Medtronic

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Clinical Evaluation Report

Device(s) Covered	MiniMed Reservoir (MMT-326A, MMT-332A, and MMT-342)
Document Date	9 March 2020

Confidentiality Statement

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1. Executive Summary

The results of pre-clinical testing and clinical evidence derived from post market surveillance activities confirm that the benefits associated with use of the MiniMed reservoirs outweigh the potential risks associated with their use.

2. Purpose and Scope of the Clinical Evaluation

Legal Manufacturer Name and Address	Medtronic MiniMed 18000 Devonshire Street Northridge, CA 91325 USA	
Name of Device	**Model Number**	**Device Class**
MiniMed Reservoir, 1.8 ml	MMT-326A	IIa
MiniMed Reservoir, 3.0 ml	MMT-332A, MMT-342	IIa

3. Device/Family/Therapy Overview

3.1 Device Description

3.1.1 Device Overview

MiniMed Reservoir

The MiniMed Reservoir (MMT-326A, MMT-332A, MMT-342) is a medication container designed for use with the Paradigm family of infusion pumps and infusion sets. These reservoirs include a removable needle system (Transfer Guard) used for filling the reservoir. The Reservoir assembly, including Transfer Guard, is designed to allow air bubbles in the system to be visible in normal indoor lighting conditions and for the purging of such bubbles.

The Transfer Guard, which contains the reservoir-filling needle, is connected to the distal end of the reservoir barrel. One side of the transfer guard needle pierces the distal end of the barrel. The other side of the needle is recessed below the end of the Transfer Guard. The side of the Transfer Guard that is not connected to the reservoir barrel snaps onto a medication vial. By pushing the reservoir assembly towards the medication vial, the user engages a locking mechanism which enables the Transfer Guard needle to pierce the medication vial. The medication vial is pressurized when the reservoir plunger is pushed down. With the medication vial inverted, releasing and pulling the plunger fills the reservoir with fluid.

Once the reservoir is filled, the Transfer Guard with the medication vial is twisted off the reservoir. The plunger rod is unscrewed from the stopper to prepare the reservoir for placement in the pump. The reservoir connector attaches to a compatible tubing connector of a (Paradigm) infusion set with a ¼ turn "snap and lock". This is intended to provide tactile and possible audible or visual feedback for correct connection. This connection will establish the fluid path to the infusion set. Once the reservoir is connected to an infusion set, the assembly is placed into a (Paradigm) Infusion Pump with a ½ to 1 turn.

The difference between Model MMT-326A and Model MMT-332A/MMT-342 is the fluid capacity and length. Model MMT-326A contains at least 1.8 ml of fluid (including 0.3 ml for priming) and a reservoir length of 1.255 in., whereas Model MMT-332A/MMT-342 is designed to contain 3.0 ml of fluid (including 0.3 ml for priming) and a reservoir length of 1.707 in. Besides these changes, Model MMT-332A/MMT-342 and Model MMT-326A are functionally similar and made from similar materials.

The MMT-332A and MMT-342 reservoirs are physically identical and differ only in labeling (the MMT-342 reservoir is specifically labeled for use with extended wear infusion sets).

3.1.2 Device Group

The MiniMed Reservoirs are non-invasive devices intended to administer insulin when used in combination with an insulin infusion pump and infusion set. Therefore, the MiniMed Reservoirs are classified as a Class IIa devices, according to the first dash of Rule 2 of Annex IX of 93/42/EEC and Annex VIII of Regulation (EU) 2017/745.

3.1.3 Degree of Novelty

Both the MiniMed reservoirs are based on well-established technology widely used in syringes used for individual injections. The MiniMed reservoirs include features that make these devices suitable for use in compatible Medtronic insulin infusion pumps. These devices have a degree of novelty of 1 (lacking or minor novelty) per ANSM criteria for innovation degrees.

