leak Adjudication

Cases Reviewed	Definitive CSF Leak	Probable CSF Leak	Possible CSF Leak	Not CSF Leak	Unspecified[a]
520	145	22	32	215	106

[a] Unadjudicated due to the timing of the data or due to the site no longer being active.

3.2.3.2Inflammatory Masses

Inflammatory mass (IM), also sometimes reported as catheter-tip inflammatory mass or an intrathecal granuloma, is a potential complication of intrathecal opioid drug therapy. In order to better quantify the incidence of inflammatory mass, all events were evaluated for a report of inflammatory mass. For these identified cases, the medical records were reviewed by Medtronic personnel together with radiographic images when available. The radiographic images were reviewed to determine if there was evidence of an intradural extramedullary enhancing lesion. The adjudication team assessed each case based upon the case definition and ascertainment guideline presented in Table 3.10. A summary of cases evaluated for IM through the data cut-off is shown in Table 3.11.

Table 3.10: Case Definition and Ascertainment of Inflammatory Mass

Case Definition	Ascertainment
Definitive IM	Surgical and histological verification or clinical symptoms plus contrast enhanced MRI or CT myelogram and resolution of lesion following cessation of drug exposure
Probable IM	No surgical or histological verification, but clinical criteria and enhanced MRI or CT myelogram criteria are present
Possible IM	Medical records document IM, but there is no surgical or histological verification, there are no clinical criteria, and no radiographic data are available

Not IM	Surgical and histological verification that lesion is another disease process rather than IM, or radiographic data do not show an intrathecal lesion

There were a total of 136 suspected cases of inflammatory mass (Table 3.11) that were discerned from evaluation of patient records and reviewed by the adjudication team. Medtronic will continue to evaluate reports of inflammatory mass. Any previously classified case of IM will be re-evaluated if new evidence is received after this report. An analysis of the adjudicated definitive and probable inflammatory mass cases in the PSR from 2003 through October 2024 indicates an incidence of 0.22% (18/8,259) for pain patients and 0.00% (0/2,293) for spasticity patients.

Table 3.11: Summary of Inflammatory Mass Adjudication

Year of Event	Cases Reviewed	Definitive IM	Probable IM	Possible IM	Not IM
2004	4	0	0	0	4
2005	4	1	0	1	2
2006	7	1	1	2	3
2007	9	1	1	2	5
2008	4	0	1	0	3
2009	3	1	0	0	2
2010	11	0	1	1	9
2011	11	1	2	1	7
2012	13	0	0	1	12
2013	6	0	0	4	2
2014	10	0	0	2	8
2015	21	1	0	6	14
2016	10	1	1	2	6
2017	9	0	0	1	8
2018	4	1	0	0	3
2019	5	1	0	0	4
2020	3	1	0	1	1
2021	2	0	1	0	1

Year of Event	Cases Reviewed	Definitive IM	Probable IM	Possible IM	Not IM
2022	0	0	0	0	0
2023	0	0	0	0	0
2024	0	0	0	0	0
Total	**136**	**10**	**8**	**24**	**94**

3.2.4 Patient Deaths

In earlier versions of the protocol, deaths were only assessed for the relatedness to the device product performance. After 2010, death assessments were expanded to also include the relationship to the implant procedure and/or therapy. As of the report cut-off, a total of 2,933 patients in the registry had expired. No deaths were reported as a direct result of a product performance event. Although, three deaths were assigned by the physician as possibly related to the implant procedure and/or therapy.

Of the three deaths possibly related to the procedure and/or therapy, one death was due to a pulmonary embolism where the treating physician stated that the event could be possibly related to the withdrawal of the intrathecal medications. The patient had experienced a lack of therapy due to a missed refill visit leading to the withdrawal and not to the device malfunctioning. Medtronic Medical Safety assessed this death event as possibly related to the to the lack of therapy. A second death was reported by the treating physician as due to acute respiratory failure possibly related to the procedure and/or therapy. This patient had a history of persistent upper respiratory tract problems, difficulties swallowing and chronic aspiration as the result of cancer-related treatments. Medtronic Medical Safety assessed this death event as possibly related to the surgery/anesthesia during the implant procedure and therapy. The third death was reported by the physician as due to respiratory distress possibly related to the intrathecal medication. This patient had multiple comorbidities with multiple concomitant medications and a decreased level of physical activity. The death records state the cause of death as probable arteriosclerotic cardiovascular disease. Medtronic Medical Safety determined this event as not assessable due to incomplete information.

Since 2003, a total of 1,476 (50.3%) deaths have been reported in this patient registry study based upon patients receiving therapy for malignant pain, 1,098 (37.4%) for non-malignant pain, 329 (11.2%) for spasticity, 26 (0.9%) for non-malignant pain & spasticity, 1 (<0.1%) for malignant pain & chemotherapy, and 3 (0.1%) for not specified primary indication (see Table 3.12). The percentage is based upon the total patient death events and not based upon the rate of occurrence. **All tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 3.12: Targeted Drug Delivery System Patient Deaths by Primary Indication

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths
Malignant pain	1476 (50.3%)
Non-malignant pain	1098 (37.4%)
Spasticity	329 (11.2%)
Non-malignant pain & Spasticity	26 (0.9%)
Malignant pain & Chemotherapy	1 (<0.1%)
Not Specified	3 (0.1%)
Total	**2933**

[a] For approved indications refer to product labeling for your geography.

3.3 Pumps

From August 7, 2003, to the report cut-off date of October 31, 2024, there were 13,848 pumps followed in the registry. The difference between the total number of patients (n=10,793) versus the total number of pumps is due to the fact that some patients were subsequently re-implanted with a pump multiple times. The aggregate prospective follow-up time for all pumps was 479,590 months (39,966 years). Table 3.13 provides the number and percentage of pumps by model number.

3.3.1 SynchroMed II Design Change: Pump Enhancements; SynchroMed III

Design changes to the SynchroMed II 20 mL and 40 mL pump models were implemented to reduce the likelihood of non-recoverable motor stalls. These changes were released incrementally, allowing for the pumps to be considered in three groups: 1) Pre-Enhancements (prior to 2016), 2) the Modified Gear Wheel Material and Encapsulated Feedthroughs (GW3/FT) enhancements (released January 2016) and 3) the Applied Diamond Like Coating (GW3/FT/DLC) enhancement (released July 2017). All enhancements were communicated in the August 2017 Medical Device Safety Notification: SynchroMed II Implantable Drug Infusion Pump Design Change Model Numbers 8637-20, 8637-40. For details, please visit https://www.medtronic.com/content/dam/medtronic-com/professional/documents/product-advisories/tdd/synchromed-pump-design-change-august-2017-hcp-letter.pdf. Table 3.13 provides the number and percentage of pumps by model and pump enhancement.

The SynchroMed III was released in 2023 and includes the same enhancements as the GW3/FT/DLC pump as well as additional enhancements.

Table 3.13: Targeted Drug Delivery Pump Counts by Model and Pump Enhancement

Model Name	N (%)
SynchroMed III 40 mL	**145 (1.0%)**
GW3/FT/DLC Enhancements	145 (1.0%)
SynchroMed III 20 mL	**45 (0.3%)**
GW3/FT/DLC Enhancements	45 (0.3%)
SynchroMed II 40 mL	**7832 (56.6%)**
Pre-Enhancements[a]	4630 (33.4%)
GW3/FT/DLC Enhancements[a]	2664 (19.2%)
GW3/FT Enhancements[a]	538 (3.9%)
SynchroMed II 20 mL	**4640 (33.5%)**
Pre-Enhancements[a]	2963 (21.4%)
GW3/FT/DLC Enhancements[a]	1315 (9.5%)
GW3/FT Enhancements[a]	362 (2.6%)
SynchroMed EL 18 mL[a]	**1146 (8.3%)**
SynchroMed EL 10 mL[a]	**34 (0.2%)**
SynchroMed Classic[a]	**5 (<0.1%)**
Other/Unspecified	**1 (<0.1%)**
Total	**13848**

[a] No longer manufactured.

The pump product performance-related events by model, pre-SynchroMed II enhancements and post-SynchroMed II enhancements are summarized in the pump models section.

3.3.2 Pump Events

There were 546 product performance-related events with an underlying reported etiology related to pump function. This includes 541 events with a pump etiology and 5 events with both a pump and other etiology (including device and non-device etiologies). Of these, 467 were the initial product performance event that affected pump survival estimates. For pumps in the

registry, the current return rate to Medtronic Returned Product Analysis (RPA) was 26.5% (1,951/7,363). The proportion was based upon the number of registry pumps received by RPA, divided by the sum of the total number of explanted devices and the total number of pumps in patients who have expired. In the 546 pump events, 35.5% (194/546) were assigned as device related by the physician, not returned to Medtronic RPA (see Figure 3.4). For the purposes of survival analysis, a device's follow-up time is cut off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For pumps:

- 467 had follow up time cut-off due to product performance-related events.
- 11,196 were censored in the survival analysis for the following reasons: patient expired, pump explanted, site termination, patient discontinued, patient lost to follow-up, or therapy suspended.
- 2,185 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

3.3.3 Pump Models

The following figures and tables represent the SynchroMed II pump characteristics, survival (including 95% confidence intervals), specifications and events by model. Since the survival estimate may become very imprecise with smaller sample sizes, the device survival curves below are truncated when the sample size is less than 20 active devices for each 3-month interval. The SynchroMed III pump survival is not shown due to small sample size of enrolled and tracked devices. The survival of SynchroMed EL model was not shown since it has no active devices in the PSR. For information on this model, please refer to the 2017 or earlier reports.

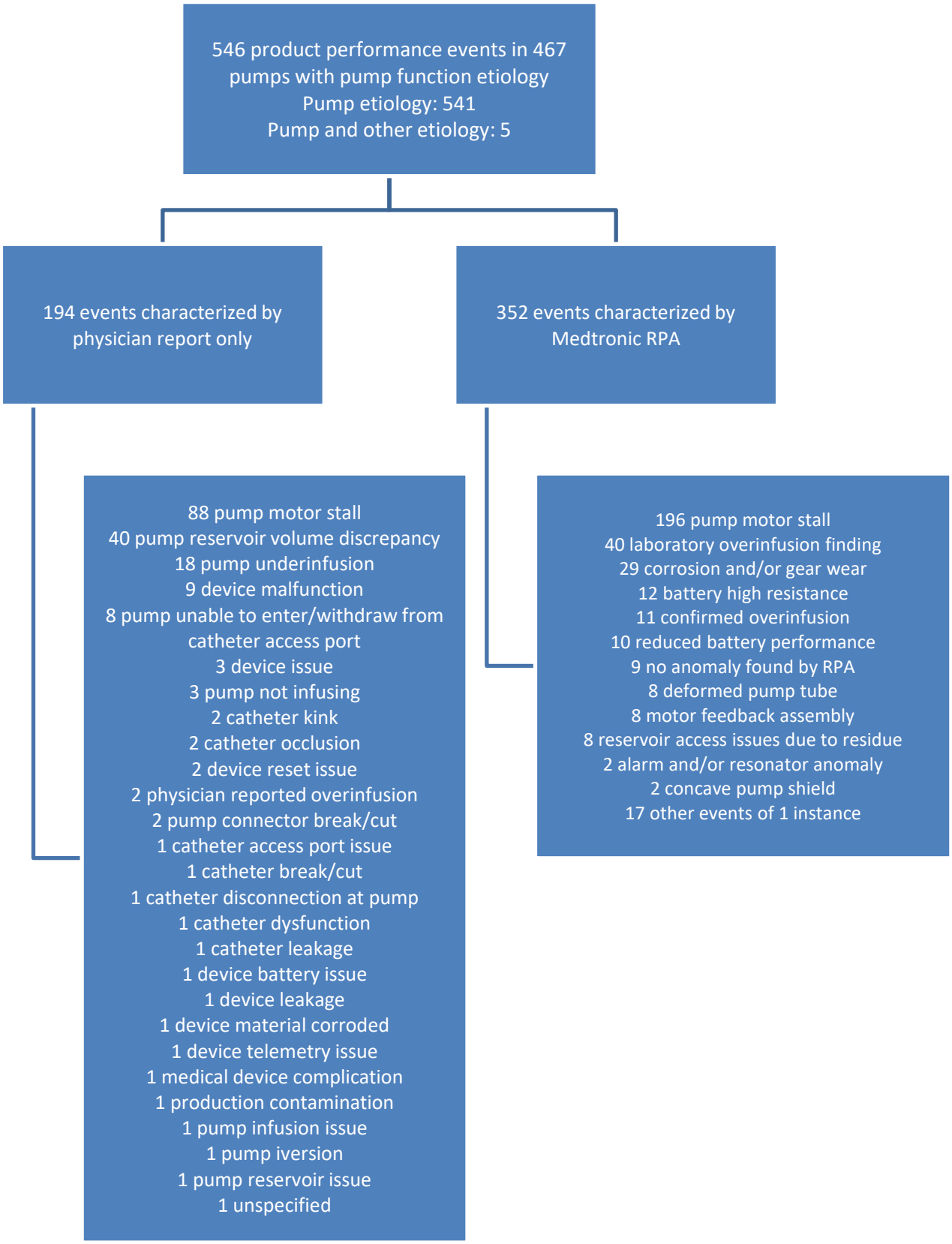
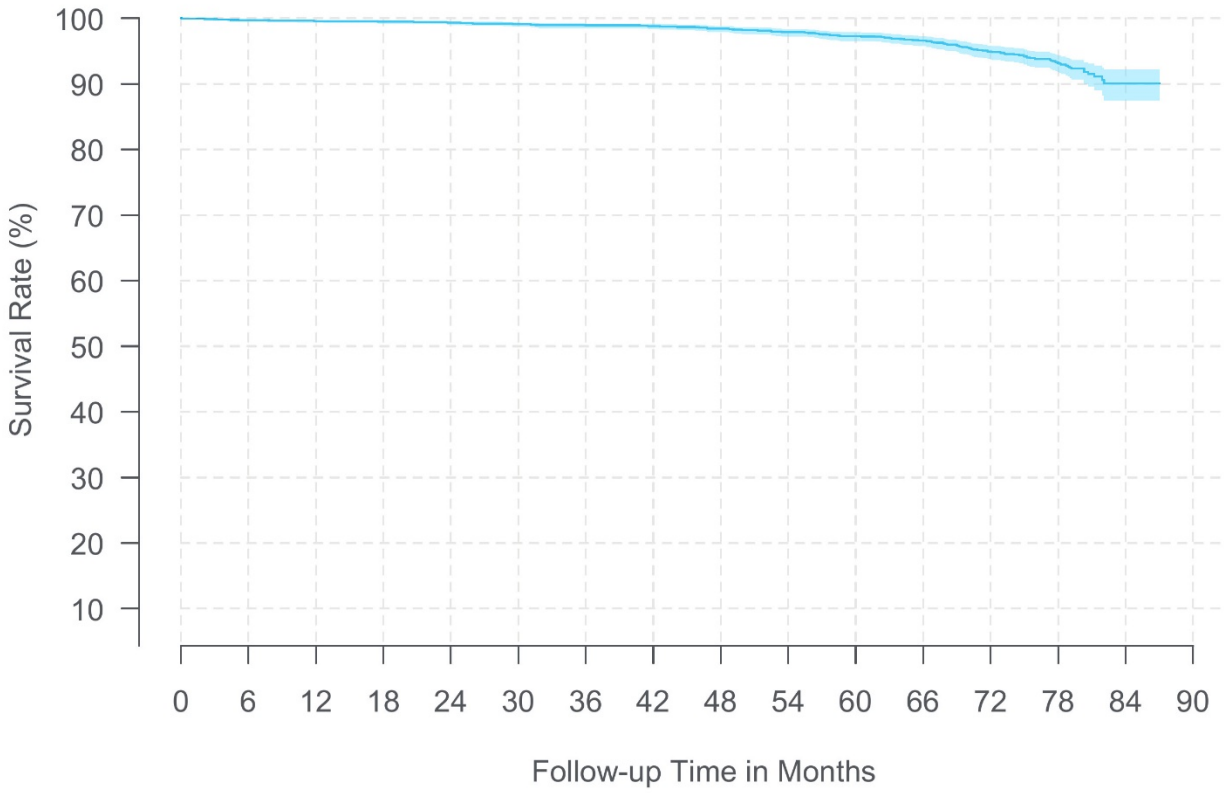


Figure 3.4: Distribution of Pump Function Etiology Product Performance Events

3.3.3.1 Model 8637-20

Model/Name	SynchroMed II 20 mL
FDA Approval Date	September 2003
Pumps Enrolled	4,640
Pumps Currently Active in Study	714
Initial Product Performance Events	129
Median Follow-up Time (Months)	39.0
Cumulative Follow-up Time (Months)	190,651



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.6% (99.3%, 99.8%)	99.4% (99.0%, 99.6%)	98.9% (98.5%, 99.2%)	98.4% (97.9%, 98.8%)	97.3% (96.6%, 97.9%)
Sample Size	3519	2995	2477	2002	1598

Time Interval	6 Years	7 Years	At 87 Months
Survival (95% CI)	94.9% (93.8%, 95.8%)	90.1% (87.5%, 92.2%)	90.1% (87.5%, 92.2%)
Sample Size	1178	44	21

Specification: 8637-20	
Expected battery life[a]	6-7 years
Thickness	0.77 in (19.5 mm)
Diameter	3.4 in (87.5 mm)
Capacity	20.0 mL
Minimal Programmable Flow Rate[b]	0.048 mL/day
Maximum Programmable Flow Rate[b]	24 mL/day
Minimum Rate Infusion Mode[c]	0.006 mL/day

[a] Dependent on flow rate. Designed to shut off at 84 months.