3.1.4 Materials Used

Table 1: Principle Device Materials for MiniMed Reservoir, MMT-326A, MMT-332A, and MMT-342

Part Description	Material	Standard	Tissue Contact Type
Barrel with connector	Polypropylene	Medical Grade USP Class VI	Indirect, fluid path
Plunger	Polypropylene	Medical Grade USP Class VI	None
Stopper/O-ring	Polypropylene with silicone rubber	Medical Grade USP Class VI	Indirect, fluid path
Transfer Guard Needle	Stainless Steel	304 ASTM I	Indirect, fluid path
Transfer Guard Housing	Polypropylene	Medical Grade USP Class VI	None
Snap Cap	Polycarbonate	Medical Grade	None
Septum	Silicone Rubber	Medical Grade	Indirect, fluid path
Barrel lubricant	Silicone Fluorosilicone	Medical Grade	Indirect, fluid path

Table 2: Additional Materials Used in Fabrication for MiniMed Reservoir, MMT-326A, MMT-332A, and MMT-342

Part Description	Material	Application	Tissue Contact Type
Adhesive	Epoxy	Cannula/hub connection	None
Ink	No-Tox® Medical Ink	Barrel markings	None
Solvent	No-Tox® Thinner	Used with barrel ink	None

3.1.5 Sterility/Radioactivity

The MiniMed reservoirs are provided sterile and do not include any radioactive substances.

3.1.6 Device Drawing or Pictures

Figure 1: MMT-326A Reservoir (with transfer guard)

Figure 2: MMT-332A, MMT-342 Reservoir (with transfer guard)

3.2 Intended Purpose of the Device

3.2.1 Intended Users

MiniMed reservoirs are used by individuals with type 1 or type 2 diabetes.

3.2.2 Single Use or Reusable

Both MiniMed reservoirs are single use devices.

3.2.3 Maximum Number of Uses

One.

3.2.4 Invasive or Non-invasive

Non-invasive.

3.2.5 Duration of Use

The MiniMed (MMT-326A, MMT-332A) reservoirs are used up to three days. The MiniMed(MMT-342) reservoirs are used for a duration of up to seven days.

3.2.6 Organs, Tissues or Body Fluids Contacted

The MiniMed reservoirs do not come into direct contact with organs, tissues or body fluids. The reservoirs contact insulin that is infused by the infusion pump into subcutaneous tissue.

3.2.7 Biocompatibility

The MiniMed reservoirs have been evaluated for biocompatibility per ISO 10993-1. The results of this testing confirm that the reservoirs meet applicable requirements for Externally Communicating Device, Tissue Contact (indirect), Permanent Duration.

3.3 Intended Target Population(s)

3.3.1 Indications

This reservoir is indicated for the subcutaneous infusion of medication, including insulin, from compatible Medtronic insulin pumps and infusion sets.

3.3.2 Contraindications

This reservoir is contraindicated for the infusion of blood or blood products.

3.3.3 Relevant Warning and Precaution

Insulin should be at room temperature before filling reservoir.

Once reservoir is filled, use promptly. Do not store.

Check for leaks after changing the reservoir and infusion set.

Conduct your first setup in the presence of your healthcare professional.

3.4 Potential Clinical Risk

The clinical risks related to the reservoirs covered by this evaluation are limited to the potential for the reservoir to leak or issues related to the interaction of insulin and the materials of the

reservoir. Reservoir leakage can lead to under-delivery of insulin leading to hyperglycemia or diabetic ketoacidosis. The potential for reservoir leakage can be fully assess through bench testing and does not require evaluation during clinical investigations. The absence of any risk related to insulin/reservoir interactions has been confirmed through extensive insulin compatibility testing and does not require evaluation through clinical investigations.

3.5 Lifetime/Stability

The MiniMed reservoirs have a shelf life up to 3 years.

The reservoir characteristics and performances are not adversely affected to such a degree that the clinical conditions and safety of the patients and, where applicable, of other persons are compromised during the lifetime of the device as indicated, when the device is subjected to the stresses which can occur during normal conditions of use.

3.6 Developmental Context of the Device

3.6.1 CE Mark Status

The MiniMed reservoir was initially CE Marked in December 1995. The MiniMed MMT-326A reservoir was initially CE Marked in April 2002. The MiniMed MMT-332A reservoir was initially CE Marked in October 2003. The MMT-342 reservoir is not CE Marked as of the date of this evaluation.

3.6.2 Marketing History

The MMT-326A and MMT-332A reservoirs have been marketed in the United States, Europe, Asia, South America and other countries. The MMT-342 reservoir has not been marketed as of the date of this evaluation.

3.6.3 Changes Since Last Evaluation

The evaluation was updated to include the MMT-342 reservoir and to include updates required for compliance with the requirements of Regulation (EU) 2017/745.

3.7 Method of Application/Procedural Method

MiniMed Reservoirs are a component of Medtronic insulin infusion systems but do not serve any stand-alone function.

3.8 Principles of Operation

MiniMed Reservoirs are user-filled to hold insulin during pump therapy. These reservoirs are simple syringes where medication is forced from the reservoir body by advancing the reservoir stopper.

3.9 Claims

None

4. State of the Art

4.1 General Background

MiniMed reservoirs are intended for use by individuals with diabetes mellitus.

4.2 Summary of State-of-the-Art Literature Search Results

Since MiniMed Reservoirs are a component of Medtronic insulin infusion systems but do not serve any stand-alone function, a state-of-the-art literature search was deemed not necessary. The state of the art related to different treatment options for diabetes is discussed in the clinical evaluation reports for the insulin infusion pumps in which these reservoirs are used.

4.3 Available Therapeutic Options

Patients with type 1 diabetes and patient with type 2 diabetes who require insulin can administer insulin using an insulin infusion pump or via periodic injections.

4.4 Applicable Standards and Guidance Documents

The connector of the MiniMed reservoir complies with the requirement of ISO 80369-7:2016. There are no other standards applicable to reservoirs used in insulin infusion pumps.

Although there are no other standards or guidance documents specific to reservoirs, the following regulations, standards and guidance are relevant to the clinical investigation and clinical evaluation of medical devices in support of commercial distribution of these devices in the European Union:

- Council Directive 93/42/EEC Concerning Medical Devices
- Regulation (EU) 2017/745 on Medical Devices
- ISO 14155:2011: Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice
- MEDDEV 2.7/1 Revision 4: Clinical Evaluation: A Guide for Manufacturers and Notified Bodies Under Directives 93/42/EEC and 90/385/EEC

5. Equivalent Device Demonstration

Not applicable.

6. Evaluation of Safety and Performance including Clinical Benefit of the Device(s)

6.1 Data Sources

Since the MiniMed reservoirs have a well-established history of use and safety and proper performance can be confirmed through preclinical testing, this clinical evaluation is based on existing scientific literature and information from post market surveillance. Prospective clinical investigations were not required prior to initial CE Marking.

6.2 Appraisal and Analysis of Relevant Available Data

6.2.1 Post Market Surveillance Data

Complaint trends for the MMT-326A and MMT-332A reservoirs are provided in Error! Reference s ource not found. through **Figure 4**.

The type and frequency of complaints associated with the MiniMed reservoir are within acceptable limits for this type of device.