[b] Actual limits depend on pump calibration constant and selected infusion mode.

[c] Nontherapeutic (if therapy is to be temporarily discontinued).

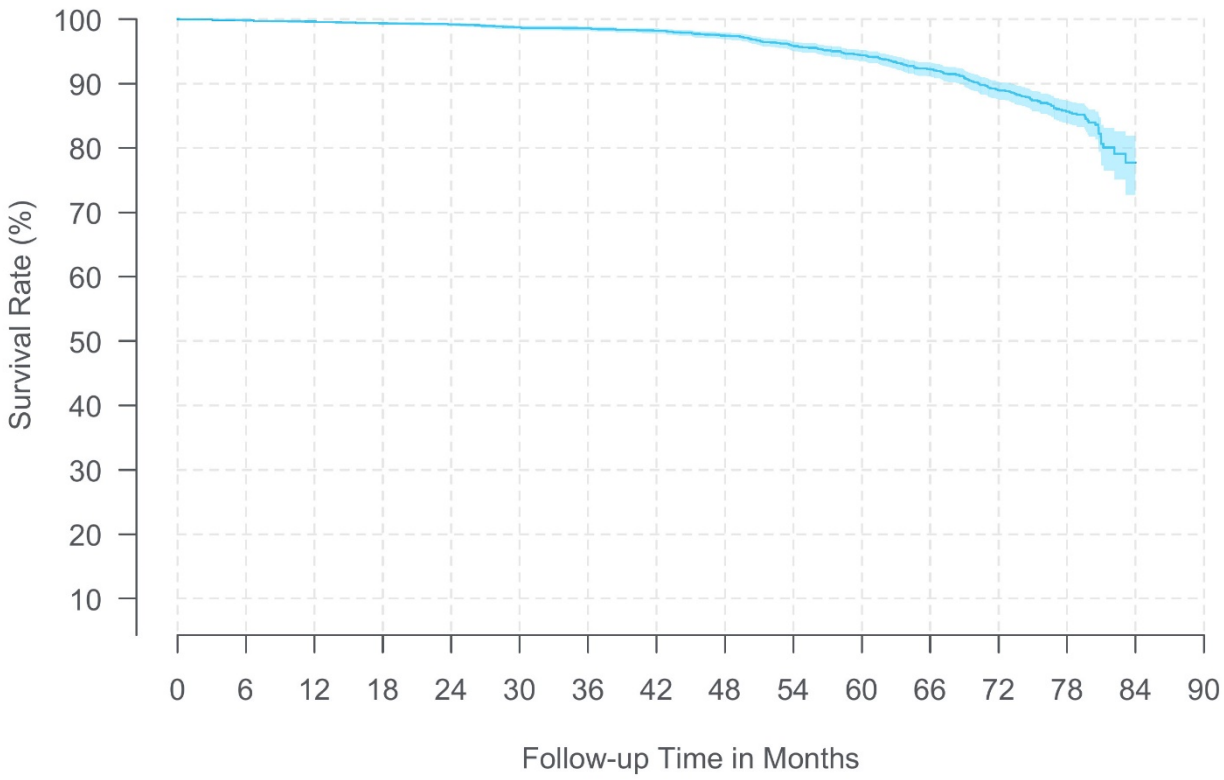
Pump Event Summary: SynchroMed II 20 mL	N
RPA Determination	**78**
Pump Motor Stall	39
Laboratory overinfusion finding	8
Battery High Resistance	7
Corrosion And/Or Gear Wear	4
Motor Feedthrough Anomaly	3

Pump Event Summary: SynchroMed II 20 mL	N
Deformed Pump Tube	2
No Anomaly Found By RPA	2
Reduced Battery Performance	2
Reservoir Access Issues Due To Residue	2
Other[a]	9
Physician's Determination	**51**
Pump Motor Stall	21
Pump Reservoir Volume Discrepancy	10
Device Malfunction	5
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Device Issue	3
Other[a]	8
Total	**129**

[a] Composed of event codes with 1 event each.

3.3.3.2 Model 8637-40

Model/Name	SynchroMed II 40 mL
FDA Approval Date	September 2003
Pumps Enrolled	7,832
Pumps Currently Active in Study	1,303
Initial Product Performance Events	304
Median Follow-up Time (Months)	26.3
Cumulative Follow-up Time (Months)	256,470



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.6% (99.4%, 99.7%)	99.2% (98.9%, 99.4%)	98.6% (98.2%, 98.9%)	97.4% (96.9%, 97.9%)	94.4% (93.5%, 95.2%)
Sample Size	5169	4102	3225	2487	1819

Time Interval	6 Years	7 Years
Survival (95% CI)	89.0% (87.5%, 90.3%)	77.7% (72.7%, 81.9%)
Sample Size	1166	23

Specification: 8637-40	
Expected battery life[a]	6-7 years
Thickness	1.0 in (26 mm)
Diameter	3.4 in (87.5 mm)
Capacity	40.0 mL
Minimal Programmable Flow Rate[b]	0.048 mL/day
Maximum Programmable Flow Rate[b]	24 mL/day
Minimum Rate Infusion Mode[c]	0.006 mL/day

[a] Dependent on flow rate. Designed to shut off at 84 months.

[b] Actual limits depend on pump calibration constant and selected infusion mode.

[c] Nontherapeutic (if therapy is to be temporarily discontinued).

Pump Event Summary: SynchroMed II 40 mL	N
RPA Determination	**212**
Pump Motor Stall	134
Laboratory overinfusion finding	29
Corrosion And/Or Gear Wear	7
No Anomaly Found By RPA	7
Reduced Battery Performance	7
Deformed Pump Tube	5
Confirmed overinfusion	4
Reservoir Access Issues Due To Residue	4
Battery High Resistance	3
Motor Feedthrough Anomaly	3
Concave Pump Shield	2
Other[a]	7
Physician's Determination	**92**
Pump Motor Stall	37
Pump Reservoir Volume Discrepancy	22

Pump Event Summary: SynchroMed II 40 mL	N
Pump Underinfusion	10
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Device Malfunction	2
Pump Not Infusing	2
Other[a]	15
Total	**304**

[a] Composed of event codes with 1 event each.

3.3.3.3 Model 8667-20

Model/Name	SynchroMed III 20 mL
FDA Approval Date	October 2023
Pumps Enrolled	45
Pumps Currently Active in Study	39
Initial Product Performance Events	0
Median Follow-up Time (Months)	0
Cumulative Follow-up Time (Months)	44

There is not sufficient data to report on SynchroMed III 20 mL (model 8667-20) survival at 1 year or later and there have been no reported product performance events for this model as of the data cut-off date.

Specification: 8637-40	
Expected battery life[a]	6-7 years
Thickness	1.0 in (26 mm)
Diameter	3.4 in (87.5 mm)
Capacity	20.0 mL
Minimal Programmable Flow Rate[b]	0.048 mL/day
Maximum Programmable Flow Rate[b]	24 mL/day
Minimum Rate Infusion Mode[c]	0.006 mL/day

[a] Dependent on flow rate. Designed to shut off at 84 months.

[b] Actual limits depend on pump calibration constant and selected infusion mode.

[c] Nontherapeutic (if therapy is to be temporarily discontinued).

3.3.3.4 Model 8667-40

Model/Name	SynchroMed III 40 mL
FDA Approval Date	October 2023
Pumps Enrolled	145
Pumps Currently Active in Study	130
Initial Product Performance Events	0
Median Follow-up Time (Months)	0.4
Cumulative Follow-up Time (Months)	165

There is not sufficient data to report on SynchroMed III 40 mL (model 8667-40) survival at 1 year or later and there have been no reported product performance events for this model as of the data cut-off date.

Specification: 8667-40	
Expected battery life[a]	6-7 years
Thickness	1.0 in (26 mm)
Diameter	3.4 in (87.5 mm)
Capacity	40.0 mL
Minimal Programmable Flow Rate[b]	0.048 mL/day
Maximum Programmable Flow Rate[b]	24 mL/day
Minimum Rate Infusion Mode[c]	0.006 mL/day

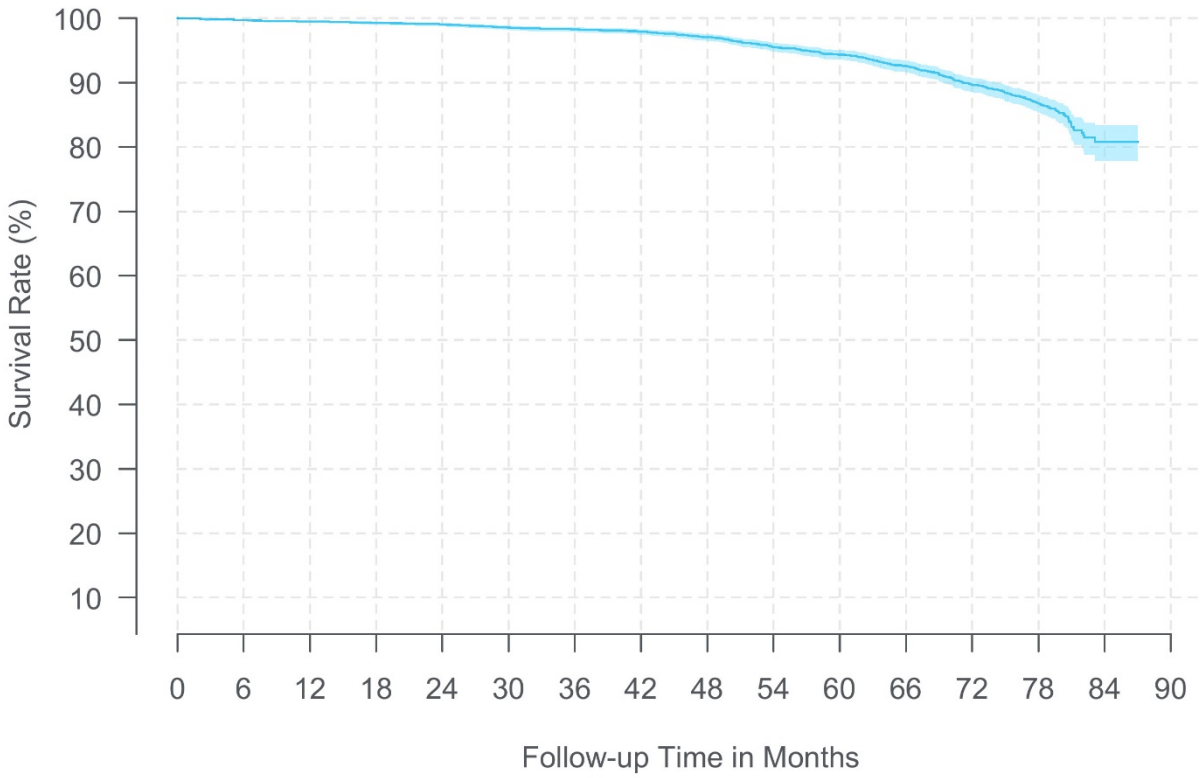
[a] Dependent on flow rate. Designed to shut off at 84 months.

[b] Actual limits depend on pump calibration constant and selected infusion mode.

[c] Nontherapeutic (if therapy is to be temporarily discontinued).

3.3.3.5 SynchroMed II 20 mL and 40 mL: Pre-enhancements

Model/Name	Pre-Enhancements
FDA Approval Date	September 2003
Pumps Enrolled	7,593
Pumps Currently Active in Study	2
Initial Product Performance Events	399
Median Follow-up Time (Months)	34.7
Cumulative Follow-up Time (Months)	294,382



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.5% (99.3%, 99.7%)	99.0% (98.7%, 99.3%)	98.3% (97.9%, 98.6%)	97.0% (96.5%, 97.5%)	94.4% (93.5%, 95.1%)
Sample Size	5294	4575	3818	3159	2567

Time Interval	6 Years	7 Years	At 87 Months
Survival (95% CI)	89.7% (88.5%, 90.8%)	80.8% (77.8%, 83.4%)	80.8% (77.8%, 83.4%)
Sample Size	1891	54	28

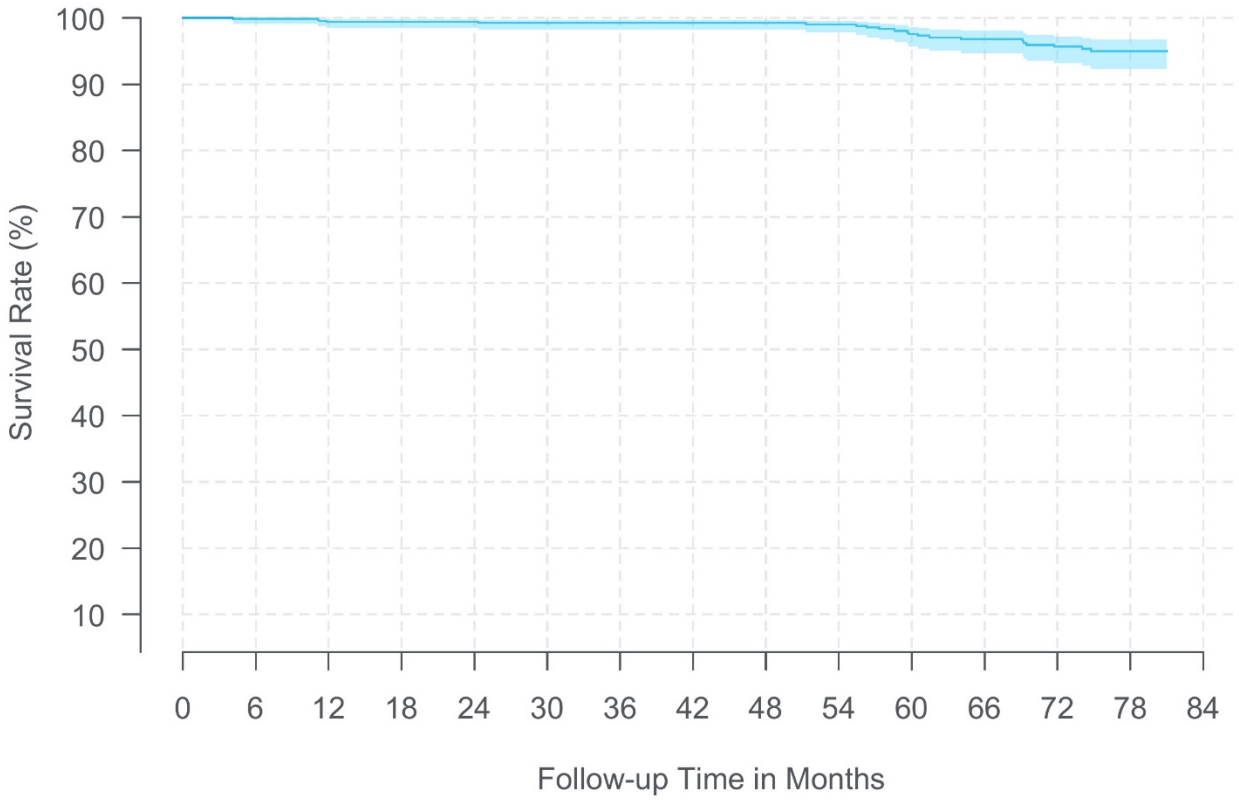
Pump Event Summary: SynchroMed II Pre-enhancements	Total
RPA Determination	**269**
Pump Motor Stall	165
Laboratory overinfusion finding	35
Battery High Resistance	10
Corrosion And/Or Gear Wear	10
Reduced Battery Performance	9
Deformed Pump Tube	6
Motor Feedthrough Anomaly	6
No Anomaly Found By RPA	6
Confirmed overinfusion	5
Reservoir Access Issues Due To Residue	4
Alarm And/Or Resonator Anomaly	2
Concave Pump Shield	2
Other[a]	9
Physician's Determination	**130**
Pump Motor Stall	57
Pump Reservoir Volume Discrepancy	28

Pump Event Summary: SynchroMed II Pre-enhancements	Total
Pump Unable To Enter/Withdraw From Catheter Access Port	8
Pump Underinfusion	8
Device Malfunction	6
Device Issue	3
Pump Not Infusing	3
Catheter Occlusion	2
Physician reported overinfusion	2
Pump Connector Break/Cut	2
Other[a]	11
Total	**399**

[a] Composed of event codes with 1 event each.