Figure 3: MMT-326A Complaint Trends

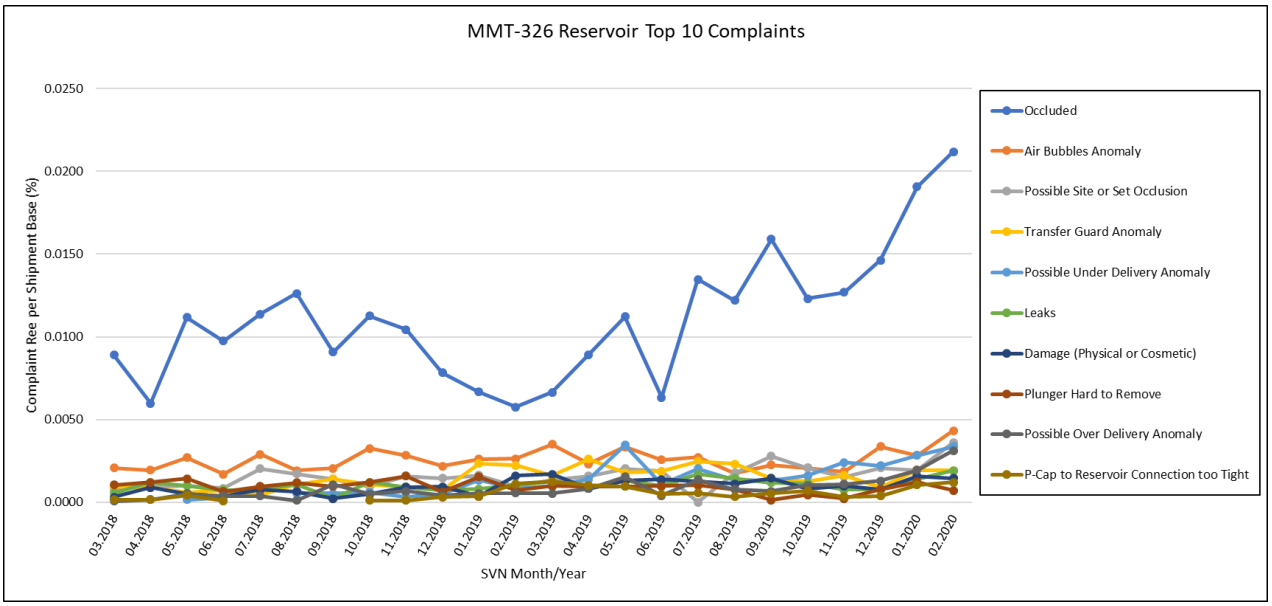
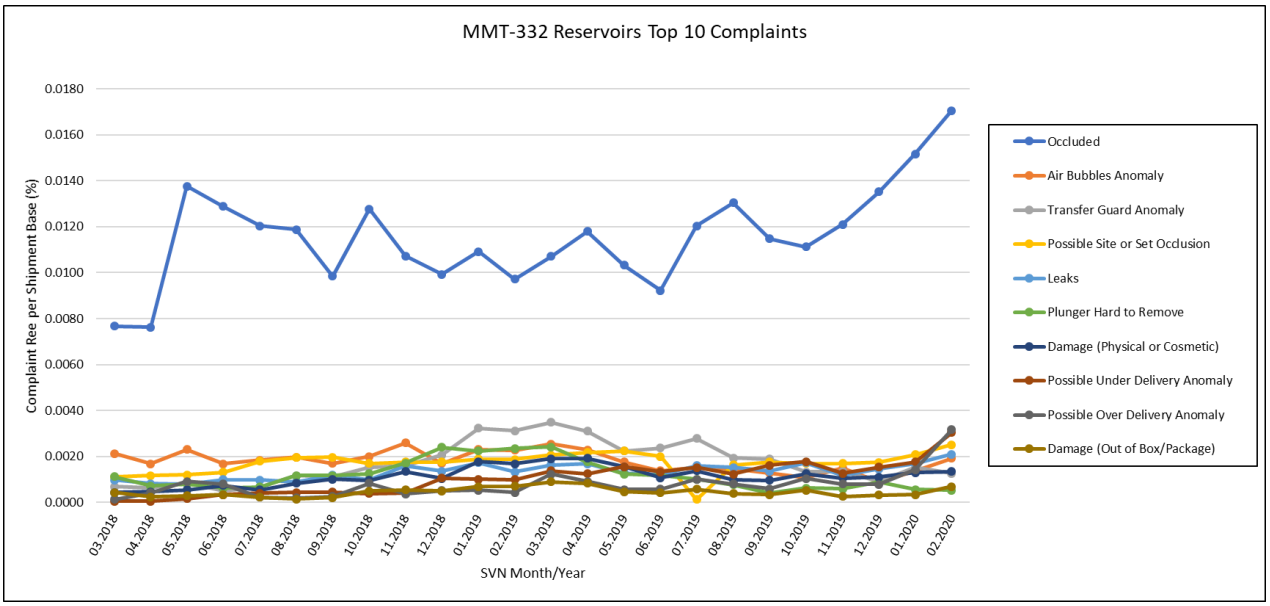


Figure 4: MMT-332A Complaint Trends



6.2.2 Scientific Literature

A literature search was conducted to identify published clinical information relevant specifically to the safety and performance of the MiniMed reservoirs. Details regarding the search protocol and search results are provided in Appendix B. The one relevant article identified is summarized in Table 5.