3.3.3.6 SynchroMed II 20 mL and 40 mL: GW3/FT Enhancements

Model/Name	GW3/FT Enhancements
FDA Approval Date	September 2015 (GW3)/November 2015 (FT)
Pumps Enrolled	900
Pumps Currently Active in Study	27
Initial Product Performance Events	21
Median Follow-up Time (Months)	48.5
Cumulative Follow-up Time (Months)	40,572



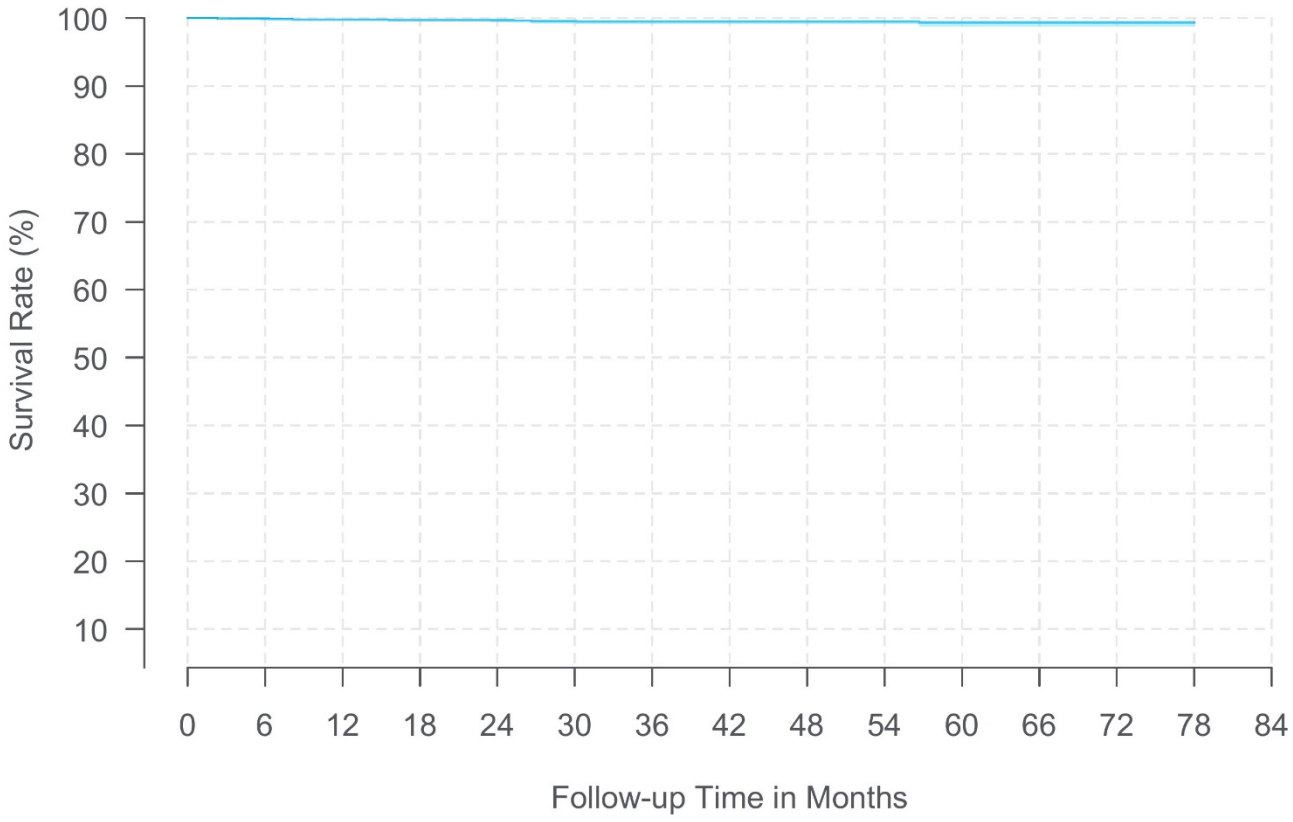
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.4% (98.5%, 99.8%)	99.4% (98.5%, 99.8%)	99.3% (98.2%, 99.7%)	99.3% (98.2%, 99.7%)	97.6% (95.7%, 98.6%)
Sample Size	686	575	507	453	393

Time Interval	6 Years	At 81 Months
Survival (95% CI)	95.7% (93.2%, 97.2%)	95.0% (92.3%, 96.8%)
Sample Size	320	64

Pump Event Summary: SynchroMed II GW3/FT Enhancements	Total
RPA Determination	**14**
Pump Motor Stall	6
No Anomaly Found By RPA	2
Reservoir Access Issues Due To Residue	2
Laboratory overinfusion finding	1
Corrosion And/Or Gear Wear	1
Failed Lab Dispense Test	1
Unknown Root Cause. Battery And Hybrid Tested, No Anomalies Found. The Pump May Have Been Exposed To Some Extreme Condition.	1
Physician's Determination	**7**
Pump Reservoir Volume Discrepancy	2
Pump Motor Stall	1
Catheter Access Port Issue	1
Catheter Disconnection At Pump	1
Pump Infusion Issue	1
Pump Reservoir Issue	1
Total	**21**

3.3.3.7 SynchroMed II 20 mL and 40 mL: GW3/FT/DLC Enhancements

Model/Name	GW3/FT/DLC Enhancements
FDA Approval Date	April 2017 (DLC)
Pumps Enrolled	3,979
Pumps Currently Active in Study	1,988
Initial Product Performance Events	13
Median Follow-up Time (Months)	23.2
Cumulative Follow-up Time (Months)	112,166



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.8% (99.6%, 99.9%)	99.7% (99.4%, 99.8%)	99.5% (99.1%, 99.7%)	99.5% (99.1%, 99.7%)	99.3% (98.7%, 99.7%)
Sample Size	2708	1947	1377	877	457

Time Interval	6 Years	At 78 Months
Survival (95% CI)	99.3% (98.7%, 99.7%)	99.3% (98.7%, 99.7%)
Sample Size	133	50

Pump Event Summary: SynchroMed II GW3/FT/DLC Enhancements	Total
RPA Determination	**7**
Pump Motor Stall[a]	2
Laboratory overinfusion finding	1
Deformed Pump Tube	1
No Anomaly Found By RPA	1
Pump Leak Due To Damage Or Missing O-Ring	1
Reservoir Septum Damage	1
Physician's Determination	**6**
Pump Reservoir Volume Discrepancy	2
Pump Underinfusion	2
Device Malfunction	1
Catheter Kink	1
Total	**13**

[a] Motor stall that occurred within 7 months of implant due to unknown cause.

3.3.4 Pump Summary

Table 3.14: Targeted Drug Delivery Pump Characteristics

Model/Name	FDA Approval Date	Pumps Enrolled	Pumps Active	Initial Product Performance Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
SynchroMed II 20 mL	September 2003	4,640	714	129	39.0	190,651
SynchroMed II 40 mL	September 2003	7,832	1,303	304	26.3	256,470
SynchroMed II Pre-enhancements[a]	September 2003	7,593	2	399	34.7	294,382
SynchroMed II GW3/FT enhancements[a]	September 2015 (GW3) November 2015 (FT)	900	27	21	48.5	40,572
SynchroMed II GW3/FT/DLC enhancements[a]	April 2017 (DLC)	3,979	1,988	13	23.2	112,166
SynchroMed III 20 mL	October 2023	45	39	0	0.0	44
SynchroMed III 40 mL	October 2023	145	130	0	0.4	165

[a] For explanation of enhancements see Section 3.3.1.

Table 3.15: Targeted Drug Delivery Pump Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
SynchroMed II 20 mL	99.6%	99.4%	98.9%	98.4%	97.3%
	(99.3%, 99.8%)	(99.0%, 99.6%)	(98.5%, 99.2%)	(97.9%, 98.8%)	(96.6%, 97.9%)
SynchroMed II 40 mL	99.6%	99.2%	98.6%	97.4%	94.4%
	(99.4%, 99.7%)	(98.9%, 99.4%)	(98.2%, 98.9%)	(96.9%, 97.9%)	(93.5%, 95.2%)
SynchroMed II Pre-Enhancements	99.5%	99.0%	98.3%	97.0%	94.4%

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
	(99.3%, 99.7%)	(98.7%, 99.3%)	(97.9%, 98.6%)	(96.5%, 97.5%)	(93.5%, 95.1%)
SynchroMed II GW3/FT Enhancements	99.4%	99.4%	99.3%	99.3%	97.6%
	(98.5%, 99.8%)	(98.5%, 99.8%)	(98.2%, 99.7%)	(98.2%, 99.7%)	(95.7%, 98.6%)
SynchroMed II GW3/FT/DLC Enhancements	99.8%	99.7%	99.5%	99.5%	99.3%
	(99.6%, 99.9%)	(99.4%, 99.8%)	(99.1%, 99.7%)	(99.1%, 99.7%)	(98.7%, 99.7%)

Model Name	6 Years	7 Years
SynchroMed II 20 mL	94.9%	90.1%
	(93.8%, 95.8%)	(87.5%, 92.2%)
SynchroMed II 40 mL	89.0%	77.7%
	(87.5%, 90.3%)	(72.7%, 81.9%)
SynchroMed II Pre-Enhancements	89.7%	80.8%
	(88.5%, 90.8%)	(77.8%, 83.4%)
SynchroMed II GW3/FT Enhancements	95.7%	
	(93.2%, 97.2%)	
SynchroMed II GW3/FT/DLC Enhancements	99.3%	
	(98.7%, 99.7%)	

Table 3.16: Targeted Drug Delivery SynchroMed II Pump Events by Enhancements

Pump Event	Pre-Enhancements	GW3/FT Enhancements	GW3/FT/DLC Enhancements
RPA Determination	**269**	**14**	**7**
Pump Motor Stall	165	6	2
Laboratory overinfusion finding	35	1	1
Battery High Resistance	10	0	0
Corrosion And/Or Gear Wear	10	1	0
Reduced Battery Performance	9	0	0
Deformed Pump Tube	6	0	1
Motor Feedthrough Anomaly	6	0	0
No Anomaly Found By RPA	6	2	1
Confirmed overinfusion	5	0	0
Reservoir Access Issues Due To Residue	4	2	0
Alarm And/Or Resonator Anomaly	2	0	0
Concave Pump Shield	2	0	0
Failed Lab Dispense Test	0	1	0
Pump Leak Due To Damage Or Missing O-Ring	0	0	1
Reservoir Septum Damage	0	0	1
Unknown Root Cause. Battery And Hybrid Tested, No Anomalies Found. The Pump May Have Been Exposed To Some Extreme Condition.	0	1	0
Other[a]	9	0	0
Physician's Determination	**130**	**7**	**6**
Pump Motor Stall	57	1	0
Pump Reservoir Volume Discrepancy	28	2	2
Pump Unable To Enter/Withdraw From Catheter Access Port	8	0	0
Pump Underinfusion	8	0	2

Pump Event	Pre-Enhancements	GW3/FT Enhancements	GW3/FT/DLC Enhancements
Device Malfunction	6	0	1
Device Issue	3	0	0
Pump Not Infusing	3	0	0
Catheter Occlusion	2	0	0
Physician reported overinfusion	2	0	0
Pump Connector Break/Cut	2	0	0
Catheter Access Port Issue	0	1	0
Catheter Disconnection At Pump	0	1	0
Pump Infusion Issue	0	1	0
Pump Reservoir Issue	0	1	0
Other[a]	11	0	0
Total	**399**	**21**	**13**

[a] Composed of event codes with 1 event each for SynchroMed II Pre-Enhancements.

3.4 SynchroMed II Pumps Exposed to On-Label and Off-Label Medications

The purpose of this analysis is to provide additional information regarding the product performance of SynchroMed II pumps exposed to On-Label and Off-Label medications. This report contains information outside the FDA approved labeling for the Medtronic SynchroMed II Infusion System. The long-term drug stability/compatibility and safety and/or efficacy of drugs not listed in the SynchroMed II Infusion System product labeling have not been established in the United States. It is recognized that healthcare providers prescribe therapies to meet specific patient needs; however, Medtronic only directs the use of its products based on approved regulatory labeling. For the purposes of this report, On-Label and Off-Label determinations have been made based on the United States FDA approved labeling. However, product labeling varies by geography, so please contact your local Medtronic representative by going to the SynchroMed™ III Intrathecal Pump | Medtronic website and clicking on "Contact and Support" for region-specific product labeling.

In this registry, patient status updates were obtained at least annually, until discontinuation of therapy, or until the patient was lost to follow-up. Medications within the pump were recorded at least annually. The interim data collection provided a snapshot of medication use at these points in time. This data is only for SynchroMed II pumps and does not include SynchroMed III pumps.

3.4.1 Pump Groups On/Off-Label Categorization

Through October 31, 2024, 9,543 patients (56.0% female, mean/SD age 54.2/17.5 years) have enrolled in the registry and have been implanted with 12,472 SynchroMed II pumps. At least one drug record was available on each of 11,786 pumps; if no drug records were available (n=686 pumps), the pump was excluded from this analysis. 11,786 pumps were categorized as being On- or Off-Label using the following criteria:

- **On-Label:** If a pump has at least one drug record in the registry, and none of the records show Off-Label drug exposure, that pump is considered On-Label even if the complete drug history of that pump is unknown.
  - For pumps used for pain patients, if the drug record has only one drug and it was morphine or ziconotide (or their brand names), and it was not a compounded drug, these pumps were considered On-Label. Note: The classification was based on the name of the drug only, not the reported concentration of the drug.
  - For pumps used for spasticity patients, if the drug record has only one drug, and it is either Lioresal® (baclofen injection) or Gablofen® (baclofen injection), that drug record was considered On-Label. Note: The classification was based on the name of the drug only, not the reported concentration of the drug. For this analysis, if only the generic chemical classification, such as baclofen, was entered then the assumption was that the drug was On-Label.
  - Pumps with an On-Label drug history and currently containing preservative free water or preservative free saline, or if previously contained preservative free water/saline and currently containing On-Label drug were considered On-Label.
- **Off-Label:** Any drugs not within the approved indications specified above are considered Off-Label. Additionally, any drug record with more than one drug at a time in the pump (admixture) was considered Off-Label.
  - If a pump had any known exposure to Off-Label drugs (i.e., the Off-Label data have been collected in the registry), that pump was considered Off-Label, regardless of the amount of exposure time.
  - If a pump is filled with a medication that was reported as compounded, that pump was considered Off-Label.

3.4.2 Data Analysis

Survival estimates were calculated using the methods described in the Methodology section of this report. Statistical testing that compared survival curves was performed using a Cox proportional-hazards model. Since the survival estimate may become very imprecise with small sample sizes, Medtronic Neuromodulation's registry truncates device survival curves when the sample size is less than 20 active devices. At this threshold, one device failure yields a 5% decrease in cumulative survival. Additionally, the standard error for this survival estimate is approximately 5% (depending on previous conditional survival estimates), with 95% confidence intervals of approximately ±10%. Overall, this large variability of 20% around the cumulative survival estimate would greatly reduce the precision for the point estimate.

Pump survival from product performance-related events was calculated and compared for the following groups:

- Total study population: On-Label vs. Off-Label Drugs (including all indications)
- Pain study population: On-Label vs. Off-Label Drugs (including all pain indications)
- Spasticity study population: On-Label vs. Off-Label Drugs (including all spasticity indications)

Additionally, the cumulative failure rate (i.e., the estimated probability that a pump will have a product performance-related event by a given time point) is presented in table and graph formats for each of the sub-groups listed above.

3.4.3 Results

A total of 3,564 (30.2%) SynchroMed II pumps were classified as On-Label where there was no evidence of Off-Label drug/admixture exposure. A total of 8,222 (69.8%) pumps were classified as Off-Label where there was evidence of pump exposure to an Off-Label drug/admixture. There were a total of 433 reported SynchroMed II pump product performance events during the study observation period. Of the 433 pump product performance events, 430 of those were the first event and included as failures in the survival analysis. In addition to the 430 pump failures, there were 15 SynchroMed II pumps explanted due to normal battery depletion by the physician, which were returned to Medtronic and had an RPA observation of high battery resistance. For this analysis, these pumps were not considered failures, because they represented normal implant duration (ranging from 5.6 to 6.8 years) with no associated physician or patient complaint.

Three of the 433 pump failure events occurred in pumps with no drug records available. Of the remaining 430 SynchroMed II pump failures, 231 were classified as pump failure due to motor stall (with or without documented motor corrosion). The remaining pump failures were due to events such as inconsistent pump reservoir volume, overinfusion, corrosion and/or gear wear, device malfunction, reduced battery performance, pump underinfusion, and other non-conforming reasons. Overall, the rate of pump failures in this cohort was 3.6% (430/11,786) with a median follow-up of 33.0 months.

For the 231 pump failures due to motor stall, 99 of the events were associated with the patient presenting clinical signs or symptoms of possible drug withdrawal or increasing pain or spasticity. The other 132 events had no patient reported signs or symptoms associated with the event but had a physician report of a motor stall occurrence.

Table 3.17: Targeted Drug Delivery Primary Indications by On/Off-Label Pump Groups

Primary Indication[a]	On-Label N=3564	Off-Label N=8222
Non-Malignant Pain	1026 (14.2%)	6212 (85.8%)
Malignant Pain	47 (2.9%)	1557 (97.1%)
Spasticity	2491 (90.7%)	255 (9.3%)
Multiple/Unknown	0 (0.0%)	198 (100%)

[a] For approved indications refer to product labeling for your geography.

3.4.3.1 Total Study Population

A total of 3,564 SynchroMed II pumps were classified as On-Label for all therapies, where there was no evidence of Off-Label drug/admixture exposure. A total of 8,222 pumps were classified as Off-Label where there was evidence of pump exposure to an Off-Label drug/admixture. The cumulative survival and failure of the SynchroMed II pump for all indications, stratified by the On-Label or Off-Label pump group, are shown in Figure 3.5 and Figure 3.6 respectively.