Table 3: Relevant Scientific Literature

Author/ Year	Device	Study Design	Study Objective	Results	Comment
Mallappa/2018[1]	MMT-332A	Single center, open label	Evaluation of safety and efficacy of long-term continuous subcutaneous hydrocortisone infusion	Six of eight patients chose to continue on long-term CSHI therapy. Compared to baseline, eighteen months of CSHI resulted in decreased (P = 0.043) 0700–hour ACTH, 17-hydroxyprogesterone, androstenedione, and progesterone; increased whole-body lean mass (P = 0.024); and improved HRQoL, especially symptoms of adrenal insufficiency (P = 0.003). Findings at six and eighteen months did not differ and improvements achieved in androgen control, lean body mass and HRQoL after six months of CSHI were maintained at eighteen months. The hydrocortisone dose appeared to decrease with time [6 vs. 18 months: 38.3 ± 8.8 vs. 33.6 ± 12.2 mg/day (P = 0.062)], especially in women receiving oral contraceptives. Reduction of testicular adrenal rest and adrenal size observed at 6 months remained stable. In one patient, an adrenal adenoma continually decreased over time. Subjective improvement in hirsutism was reported.	This study involved an off-label use of the MMT-332A reservoir, there were no major pump related mechanical issues suggesting that there were no performance issue specific to the reservoir. Since this study involved an off-label use of the MMT-332A reservoir, the result are not directly applicable to the reservoir when used with insulin.

6.3 Safety and Performance

6.3.1 Device Safety

Data from post market surveillance and available scientific literature does not indicate any safety issues associated with use of MiniMed reservoirs.

6.3.2 Device Performance

There are no specific clinical performance requirements for MiniMed a reservoirs. All performance requirements were verified during preclinical testing.

6.4 Potential Emerging Clinical Risks/Issues That Require Evaluation

There are no emerging clinical risks or issues that require further evaluation.

7. Benefit-Risk Profile

Based on the absence of any data suggesting any safety risks associated with use of MiniMed reservoirs, the potential benefits provided by these products outweigh any risks related to their use.

8. General Safety and Performance Requirements (GSPR)/Essential Requirements

With respect to the essential requirements of Council Directive 93/42/EEC, clinical evidence was evaluated to confirm that the MiniMed reservoirs meet the requirements for safety and acceptable risk/benefit profile (ER1), performance (ER3) and acceptability of side-effects (ER6). With respect to the General Safety and Performance Requirements of Regulation (EU) 2017/745, clinical evidence was evaluated to confirm that the MiniMed reservoirs meet the General Requirements described in Annex I, Sections 1 and 8.

As discussed throughout this report, the available information continues to indicate that the MiniMed reservoirs meet the applicable GSPRs/ERs.

9. Post Market Clinical Follow-Up

The MiniMed a reservoirs comply with applicable requirements and harmonized standards for the design, manufacture, and packaging of medical devices. Pre-clinical testing is performed to demonstrate that the products perform as intended and are safe for market release.

Ongoing evaluation of available clinical data has not raised any performance or safety concerns for these devices. Clinical experience data is continually monitored and trended by Medtronic per an established quality management system. This system includes but is not limited to monitoring and trending of field performance through analysis of customer complaints, analysis of returned products, and review of published literature; assessment of risks associated with changes to manufacturing processes or product design; and assessment of risks associated with non-conformances detected in manufacturing.

The post-market surveillance activities in place are sufficient to identify and analyze emergent risks, and to ensure acceptability of the benefit-risk ratio is continually demonstrated.