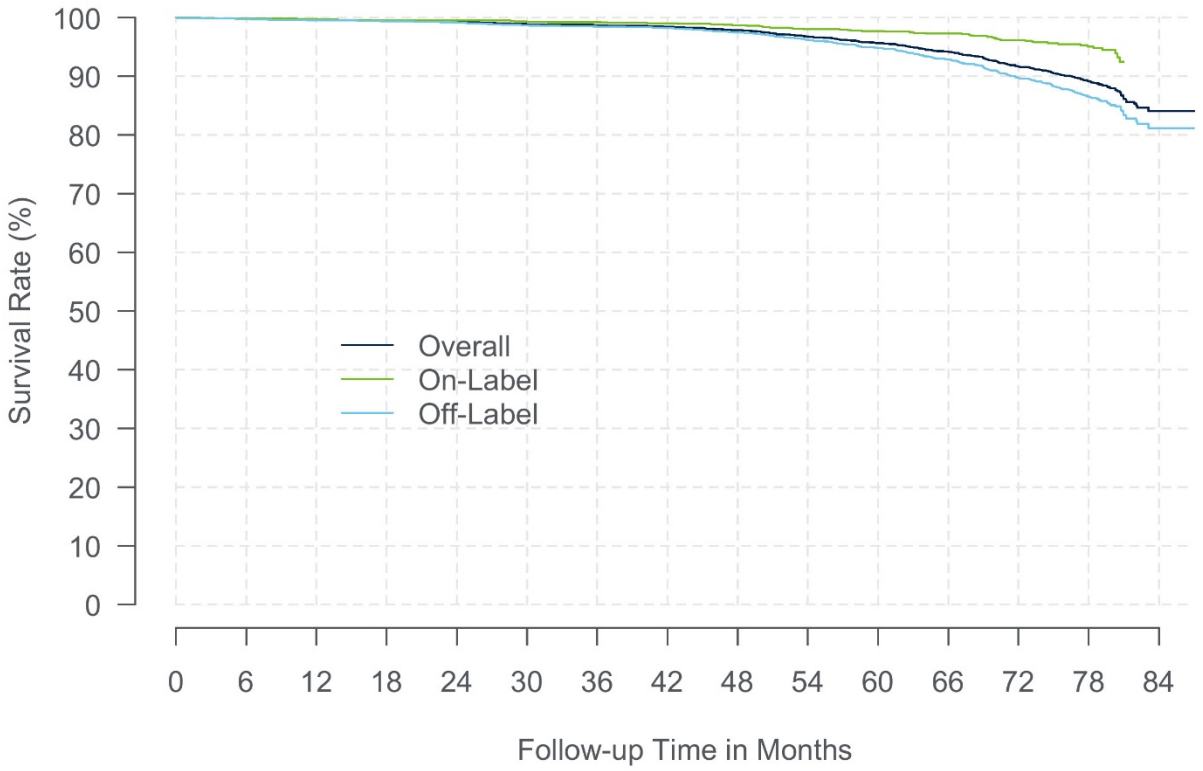


Figure 3.5: SynchroMed II Cumulative Survival (All Therapies)

Table 3.18: Survival Summary Table: All Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	At 87 Mos
Overall	Survival	99.6%	99.3%	98.7%	97.8%	95.7%	91.7%	84.1%	84.1%
	Sample Size	8468	7002	5658	4454	3397	2335	66	31
On-Label	Survival	99.7%	99.5%	99.2%	98.7%	97.7%	96.2%	-	-
	Sample Size	2598	2145	1704	1311	1024	783	-	-
Off-Label	Survival	99.6%	99.2%	98.5%	97.5%	94.8%	89.8%	81.2%	81.2%
	Sample Size	5870	4857	3954	3143	2373	1552	48	24

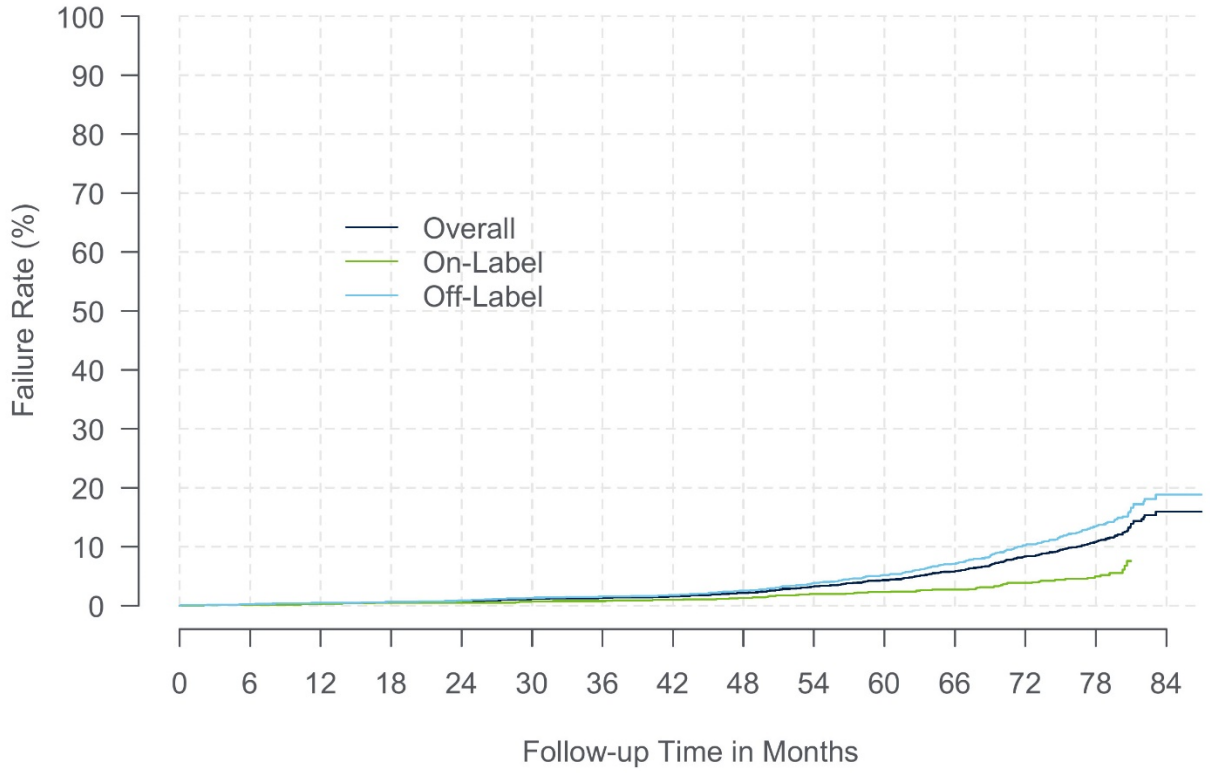


Figure 3.6: SynchroMed II Cumulative Failure (All Therapies)

Table 3.19: Failure Summary Table: All Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	At 87 Mos
Overall	Failure	0.4%	0.7%	1.3%	2.2%	4.3%	8.3%	15.9%	15.9%
	Sample Size	8468	7002	5658	4454	3397	2335	66	31
On-Label	Failure	0.3%	0.5%	0.8%	1.3%	2.3%	3.8%	-	-
	Sample Size	2598	2145	1704	1311	1024	783	-	-
Off-Label	Failure	0.4%	0.8%	1.5%	2.5%	5.2%	10.2%	18.8%	18.8%
	Sample Size	5870	4857	3954	3143	2373	1552	48	24

3.4.3.2 Pain Study Population

A total of 1,073 SynchroMed II pumps were classified as On-Label for pain therapies, where there was no evidence of Off-Label drug/admixture exposure. A total of 7,769 pumps were classified as Off-Label where there was evidence of pump exposure to an Off-Label drug/admixture. The cumulative survival and failure of the SynchroMed II pump for pain indications, stratified by the On-Label or Off-Label pump group, are shown in Figure 3.7 and Figure 3.8 respectively.

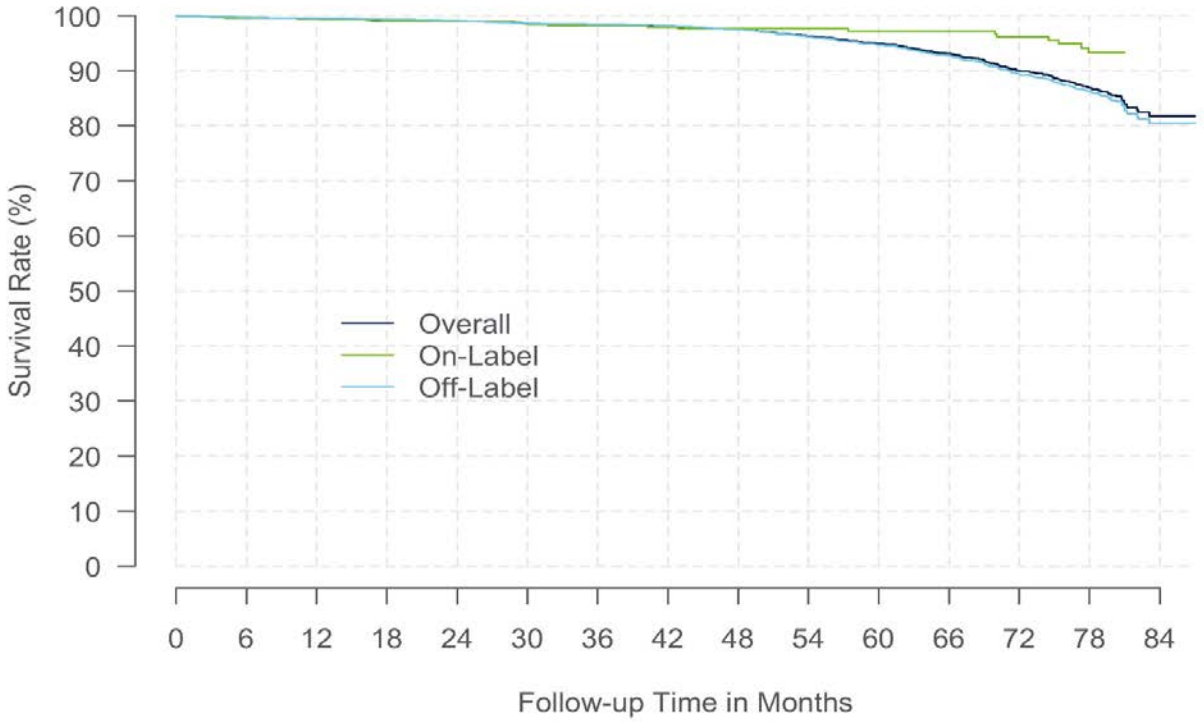


Figure 3.7: SynchroMed II Cumulative Survival (Pain Therapies)

Table 3.20: Survival Summary Table: Pain Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	At 87 Mos
Pain Overall	Survival	99.5%	99.1%	98.5%	97.5%	95.0%	90.0%	81.8%	81.8%
	Sample Size	6228	5108	4107	3214	2431	1605	52	25
On Label	Survival	99.5%	99.1%	98.2%	97.7%	97.3%	96.2%	-	-
	Sample Size	727	556	408	286	225	175	-	-
Off Label	Survival	99.5%	99.1%	98.5%	97.5%	94.8%	89.4%	80.5%	80.5%
	Sample Size	5501	4552	3699	2928	2206	1430	45	22

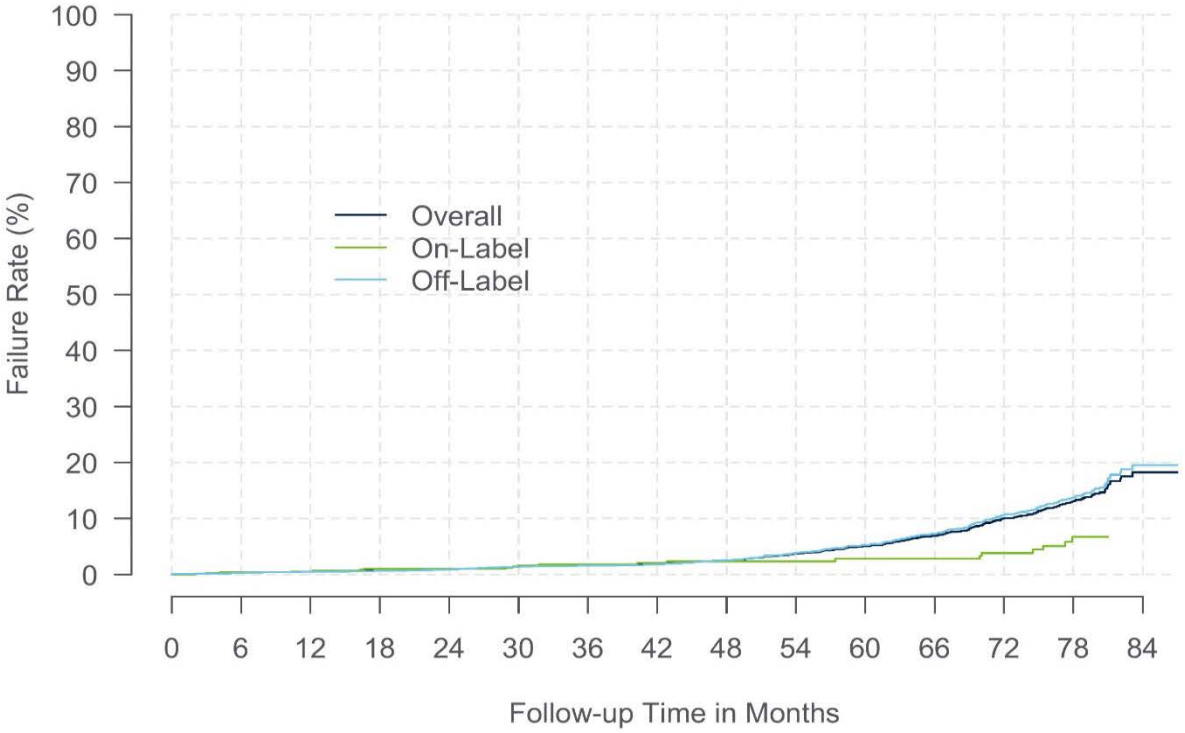


Figure 3.8: SynchroMed II Cumulative Failure (Pain Therapies)

Table 3.21: Failure Summary Table: Pain Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	At 87 Mos
Overall	Failure	0.5%	0.9%	1.5%	2.5%	5%	10%	18.2%	18.2%
	Sample Size	6228	5108	4107	3214	2431	1605	52	25
On-Label	Failure	0.5%	0.9%	1.8%	2.3%	2.7%	3.8%	-	-
	Sample Size	727	556	408	286	225	175	-	-
Off-Label	Failure	0.5%	0.9%	1.5%	2.5%	5.2%	10.6%	19.5%	19.5%
	Sample Size	5501	4552	3699	2928	2206	1430	45	22

3.4.3.3 Spasticity Study Population

A total of 2,491 SynchroMed II pumps were classified as On-Label for spasticity therapies, where there was no evidence of Off-Label drug/admixture exposure. A total of 255 pumps were classified as Off-Label where there was evidence of pump exposure to an Off-Label drug/admixture. The cumulative survival and failure of the SynchroMed II pump for spasticity indications, stratified by the On-Label or Off-Label pump group, are shown in Figure 3.9 and Figure 3.10 respectively.

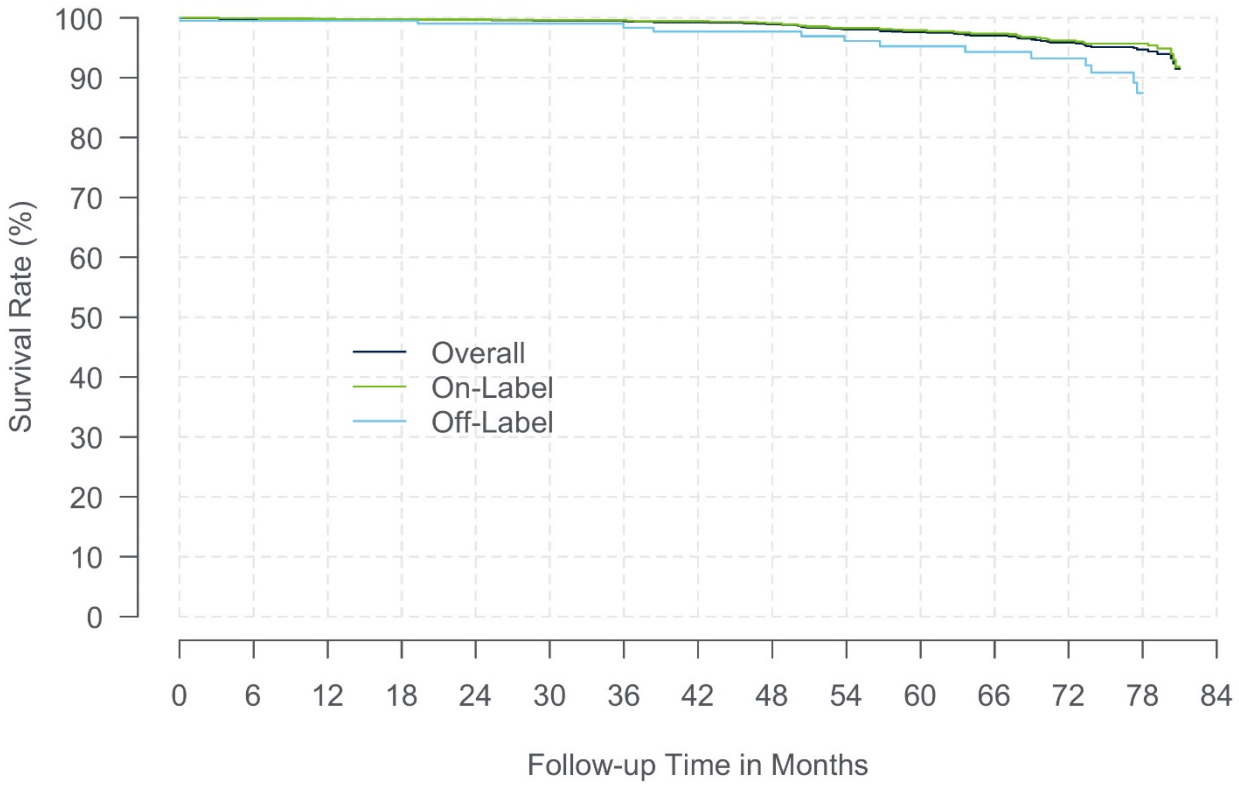


Figure 3.9: SynchroMed II Cumulative Survival (Spasticity Therapies)

Table 3.22: Survival Summary Table: Spasticity Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	At 81 Mos
Overall	Survival	99.8%	99.7%	99.5%	98.9%	97.6%	95.9%	91.5%
	Sample Size	2078	1766	1445	1157	904	690	77
On-Label	Survival	99.8%	99.7%	99.6%	99.1%	97.9%	96.2%	91.8%
	Sample Size	1871	1589	1296	1025	799	608	60
Off-Label	Survival	99.5%	99.0%	98.4%	97.7%	95.3%	93.3%	-
	Sample Size	207	177	149	132	105	82	-

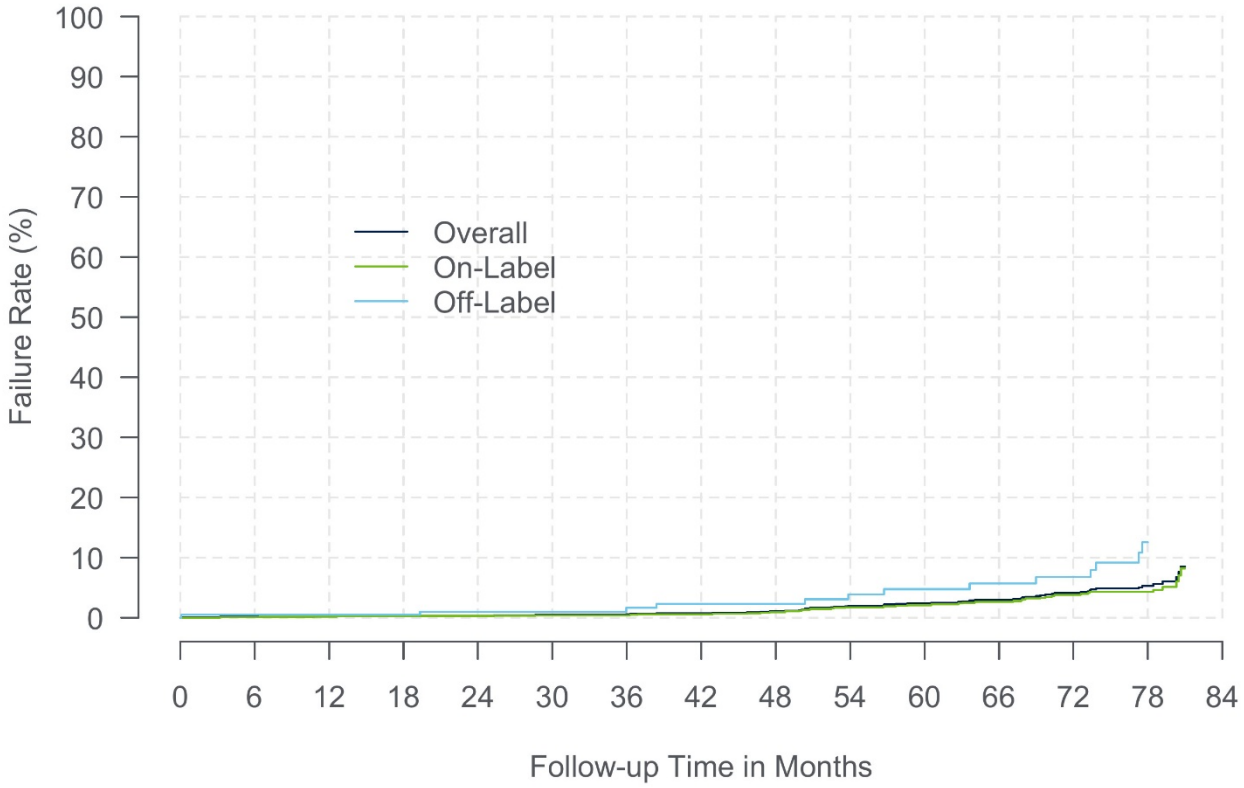


Figure 3.10: SynchroMed II Cumulative Failure (Spasticity Therapies)

Table 3.23: Failure Summary Table: Spasticity Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	At 81 Mos
Overall	Failure	0.2%	0.3%	0.5%	1.1%	2.4%	4.1%	8.5%
	Sample Size	2078	1766	1445	1157	904	690	77
On-Label	Failure	0.2%	0.3%	0.4%	0.9%	2.1%	3.8%	8.2%
	Sample Size	1871	1589	1296	1025	799	608	60
Off-Label	Failure	0.5%	1%	1.6%	2.3%	4.7%	6.7%	-
	Sample Size	207	177	149	132	105	82	-

3.4.4 Overall Summary and Limitations

- Pump failures have been observed in pumps with both On-Label and Off-Label medications used for all indications over the follow-up period.
- Among pre-enhanced devices (n = 7,593), Off-Label medication exposure is associated with an overall 2.6 times greater risk of pump failures (95% confidence interval [1.963, 3.367]) compared to On-Label medication exposure for the entire pump population. The rate of pump failure accelerates in the Off-Label group after 48 months of follow-up. At 81 months of follow-up the survival from pump failure for On-Label pumps was 91.9% compared to a survival of 81.7% for Off-Label pumps.
- Among fully enhanced devices (n = 3,583), Off-Label medication exposure is associated with an overall 1.4 times greater risk of pump failures (95% confidence interval [0.384, 5.075]) compared to On-Label medication exposure for the entire pump population. At 6 years of follow-up the survival from pump failure for On-Label pumps was 99.1% compared to a survival of 99.4% for Off-Label pumps.
- The data represent the reported registry experience with a median follow-up time of 34.7 months for pre-enhanced devices and 19.8 months for fully enhanced devices. The longer-term data are based on a lower number of pumps and are subject to change as more follow-up data are obtained via the registry. Survival curve truncation or plateaus do not imply that the implanted devices will not be adversely impacted beyond the time points of the current data.
- The On-Label pump group for all devices (pre-enhanced and fully enhanced) was comprised of 69.9% of pumps with Spasticity as the indication (2,491/2,746 total spasticity pumps vs. 1,073/8,842 total pain pumps: Spasticity versus Pain pumps respectively). While the Off-Label group consisted of 94.5% of pumps with pain indications (7,769 vs. 255: Pain versus Spasticity pumps respectively).
- Medication use was recorded as a snapshot at the time of follow-up. It is possible that some On-Label pumps received Off-Label medications in between follow-up periods. In addition, it is possible that some pumps designated as On-Label received compounded formulation of an On-Label equivalent but was not designated as such in the registry database. The time a pump was exposed to an Off-Label medication was not assessed. It is possible that some Off-Label pumps were exposed only for a brief period of time (e.g. < 6 months).
- The risk of pump failure by type of Off-Label drug was not assessed. Many Off-Label pumps were exposed to multiple medications over the life span of the pump. This limits the ability to associate a specific drug, compounded drug, drug concentration, or drug combination with increased pump failure risk.

3.5 Catheters

From August 7, 2003, to the report cut-off date of October 31, 2024, there were 12,199 catheters followed in the registry. The total number of catheters was not equal to the total number of pumps (n=13,848) because patients may have undergone pump replacements but used the same catheters, or patients may have been implanted with Medtronic pumps and non-Medtronic catheters which were not registered with Medtronic Device And Registrant Tracking (DART) system. The use of a non-Medtronic catheter with a Medtronic pump is considered off-label. The aggregate prospective follow-up time for all catheters was 473,340 months (39,445 years). Table 3.24 provides the number and percentage of catheters by model.

Table 3.24: Targeted Drug Delivery Catheter Counts by Model

Model Name	N (%)
Currently Manufactured[a]	**3495 (28.6%)**
8780 (US & OUS)	1659 (13.6%)
8781 (US & OUS)	1552 (12.7%)
8731SC (OUS)	284 (2.3%)
Revised Catheters	**2816 (23.1%)**
Revised As Designed[b]	872 (7.1%)
Revised Not As Designed[c]	742 (6.1%)
Ascenda Revised As Designed[d]	681 (5.6%)
Grafted Not As Designed[e]	521 (4.3%)
No Longer Manufactured	**5425 (44.5%)**
8709	2925 (24%)
8709SC	1110 (9.1%)
8711	665 (5.5%)
8731	538 (4.4%)
8703W	187 (1.5%)
Other/Unspecified	**463 (3.8%)**
Total	**12199 (100%)**

[a] Manufactured for designated region; US=United States; OUS=Outside United States.

[b] 8731 catheters repaired with an 8596 proximal or 8598 distal revision kit.

[c] Medtronic non-Ascenda catheters repaired with aMedtronic revision kit, but not for the model it was intended.

[d] 8780 or 8781 Ascenda catheters repaired with the 8782 or 8784 revision kit.

[e] Catheters that involve the ad-hoc assembly of components other than a Medtronic repair kit or brand-new catheter.

3.5.1 Catheter Events

There were 1,876 product performance-related events with an underlying reported etiology related to catheter function. This includes 1,862 events with a catheter etiology and 14 events with both a catheter and other etiology (including device and non-device etiologies). The majority of the events were catheter occlusion (n=531), catheter dislodgement (n=424), catheter kink (n=277), or catheter break/cut (n=271). Of the 1,876 events, 1,599 were the initial product performance event that affected catheter survival estimates.

The catheter product performance-related events are summarized by model in the catheter models section.

For the purposes of survival analysis, a device's follow-up time is cut off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For catheters:

- 1,599 had follow-up time cut-off due to product performance-related events.
- 8,577 were censored in the survival analysis for the following reasons: patient expired, catheter explanted/capped, site termination, patient discontinued, patient lost to follow-up, or therapy suspended.
- 2,023 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

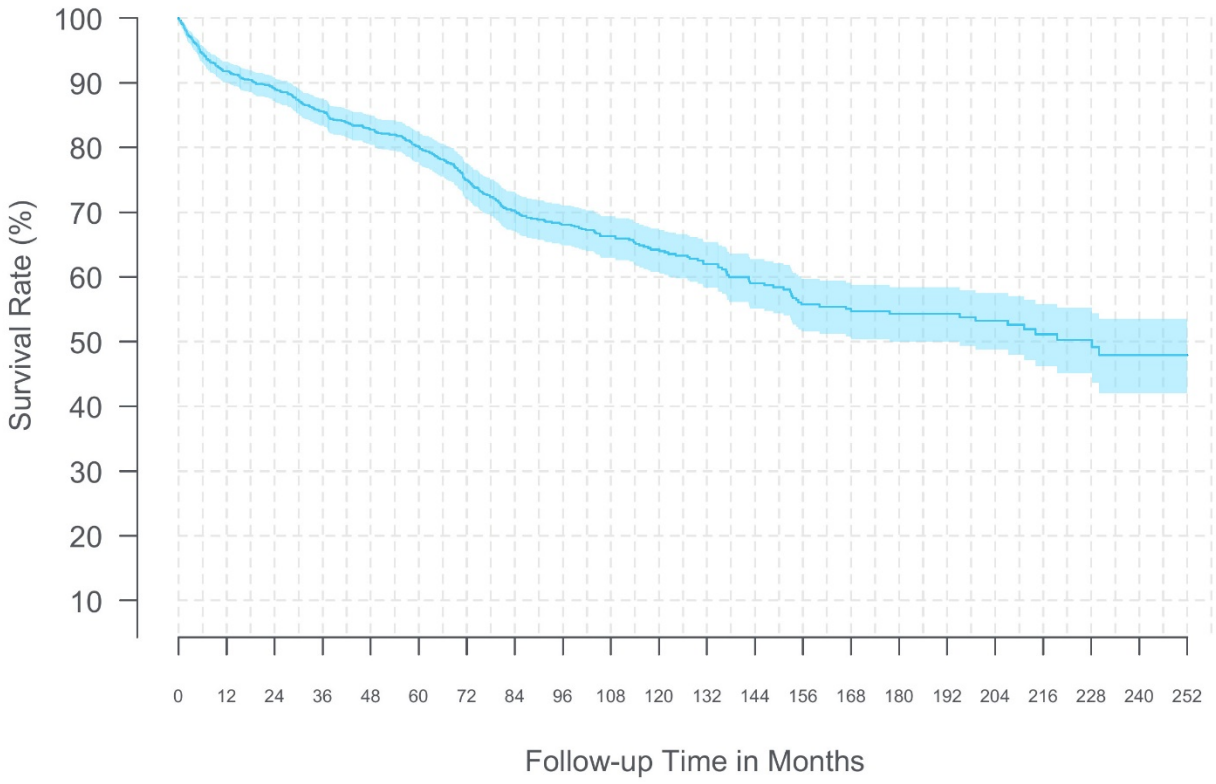
3.5.2 Catheter Models

The figures and tables below represent catheter survival and 95% confidence intervals where at least 20 catheters contributed to each 3-month interval. Survival curves are only shown if more than 20 devices had at least 12 months of follow-up at the time of the report cut-off for each model.

Medtronic catheter repair kits and 2-piece catheters include specially designed connector pins and strain relief sleeves to splice the catheter segments together. Catheters grafted not as designed, by definition, involve the ad-hoc assembly of components other than those from a Medtronic repair kit or brand-new catheter. Medtronic recommends that clinicians follow the labeling for the catheter revision kits.

3.5.2.1 Model 8709

Model/Name	8709/InDura
FDA Approval Date	May 1998
Catheters Enrolled	2,925
Catheters Currently Active in Study	92
Initial Product Performance Events	366
Median Follow-up Time (Months)	18.0
Cumulative Follow-up Time (Months)	102,675



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.8% (90.1%, 93.3%)	89.1% (87.1%, 90.8%)	85.6% (83.4%, 87.5%)	82.8% (80.4%, 84.9%)	80.1% (77.6%, 82.4%)
Sample Size	996	943	876	781	670

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	75.0% (72.1%, 77.6%)	70.3% (67.2%, 73.1%)	68.1% (64.9%, 71.0%)	66.3% (63.0%, 69.4%)	64.2% (60.8%, 67.5%)
Sample Size	577	505	422	338	286

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	62.0% (58.4%, 65.4%)	59.0% (55.1%, 62.7%)	55.7% (51.5%, 59.7%)	54.7% (50.4%, 58.8%)	54.3% (50.0%, 58.4%)
Sample Size	232	185	163	150	137

Time Interval	16 Years	17 Years	18 Years	19 Years	20 Years
Survival (95% CI)	54.3% (50.0%, 58.4%)	53.2% (48.7%, 57.5%)	51.1% (46.2%, 55.9%)	50.3% (45.1%, 55.2%)	47.9% (42.0%, 53.5%)
Sample Size	114	87	61	45	27

Time Interval	21 Years
Survival (95% CI)	47.9% (42.0%, 53.5%)
Sample Size	20

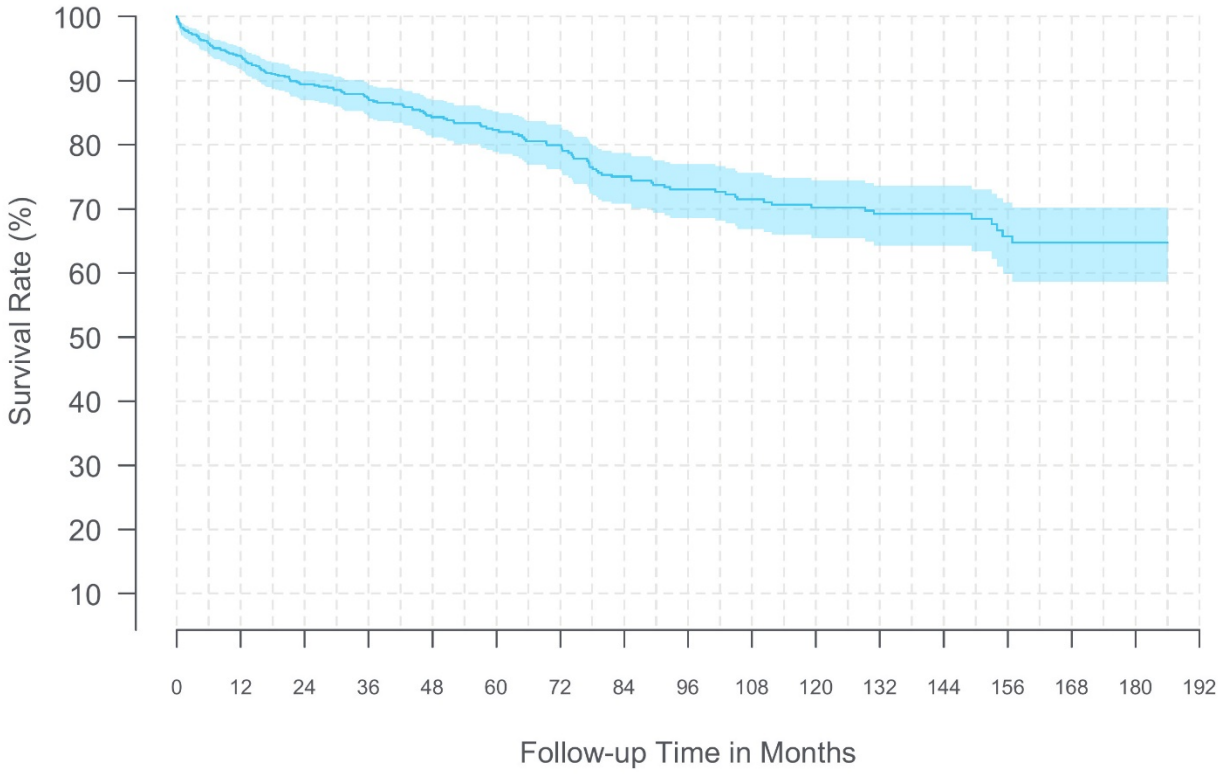
Specification: 8709	
Total Length	89 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Pump end

Catheter Event Summary: 8709	N
Catheter Dislodgement	95
Catheter Occlusion	88
Catheter Break/Cut	79
Catheter Kink	31
Catheter Disconnection At Pump	20
Catheter Leakage	16
Pump Connector Break/Cut	10
Catheter Dysfunction	6
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Catheter Related Complication	3
Device Issue	2
Device Malfunction	2
Other[a]	10
Total	**366**

[a] Composed of event codes with 1 event each.