With regard to the functionality, final users of the MiniMed reservoirs proactively contact Medtronic directly to report issues or feedback related to the device, yielding a high volume of clinical experience. Therefore, there are no gaps identified or needs that would warrant a post-

market clinical follow-up study. The identification of systematic misuse or off-label use will be accomplished through a structured scientific literature search as part of the CER.

10. Overall Conclusion of the Clinical Evaluation

The clinical evidence derived from use data and relevant literature for the MiniMed Reservoir Reservoir confirm conformity with the applicable essential requirements and general safety and performance requirements related to clinical safety and clinical performance.

The evidence also demonstrates that the performance, efficacy and safety of the MiniMed Reservoir a Reservoir as claimed have been established, and that the risks associated with the use of the devices are acceptable when weighed against the benefits to the patient.

11. Expert Reviewer/Evaluator/Approver Statement

The expert medical evaluator/reviewer/approver for this clinical evaluation report is Dr. Robert Vigersky. Dr. Vigersky's qualifications as an expert on diabetes and devices used for the treatment of diabetes are detailed in Appendix C of this report.

By electronically approving this document in the Medtronic Diabetes document control system, Dr. Vigersky confirms that he has reviewed and evaluated the information included in this document and agrees with the conclusion described herein regarding the acceptable risk benefit profile of the devices covered by this evaluation.

12. Clinical Evaluation Update Cadence

Since the MiniMed reservoirs are low risk, well established devices, this evaluation will be updated at least every three years.

13. Report Author

The author of this report is Mark Faillace. Marks's qualifications are detailed in Appendix C of this report.

14. Signature Page

By approving electronically, the approvers of this document confirm that they agree with the contents of this report. Approvals for this clinical evaluation report are maintained in the Agile PLM system.

15. Revision History

Revision history is maintained in the Agile PLM system.

Appendix A – State of the Art Literature Search Methods and Results

Since MiniMed Reservoirs are components of Medtronic insulin infusion systems but do not serve any stand-alone function, a state-of-the-art literature search was deemed not necessary. The state of the art related to different treatment options for diabetes is discussed in the clinical evaluation reports for the insulin infusion pumps in which these reservoirs are used.

Appendix B – Device Literature Search Methods, Results and Assessment

Scope of the Device Literature Search

A literature search was conducted using the Medtronic Knowledge Center Embase search platform to ensure comprehensive coverage of globally published clinical evidence for medical device products and therapies. Embase, from Elsevier, provides access to Embase, Medline, and SCIENCEDIRECT on a single search platform.

EMBASE, published by Elsevier, contains over 11 million records with over 500,000 citations added annually. EMBASE's international journal collection contains over 5,000 biomedical journals from 70 countries.

MEDLINE is the U.S. National Library of Medicine's premier bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the health care system, and the preclinical sciences. MEDLINE contains bibliographic citations and author abstracts from more than 5,000 biomedical journals published in the United States and 80 other countries. The database contains over 15 million citations.

SCIENCEDIRECT from Elsevier is a full text searchable scientific and technical database featuring over 3,800 journals.

Search Protocol

Details of the search protocol are provided in **Table 4** below.

Table 4: Search Protocol

Date of Search	5 March 2020
Individual Performing Search	Mark Faillace
Databases	Embase, Medline and SCIENCEDIRECT (databases search simultaneously using Medtronic Knowledge Center Embase Quick Search)
Timeframe	There were no date limitations applied during the search.
**Search Logic*, ** **	Medtronic AND ('mmt 103' OR 'mmt 103a' OR 'mmt 326' OR 'mmt 326a' OR 'mmt 332' OR 'mmt 332a')
Publication Types	Results limited to "article" publication type

*MMT 342 was not included as a search term since this configuration has not been produced as of the date of this report.

** Since MMT-103 and MMT-103a are no longer marketed in Europe, they will not be included in future searches.

Results

The search resulted in one citation for review. Based on review of the article abstract, the article was selected for full text review. Since only one publication was selected for review, a detailed weighting of each article was not performed however since this article discussed an off-label use of the reservoir, it was considered partially relevant to the clinical evaluation. A summary of this article is provided in **Table 3**. The article did not include any safety or clinical performance information specific to the reservoir.