3.5.2.2 Model 8709SC

Model/Name	8709SC/InDura 1P
FDA Approval Date	March 2006
Catheters Enrolled	1,110
Catheters Currently Active in Study	106
Initial Product Performance Events	155
Median Follow-up Time (Months)	28.3
Cumulative Follow-up Time (Months)	50,935



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.8% (91.9%, 95.3%)	89.4% (87.0%, 91.5%)	87.2% (84.4%, 89.5%)	84.3% (81.2%, 87.0%)	82.3% (78.9%, 85.2%)
Sample Size	668	520	437	361	298

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	80.0% (76.3%, 83.1%)	75.0% (70.8%, 78.8%)	73.0% (68.6%, 77.0%)	71.5% (66.9%, 75.6%)	70.2% (65.4%, 74.5%)
Sample Size	259	242	199	174	155

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	69.2% (64.3%, 73.6%)	69.2% (64.3%, 73.6%)	65.7% (59.9%, 70.9%)	64.7% (58.6%, 70.2%)	64.7% (58.6%, 70.2%)
Sample Size	135	103	68	43	26

Time Interval	At 186 Months
Survival (95% CI)	64.7% (58.6%, 70.2%)
Sample Size	23

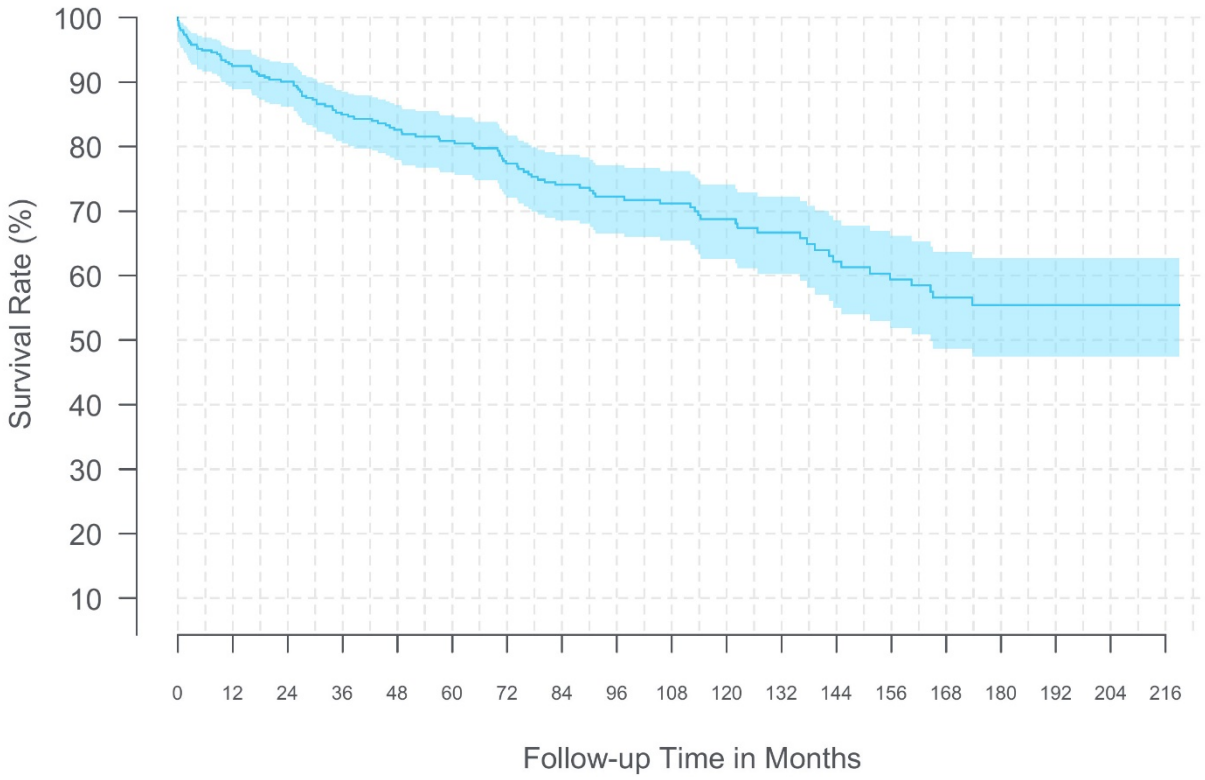
Specification: 8709SC	
Total Length	89 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed tip, radiopaque, titanium with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Pump end

Catheter Event Summary: 8709SC	N
Catheter Occlusion	42
Catheter Break/Cut	36
Catheter Dislodgement	34
Catheter Leakage	9
Catheter Disconnection At Pump	6
Catheter Kink	6
Catheter Dysfunction	5
Catheter Related Complication	3
Pump Unable To Enter/Withdraw From Catheter Access Port	3
Catheter Damage	2
Device Damage	2
Device Malfunction	2
Other[a]	5
Total	**155**

[a] Composed of event codes with 1 event each.

3.5.2.3 Model 8711

Model/Name	8711/InDura
FDA Approval Date	October 1999
Catheters Enrolled	665
Catheters Currently Active in Study	43
Initial Product Performance Events	103
Median Follow-up Time (Months)	31.9
Cumulative Follow-up Time (Months)	33,220



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.5% (88.9%, 95.0%)	90.1% (86.2%, 92.9%)	85.0% (80.5%, 88.5%)	82.6% (77.9%, 86.4%)	80.8% (76.0%, 84.8%)
Sample Size	308	287	259	238	225

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	77.3% (72.1%, 81.7%)	74.1% (68.6%, 78.7%)	72.3% (66.6%, 77.1%)	71.2% (65.4%, 76.2%)	68.7% (62.6%, 74.1%)
Sample Size	189	179	148	124	105

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	66.7% (60.3%, 72.3%)	62.2% (55.0%, 68.5%)	59.4% (51.9%, 66.2%)	56.6% (48.7%, 63.7%)	55.4% (47.4%, 62.7%)
Sample Size	82	69	64	53	41

Time Interval	16 Years	17 Years	18 Years	At 219 Months
Survival (95% CI)	55.4% (47.4%, 62.7%)	55.4% (47.4%, 62.7%)	55.4% (47.4%, 62.7%)	55.4% (47.4%, 62.7%)
Sample Size	32	21	21	20

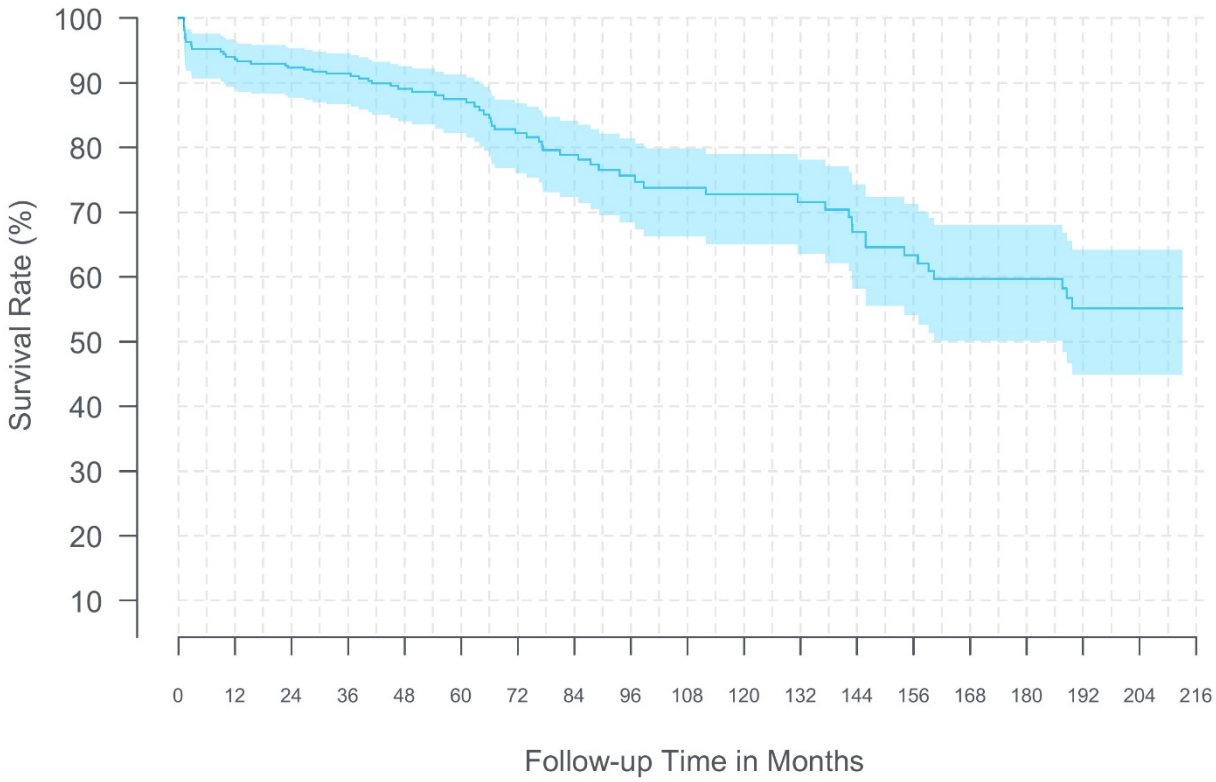
Specification: 8711	
Total Length	104.1 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Spinal and pump ends

Catheter Event Summary: 8711	N
Catheter Occlusion	33
Catheter Break/Cut	20
Catheter Dislodgement	13
Catheter Dysfunction	9
Catheter Kink	9
Catheter Leakage	4
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Catheter Disconnection At Pump	2
Catheter Related Complication	2
Device Issue	2
Other[a]	5
Total	**103**

[a] Composed of event codes with 1 event each.

3.5.2.4 Model 8731

Model/Name	8731
FDA Approval Date	October 2002
Catheters Enrolled	538
Catheters Currently Active in Study	34
Initial Product Performance Events	66
Median Follow-up Time (Months)	33.0
Cumulative Follow-up Time (Months)	25,141



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.7% (89.0%, 96.4%)	92.4% (87.7%, 95.3%)	91.4% (86.7%, 94.5%)	89.1% (84.1%, 92.5%)	87.5% (82.3%, 91.3%)
Sample Size	262	306	256	198	150

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	82.2% (76.1%, 86.9%)	78.9% (72.3%, 84.1%)	75.6% (68.5%, 81.4%)	73.8% (66.3%, 79.9%)	72.8% (65.1%, 79.0%)
Sample Size	134	107	83	72	66

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	71.6% (63.6%, 78.1%)	67.0% (58.2%, 74.3%)	63.4% (54.1%, 71.3%)	59.7% (50.1%, 68.1%)	59.7% (50.1%, 68.1%)
Sample Size	61	56	49	47	41

Time Interval	16 Years	17 Years	At 213 Months
Survival (95% CI)	55.1% (44.9%, 64.2%)	55.1% (44.9%, 64.2%)	55.1% (44.9%, 64.2%)
Sample Size	32	27	21

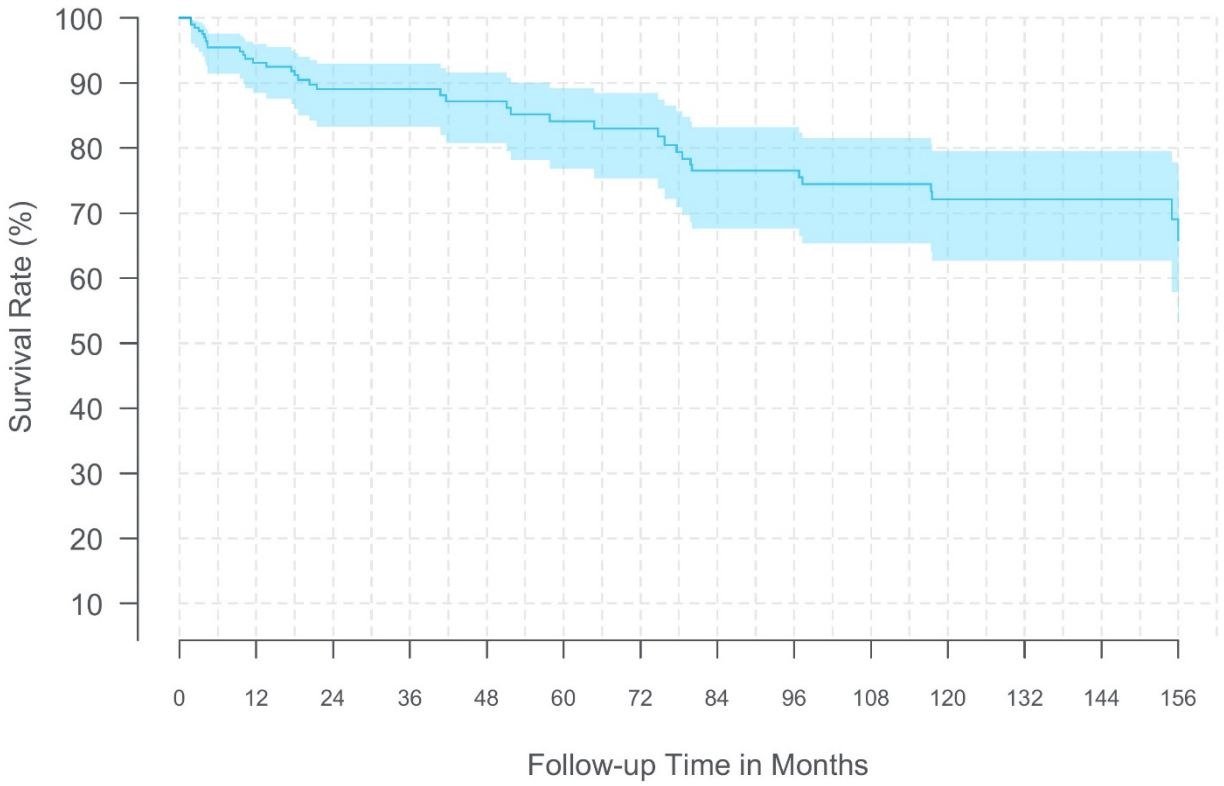
Specification: 8731	
Total Length	104.1 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed tip, radiopaque, titanium with 6 side holes
Catheter Volume	2.22 mL/cm
Trimmable Segments	Spinal end

Catheter Event Summary: 8731	N
Catheter Occlusion	25
Catheter Dislodgement	19
Catheter Break/Cut	5
Catheter Kink	5
Catheter Disconnection At Pump	3
Catheter Related Complication	3
Catheter Dysfunction	2
Other[a]	4
Total	**66**

[a] Composed of event codes with 1 event each.

3.5.2.5 Model 8731SC

Model/Name	8731SC
FDA Approval Date	March 2006
Catheters Enrolled	284
Catheters Currently Active in Study	52
Initial Product Performance Events	39
Median Follow-up Time (Months)	38.9
Cumulative Follow-up Time (Months)	14,071



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.1% (88.5%, 96.0%)	89.1% (83.3%, 92.9%)	89.1% (83.3%, 92.9%)	87.2% (80.8%, 91.5%)	84.1% (76.8%, 89.3%)
Sample Size	155	117	100	89	78

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	83.0% (75.4%, 88.4%)	76.5% (67.6%, 83.2%)	76.5% (67.6%, 83.2%)	74.5% (65.4%, 81.5%)	72.1% (62.7%, 79.6%)
Sample Size	68	82	77	67	61

Time Interval	11 Years	12 Years	13 Years
Survival (95% CI)	72.1% (62.7%, 79.6%)	72.1% (62.7%, 79.6%)	65.9% (53.2%, 75.8%)
Sample Size	49	37	21

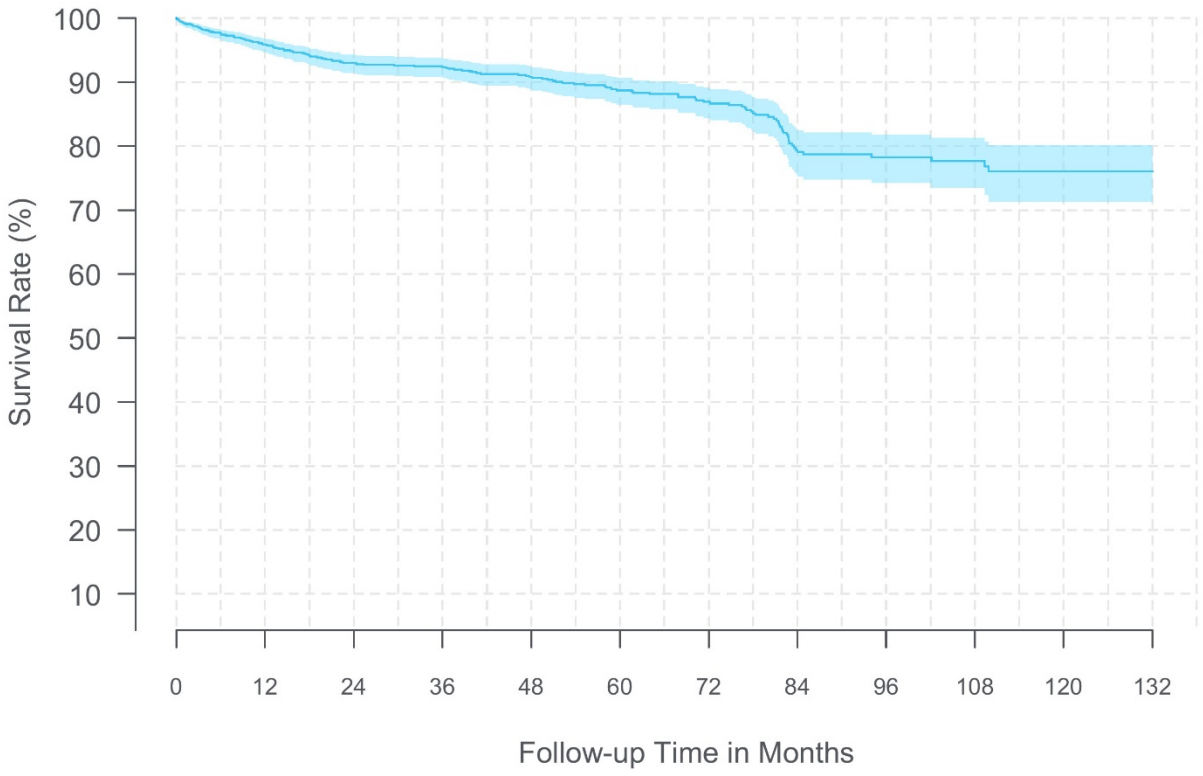
Specification: 8731SC	
Total Length	104.1 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Spinal and pump ends

Catheter Event Summary: 8731SC	N
Catheter Occlusion	15
Catheter Dislodgement	8
Catheter Kink	4
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Catheter Dysfunction	3
Catheter Leakage	2
Other[a]	3
Total	**39**

[a] Composed of event codes with 1 event each.

3.5.2.6 Model 8780

Model/Name	8780/Ascenda
FDA Approval Date	May 2012
Catheters Enrolled	1,659
Catheters Currently Active in Study	574
Initial Product Performance Events	156
Median Follow-up Time (Months)	30.3
Cumulative Follow-up Time (Months)	67,308



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	95.8% (94.6%, 96.8%)	93.0% (91.4%, 94.3%)	92.5% (90.8%, 93.9%)	90.8% (88.9%, 92.4%)	88.7% (86.5%, 90.6%)
Sample Size	1115	873	719	580	450

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	86.9% (84.3%, 89.1%)	79.1% (75.2%, 82.4%)	78.3% (74.2%, 81.8%)	77.7% (73.4%, 81.3%)	76.0% (71.2%, 80.1%)
Sample Size	351	232	156	100	60

Time Interval	11 Years
Survival (95% CI)	76.0% (71.2%, 80.1%)
Sample Size	20

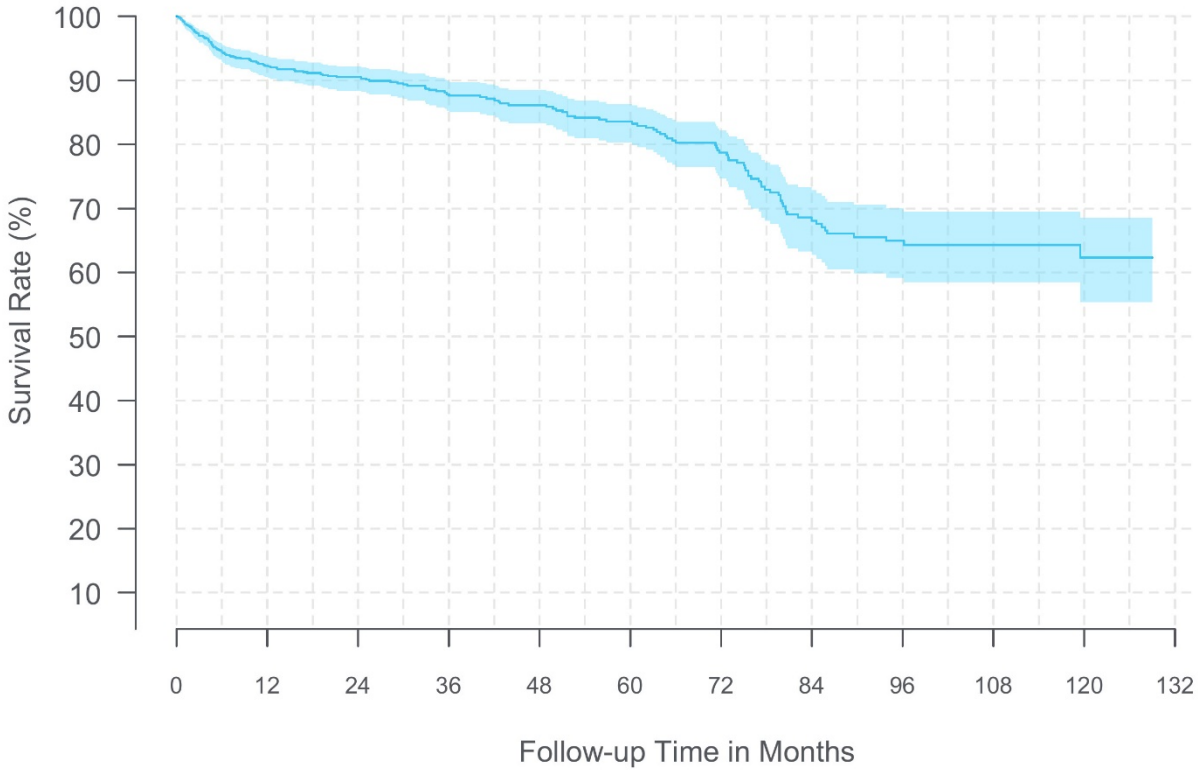
Specification: 8780	
Total Length	114 cm
Outer Diameter (spinal segment)	1.2 mm (4.0 French)
Inner Diameter (spinal segment)	0.5 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Connector end of the spinal segment

Catheter Event Summary: 8780	N
Catheter Occlusion	57
Catheter Kink	36
Catheter Break/Cut	18
Catheter Dislodgement	18
Catheter Damage	6
Catheter Leakage	6
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Catheter Disconnection At Pump	2
Catheter Dysfunction	2
Device Damage	2
Other[a]	5
Total	**156**

[a] Composed of event codes with 1 event each.

3.5.2.7 Model 8781

Model/Name	8781/Ascenda
FDA Approval Date	May 2012
Catheters Enrolled	1,552
Catheters Currently Active in Study	439
Initial Product Performance Events	174
Median Follow-up Time (Months)	12.4
Cumulative Follow-up Time (Months)	43,084



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.3% (90.5%, 93.8%)	90.5% (88.4%, 92.2%)	87.8% (85.3%, 90.0%)	86.1% (83.3%, 88.5%)	83.6% (80.3%, 86.3%)
Sample Size	698	497	396	318	260

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	78.7% (74.7%, 82.2%)	68.1% (62.7%, 72.9%)	64.9% (59.2%, 70.1%)	64.3% (58.5%, 69.5%)	62.3% (55.4%, 68.5%)
Sample Size	203	138	104	72	30

Time Interval	At 129 Months
Survival (95% CI)	62.3% (55.4%, 68.5%)
Sample Size	20

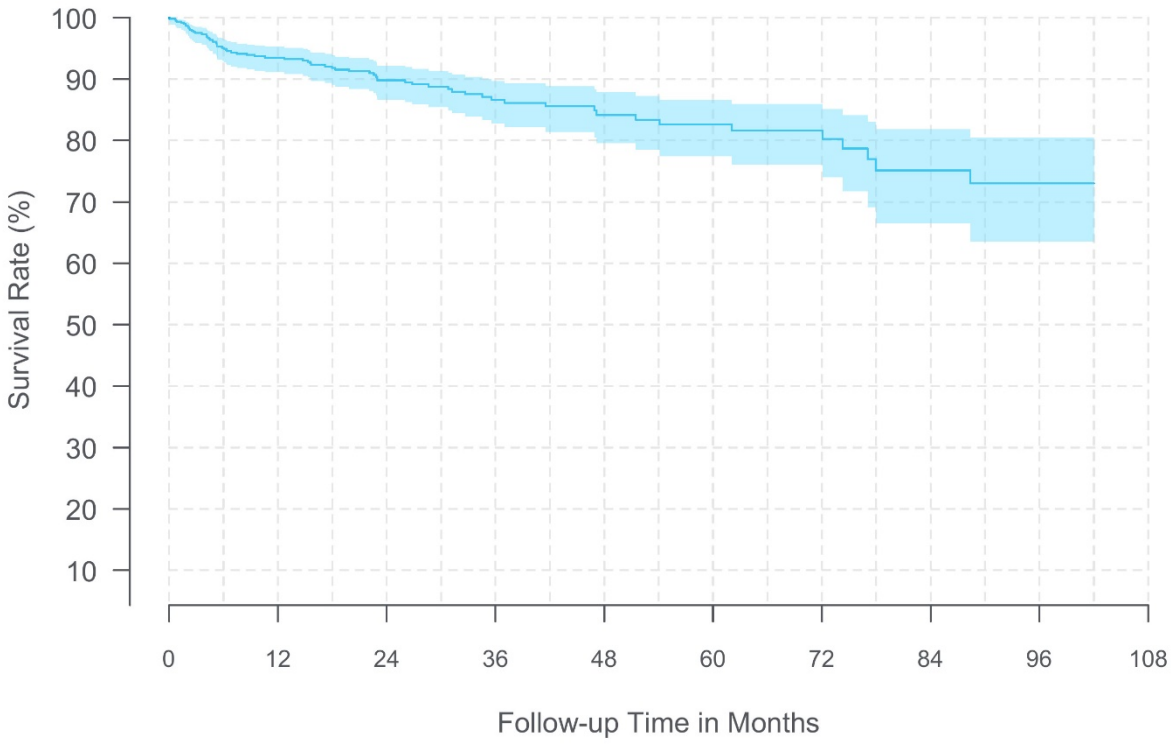
Specification: 8781	
Total Length	140 cm
Outer Diameter (spinal segment)	1.2 mm (4.0 French)
Inner Diameter (spinal segment)	0.5 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Catheter connector ends of the spinal and pump segments

Catheter Event Summary: 8781	N
Catheter Kink	61
Catheter Occlusion	47
Catheter Dislodgement	34
Catheter Break/Cut	9
Catheter Leakage	5
Catheter Dysfunction	4
Catheter Disconnection At Pump	3
Pump Reservoir Volume Discrepancy	3
Device Malfunction	2
Other[a]	6
Total	**174**

[a] Composed of event codes with 1 event each.

3.5.2.8 Ascenda Revised As Designed

Model/Name	Ascenda Revised As Designed
FDA Approval Date	May 2012
Catheters Enrolled	681
Catheters Currently Active in Study	240
Initial Product Performance Events	70
Median Follow-up Time (Months)	21.1
Cumulative Follow-up Time (Months)	19,094



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.5% (91.1%, 95.3%)	89.8% (86.7%, 92.2%)	86.6% (82.7%, 89.7%)	84.2% (79.5%, 87.8%)	82.6% (77.5%, 86.7%)
Sample Size	424	295	184	117	89

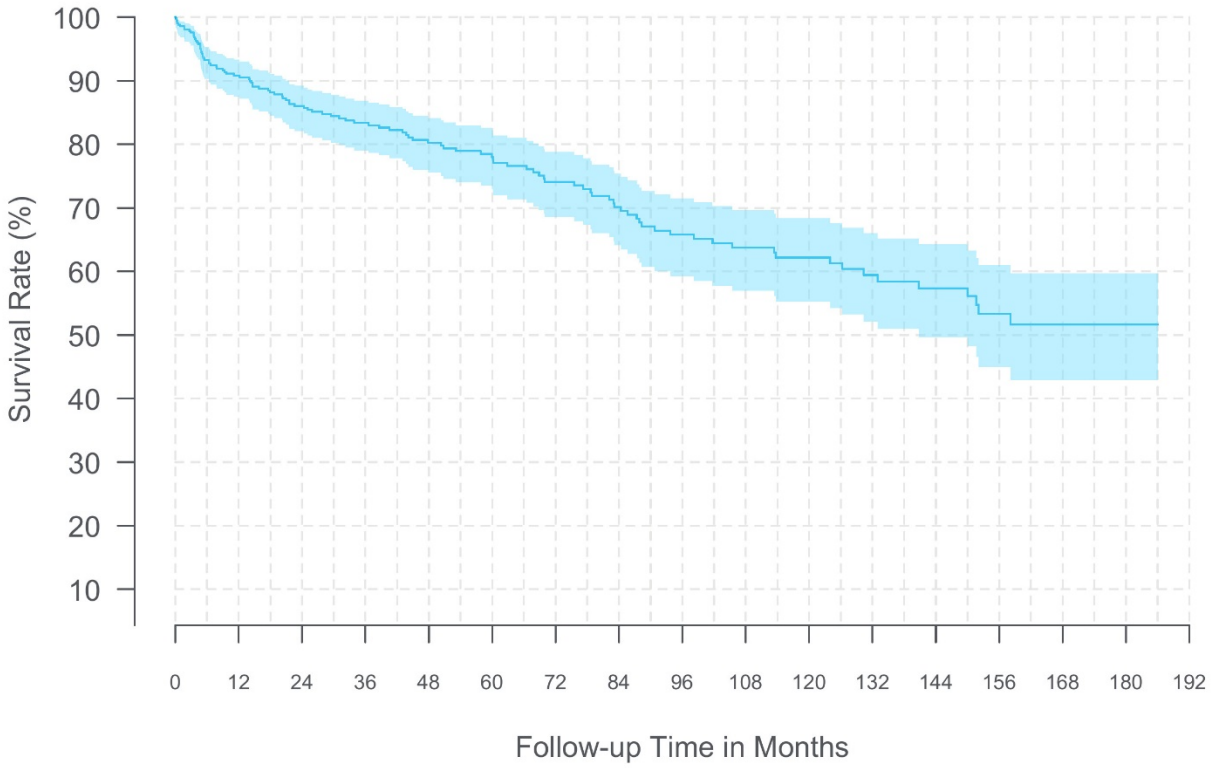
Time Interval	6 Years	7 Years	8 Years	At 102 Months
Survival (95% CI)	81.6% (76.1%, 86.0%)	75.1% (66.5%, 81.8%)	73.0% (63.5%, 80.5%)	73.0% (63.5%, 80.5%)
Sample Size	58	38	30	21

Catheter Event Summary: Ascenda RAD	N
Catheter Occlusion	25
Catheter Kink	18
Catheter Dislodgement	15
Catheter Break/Cut	3
Device Component Migration	3
Other[a]	6
Total	**70**

[a] Composed of event codes with 1 event each.

3.5.2.9 Grafted Not As Designed

Model/Name	Grafted Not As Designed
FDA Approval Date	NA
Catheters Enrolled	521
Catheters Currently Active in Study	69
Initial Product Performance Events	113
Median Follow-up Time (Months)	39.0
Cumulative Follow-up Time (Months)	27,080



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	90.8% (87.5%, 93.3%)	86.0% (82.1%, 89.2%)	83.4% (79.1%, 86.9%)	80.2% (75.5%, 84.2%)	78.0% (73.0%, 82.2%)
Sample Size	323	270	231	191	168

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	74.1% (68.5%, 78.8%)	70.1% (64.1%, 75.3%)	65.8% (59.3%, 71.5%)	63.7% (57.0%, 69.7%)	62.2% (55.2%, 68.3%)
Sample Size	142	118	98	89	75

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	59.4% (52.1%, 66.0%)	57.3% (49.7%, 64.3%)	53.3% (44.9%, 61.0%)	51.6% (42.9%, 59.7%)	51.6% (42.9%, 59.7%)
Sample Size	59	49	32	24	21

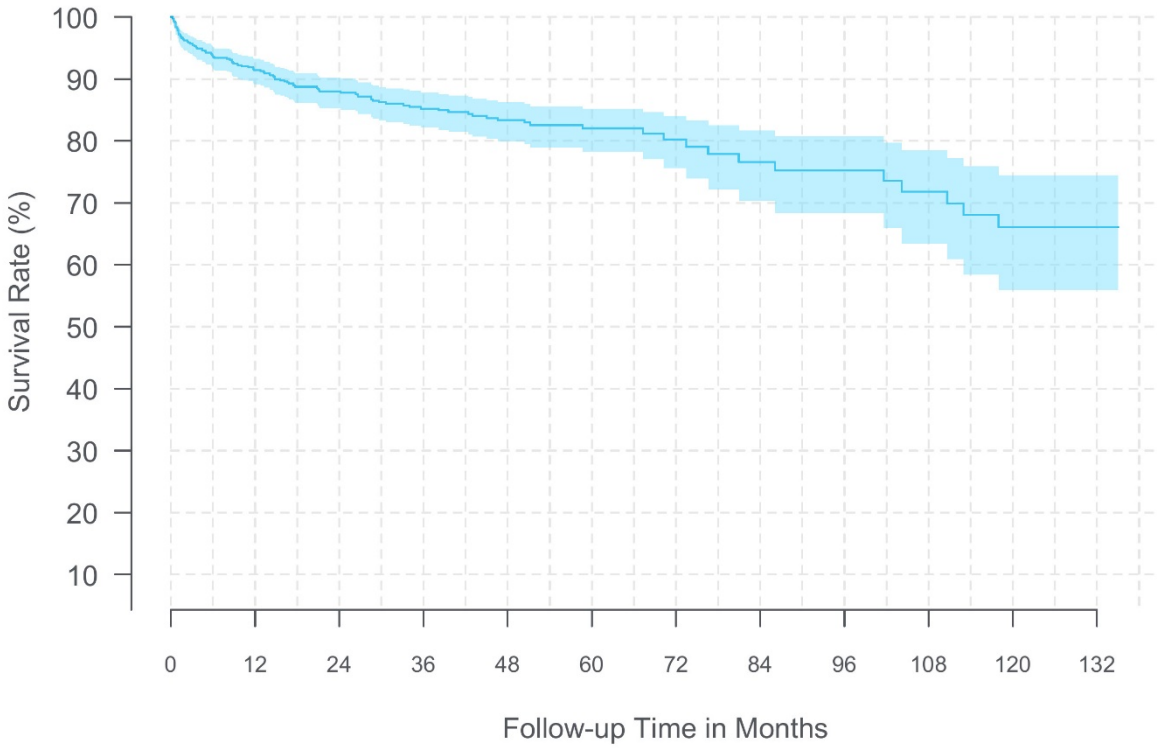
Time Interval	At 186 Months
Survival (95% CI)	51.6% (42.9%, 59.7%)
Sample Size	20

Catheter Event Summary: Grafted Not As Designed	N
Catheter Occlusion	34
Catheter Dislodgement	28
Catheter Break/Cut	15
Catheter Kink	8
Catheter Leakage	7
Catheter Related Complication	4
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Catheter Dysfunction	3
Catheter Damage	2
Device Malfunction	2
Other[a]	6
Total	**113**

[a] Composed of event codes with 1 event each.