Appendix C – Qualifications of Author and Expert Approver

Report Author:

The primary author of this report was Mark Faillace. Mr. Faillace has a degree in BioMedical Engineering from the University of Southern California and over 41 years of experience in medical device clinical research and regulatory affairs. Mr. Faillace has been employee by Medtronic MiniMed since 1998 and is intimately familiar with insulin pumps and continuous glucose monitoring systems.

Expert Reviewer/Evaluator/Approver:

The reviewer/evaluator/approver of this report is Robert A. Vigersky, M.D. Dr. Vigersky is currently the Principal Medical Officer, Global Clinical and Medical Affairs, for Medtronic Diabetes overseeing national and international studies on Medical Device Therapy. He is Professor of Medicine at the Uniformed Services University of the Health Sciences, Bethesda, MD. He was the Founder and Director of the Diabetes Institute at Walter Reed National Military Medical Center where he continues to volunteer.

He graduated as the Valedictorian from Boston University School of Medicine, did his Internal Medicine training at The Johns Hopkins Hospital, Baltimore, MD and completed a 3-year Fellowship in Endocrinology at the National Institutes of Health, Bethesda, MD. He is Board Certified in Internal Medicine and Endocrinology. Dr. Vigersky held the rank of Colonel in the Army Medical Corps before retiring in 2015. He served in Iraq, Korea, and Germany. He held the "A" proficiency designation from the Department of the Army and received numerous military awards including the Legion of Merit in 2009. He was elected as a member of the Order of Medical Military Merit. He was a member of the VA/DoD guideline committee and represented the Department of Defense on the Advisory Council of the National Institute of Diabetes, Digestive and Kidney Disease.

He has been an active participant in the Endocrine Society where established Clinical Practice Guideline program and served as President from 2009-2010. The Diabetes Technology Society gave him its Leadership Award in 2011. Dr. Vigersky has published over 280 scholarly papers and abstracts focusing on the use of technology to improve outcomes of patients with diabetes.

Curriculum Vitaes for Mark and Dr. Vigersky are provided in **Attachment 1**.

Appendix D – Declaration of Interests

Both the author and the reviewer/evaluator/approver of this report are full time employees of Medtronic Diabetes, the manufacturer of MiniMed Reservoirs. Declarations of interest for both the report author and reviewer/evaluator/approver are provided in **Attachment 2** to this report.

Appendix E - Abbreviations, Acronyms, and Definitions

Table 5. List of Abbreviations, Acronyms, and Definitions

Term	Definition
AIMDD	Active Implantable Medical Device Directive
CGM	Continous Glucose Monitoring
CER	Clinical Evaluation Report
COI	Conflict of Interest
DCCT	Diabetes Control and Complications
DKA	Diabetic ketoacidosis
EDIC	Epidemiology of Diabetes Interventions and Complications
EU MDR	European Medical Device Regulation
FST	Frequent Sample Testing
GCH	Global Complaint Handling
GMI	Glucose Management Indicator
GSPR	General Safety and Performance Requirements
HAS	Human Serum Albumin
HCL	Hybrid Closed-Loop
HIIE	High-Intensity Interval Exercise
MARD	Mean Absolute Relsative Difference
MDD	Medical Devices Directive
MDI	Multiple Daily Injections
MDR	Medical Device Report
MIE	Moderate Intensity Exercise
MEDDEV	Commission guideline relating to medical devices directives
PLGM	Predictive Low Glucose Management
PMCF	Post Market Clinical Follow-up
SAP	Sensor Augmented Pump
SG	Sensor Glucose
SMBG	Self Monitored Blood Glucose
T1D	Type 1 Diabetes
YSI	Yellow Springs Instrument

Appendix F - References

1. Mallappa A, Nella AA, Sinaii N, et al. Long-term use of continuous subcutaneous hydrocortisone infusion therapy in patients with congenital adrenal hyperplasia. *Clin Endocrinol (Oxf).* 2018;89(4):399-407.