3.5.2.10 Revised As Designed

Model/Name	Revised As Designed
FDA Approval Date	October 2002
Catheters Enrolled	872
Catheters Currently Active in Study	274
Initial Product Performance Events	117
Median Follow-up Time (Months)	25.6
Cumulative Follow-up Time (Months)	29,499



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.4% (89.1%, 93.2%)	88.0% (85.3%, 90.2%)	85.2% (82.1%, 87.8%)	83.3% (79.9%, 86.2%)	82.0% (78.3%, 85.2%)
Sample Size	578	435	311	228	146

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	80.2% (75.6%, 84.0%)	76.6% (70.4%, 81.7%)	75.2% (68.4%, 80.8%)	71.8% (63.5%, 78.5%)	66.1% (55.9%, 74.4%)
Sample Size	74	55	48	38	31

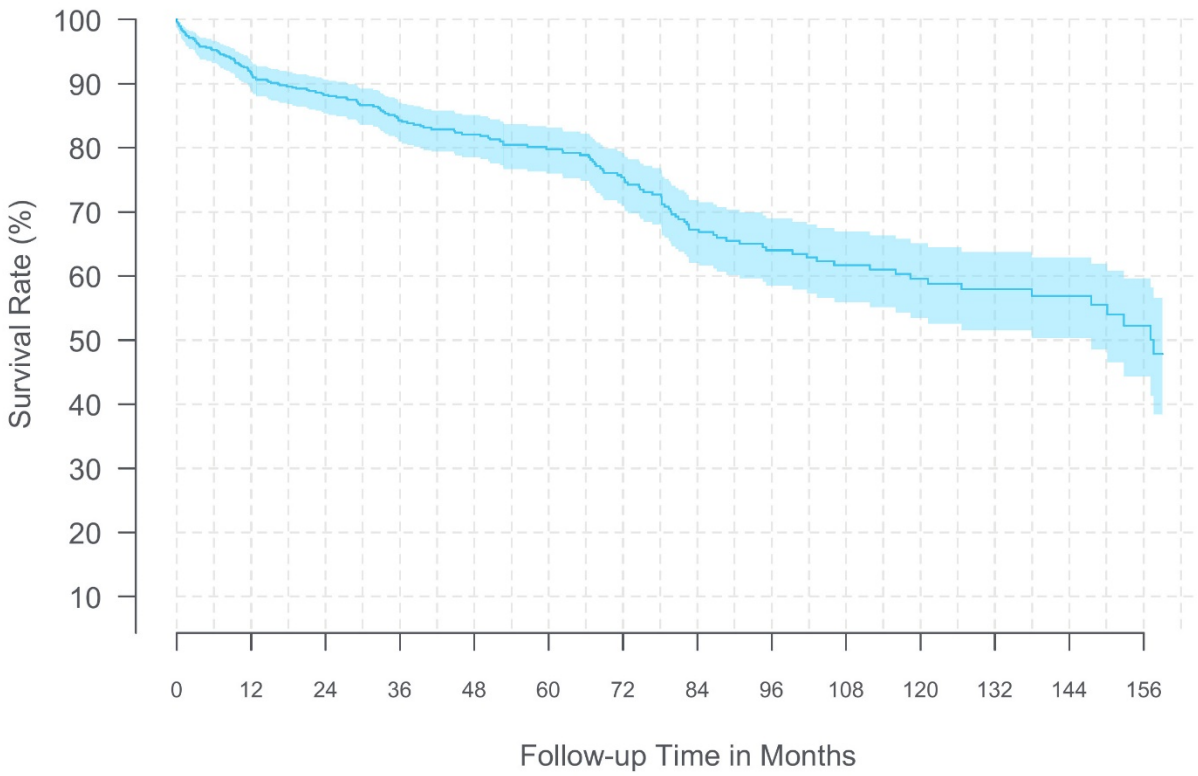
Time Interval	11 Years	At 135 Months
Survival (95% CI)	66.1% (55.9%, 74.4%)	66.1% (55.9%, 74.4%)
Sample Size	23	21

Catheter Event Summary: Revised As Designed	N
Catheter Dislodgement	57
Catheter Occlusion	30
Catheter Kink	8
Catheter Break/Cut	6
Device Component Migration	6
Catheter Leakage	3
Catheter Dysfunction	2
Pump Unable To Enter/Withdraw From Catheter Access Port	2
Other[a]	3
Total	**117**

[a] Composed of event codes with 1 event each.

3.5.2.11 Revised Not As Designed

Model/Name	Revised Not As Designed
FDA Approval Date	NA
Catheters Enrolled	742
Catheters Currently Active in Study	86
Initial Product Performance Events	161
Median Follow-up Time (Months)	41.4
Cumulative Follow-up Time (Months)	38,246



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.5% (88.9%, 93.5%)	88.3% (85.3%, 90.6%)	84.2% (80.9%, 87.1%)	82.1% (78.5%, 85.1%)	79.8% (76.0%, 83.1%)
Sample Size	527	462	378	315	254

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	75.4% (71.0%, 79.2%)	67.3% (62.1%, 71.9%)	64.0% (58.5%, 69.0%)	61.7% (55.9%, 66.9%)	59.6% (53.5%, 65.1%)
Sample Size	205	161	120	99	77

Time Interval	11 Years	12 Years	13 Years	At 159 Months
Survival (95% CI)	57.9% (51.6%, 63.8%)	56.9% (50.3%, 62.9%)	52.3% (44.3%, 59.6%)	47.8% (38.4%, 56.6%)
Sample Size	61	41	25	21

Catheter Event Summary: Revised Not As Designed	N
Catheter Occlusion	62
Catheter Dislodgement	24
Catheter Break/Cut	18
Catheter Kink	18
Catheter Leakage	11
Pump Unable To Enter/Withdraw From Catheter Access Port	5
Catheter Disconnection At Pump	4
Device Component Migration	4
Catheter Dysfunction	3
Catheter Related Complication	2
Other[a]	10
Total	**161**

[a] Composed of event codes with 1 event each.

3.5.3 Catheter Summary

Table 3.25: Targeted Drug Delivery Catheter Characteristics

Model/Name	FDA Approval Date	Catheters Enrolled	Catheters Active	Initial Product Performance Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
8709	May 1998	2,925	92	366	18.0	102,675
8709SC	March 2006	1,110	106	155	28.3	50,935
8711	October 1999	665	43	103	31.9	33,220
8731	October 2002	538	34	66	33.0	25,141
8731SC	March 2006	284	52	39	38.9	14,071
8780	May 2012	1,659	574	156	30.3	67,308
8781	May 2012	1,552	439	174	12.4	43,084
Ascenda Revised As Designed	May 2012	681	240	70	21.1	19,094
Grafted Not As Designed	NA	521	69	113	39.0	27,080
Revised As Designed	October 2002	872	274	117	25.6	29,499
Revised Not As Designed	NA	742	86	161	41.4	38,246

Table 3.26: Targeted Drug Delivery Catheter Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
8709	91.8%	89.1%	85.6%	82.8%	80.1%
	(90.1%, 93.3%)	(87.1%, 90.8%)	(83.4%, 87.5%)	(80.4%, 84.9%)	(77.6%, 82.4%)
8709SC	93.8%	89.4%	87.2%	84.3%	82.3%
	(91.9%, 95.3%)	(87.0%, 91.5%)	(84.4%, 89.5%)	(81.2%, 87.0%)	(78.9%, 85.2%)
8711	92.5%	90.1%	85.0%	82.6%	80.8%
	(88.9%, 95.0%)	(86.2%, 92.9%)	(80.5%, 88.5%)	(77.9%, 86.4%)	(76.0%, 84.8%)
8731	93.7%	92.4%	91.4%	89.1%	87.5%
	(89.0%, 96.4%)	(87.7%, 95.3%)	(86.7%, 94.5%)	(84.1%, 92.5%)	(82.3%, 91.3%)
8731SC	93.1%	89.1%	89.1%	87.2%	84.1%
	(88.5%, 96.0%)	(83.3%, 92.9%)	(83.3%, 92.9%)	(80.8%, 91.5%)	(76.8%, 89.3%)
8780	95.8%	93.0%	92.5%	90.8%	88.7%
	(94.6%, 96.8%)	(91.4%, 94.3%)	(90.8%, 93.9%)	(88.9%, 92.4%)	(86.5%, 90.6%)
8781	92.3%	90.5%	87.8%	86.1%	83.6%
	(90.5%, 93.8%)	(88.4%, 92.2%)	(85.3%, 90.0%)	(83.3%, 88.5%)	(80.3%, 86.3%)
Ascenda RAD	93.5%	89.8%	86.6%	84.2%	82.6%
	(91.1%, 95.3%)	(86.7%, 92.2%)	(82.7%, 89.7%)	(79.5%, 87.8%)	(77.5%, 86.7%)
Grafted Not As Designed	90.8%	86.0%	83.4%	80.2%	78.0%
	(87.5%, 93.3%)	(82.1%, 89.2%)	(79.1%, 86.9%)	(75.5%, 84.2%)	(73.0%, 82.2%)
Revised As Designed	91.4%	88.0%	85.2%	83.3%	82.0%
	(89.1%, 93.2%)	(85.3%, 90.2%)	(82.1%, 87.8%)	(79.9%, 86.2%)	(78.3%, 85.2%)
Revised Not As	91.5%	88.3%	84.2%	82.1%	79.8%

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
Designed					
	(88.9%, 93.5%)	(85.3%, 90.6%)	(80.9%, 87.1%)	(78.5%, 85.1%)	(76.0%, 83.1%)

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
8709	75.0%	70.3%	68.1%	66.3%	64.2%
	(72.1%, 77.6%)	(67.2%, 73.1%)	(64.9%, 71.0%)	(63.0%, 69.4%)	(60.8%, 67.5%)
8709SC	80.0%	75.0%	73.0%	71.5%	70.2%
	(76.3%, 83.1%)	(70.8%, 78.8%)	(68.6%, 77.0%)	(66.9%, 75.6%)	(65.4%, 74.5%)
8711	77.3%	74.1%	72.3%	71.2%	68.7%
	(72.1%, 81.7%)	(68.6%, 78.7%)	(66.6%, 77.1%)	(65.4%, 76.2%)	(62.6%, 74.1%)
8731	82.2%	78.9%	75.6%	73.8%	72.8%
	(76.1%, 86.9%)	(72.3%, 84.1%)	(68.5%, 81.4%)	(66.3%, 79.9%)	(65.1%, 79.0%)
8731SC	83.0%	76.5%	76.5%	74.5%	72.1%
	(75.4%, 88.4%)	(67.6%, 83.2%)	(67.6%, 83.2%)	(65.4%, 81.5%)	(62.7%, 79.6%)
8780	86.9%	79.1%	78.3%	77.7%	76.0%
	(84.3%, 89.1%)	(75.2%, 82.4%)	(74.2%, 81.8%)	(73.4%, 81.3%)	(71.2%, 80.1%)
8781	78.7%	68.1%	64.9%	64.3%	62.3%
	(74.7%, 82.2%)	(62.7%, 72.9%)	(59.2%, 70.1%)	(58.5%, 69.5%)	(55.4%, 68.5%)
Ascenda RAD	81.6%	75.1%	73.0%	-	-
	(76.1%, 86.0%)	(66.5%, 81.8%)	(63.5%, 80.5%)	-	-
Grafted Not As Designed	74.1%	70.1%	65.8%	63.7%	62.2%
	(68.5%, 78.8%)	(64.1%, 75.3%)	(59.3%, 71.5%)	(57.0%, 69.7%)	(55.2%, 68.3%)
Revised As Designed	80.2%	76.6%	75.2%	71.8%	66.1%

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
	(75.6%, 84.0%)	(70.4%, 81.7%)	(68.4%, 80.8%)	(63.5%, 78.5%)	(55.9%, 74.4%)
Revised Not As Designed	75.4%	67.3%	64.0%	61.7%	59.6%
	(71.0%, 79.2%)	(62.1%, 71.9%)	(58.5%, 69.0%)	(55.9%, 66.9%)	(53.5%, 65.1%)

Model Name	11 Years	12 Years	13 Years	14 Years	15 Years
8709	62.0%	59.0%	55.7%	54.7%	54.3%
	(58.4%, 65.4%)	(55.1%, 62.7%)	(51.5%, 59.7%)	(50.4%, 58.8%)	(50.0%, 58.4%)
8709SC	69.2%	69.2%	65.7%	64.7%	64.7%
	(64.3%, 73.6%)	(64.3%, 73.6%)	(59.9%, 70.9%)	(58.6%, 70.2%)	(58.6%, 70.2%)
8711	66.7%	62.2%	59.4%	56.6%	55.4%
	(60.3%, 72.3%)	(55.0%, 68.5%)	(51.9%, 66.2%)	(48.7%, 63.7%)	(47.4%, 62.7%)
8731	71.6%	67.0%	63.4%	59.7%	59.7%
	(63.6%, 78.1%)	(58.2%, 74.3%)	(54.1%, 71.3%)	(50.1%, 68.1%)	(50.1%, 68.1%)
8731SC	72.1%	72.1%	65.9%	-	-
	(62.7%, 79.6%)	(62.7%, 79.6%)	(53.2%, 75.8%)	-	-
8780	76.0%	-	-	-	-
	(71.2%, 80.1%)	-	-	-	-
8781	-	-	-	-	-
	-	-	-	-	-
Ascenda RAD	-	-	-	-	-
	-	-	-	-	-
Grafted Not As Designed	59.4%	57.3%	53.3%	51.6%	51.6%
	(52.1%,	(49.7%,	(44.9%,	(42.9%,	(42.9%,

Model Name	11 Years	12 Years	13 Years	14 Years	15 Years
	66.0%)	64.3%)	61.0%)	59.7%)	59.7%)
Revised As Designed	66.1%	-	-	-	-
	(55.9%, 74.4%)	-	-	-	-
Revised Not As Designed	57.9%	56.9%	52.3%	-	-
	(51.6%, 63.8%)	(50.3%, 62.9%)	(44.3%, 59.6%)	-	-

Model Name	16 Years	17 Years	18 Years	19 Years	20 Years
8709	54.3%	53.2%	51.1%	50.3%	47.9%
	(50.0%, 58.4%)	(48.7%, 57.5%)	(46.2%, 55.9%)	(45.1%, 55.2%)	(42.0%, 53.5%)
8709SC	-	-	-	-	-
	-	-	-	-	-
8711	55.4%	55.4%	55.4%	-	-
	(47.4%, 62.7%)	(47.4%, 62.7%)	(47.4%, 62.7%)	-	-
8731	55.1%	55.1%	-	-	-
	(44.9%, 64.2%)	(44.9%, 64.2%)	-	-	-
8731SC	-	-	-	-	-
	-	-	-	-	-
8780	-	-	-	-	-
	-	-	-	-	-
8781	-	-	-	-	-
	-	-	-	-	-
Ascenda RAD	-	-	-	-	-
	-	-	-	-	-
Grafted Not As Designed	-	-	-	-	-

Model Name	16 Years	17 Years	18 Years	19 Years	20 Years
	-	-	-	-	-
Revised As Designed	-	-	-	-	-
	-	-	-	-	-
Revised Not As Designed	-	-	-	-	-
	-	-	-	-	-

Model Name	21 Years
8709	47.9%
	(42.0%, 53.5%)
8709SC	-
	-
8711	-
	-
8731	-
	-
8731SC	-
	-
8780	-
	-
8781	-
	-
Ascenda RAD	-
	-
Grafted Not As Designed	-
	-
Revised As Designed	-
	-
Revised Not As	-

Model Name	21 Years
Designed	
	-