Clinical Evaluation Report (CER) for Irrigation Sets

Revision History		
Revision	**Date**	**Reason for Update/Summary of Changes**
Rev A	SEE STAMP	Initial Clinical Evaluation Report in compliance with Medical Device Regulation (MDR) 2017/745. The corresponding Clinical Evaluation Report in compliance with Medical Device Directive (MDD) 93/42/EEC is 1248528_CER

Approval Page

Declaration of Interest (DOI): The author(s) and approvers of this document are either Baxter employees or approved Baxter Service Providers. By signing this document, the approvers declare that they have objectively analyzed the data in this Clinical Evaluation for Irrigation Sets.

The approvers signature represents agreement to the DOI statements included in the table below (adapted from A11 of MEDDEV 2.7/1 Rev 4) unless a specific declaration of a potential conflict of interest is included in the approver's signature line below.

1. Has not participated as an investigator in clinical studies of the device, or in pre-clinical testing of the device within 36 months prior to the clinical evaluation
2. Does not have ownership/shareholding whose value could possibly be affected by the outcome of the evaluation
3. No family members (namely spouse or partner living in the same residence as the evaluator, children and adults for whom the evaluator is legally responsible) have financial interests affected by the outcome of the evaluation
4. Is not a recipient of grants sponsored by the manufacturer within 36 months prior to the clinical evaluation
5. Does not receive benefits such as travelling or hospitality (beyond what is reasonably necessary for the work as an employee or external evaluator)
6. Does not have interests in connection with intellectual property, such as patents, copyrights, and royalties (whether pending, issued, or licensed) possibly affected by the outcome of the evaluation
7. Does not have interests related to the manufacturing of the device or its constituents
8. Does not have other interests or sources of revenues possibly affected by the outcome of the evaluation

The undersigned have read this clinical evaluation report and hereby confirm that, to the best of their knowledge, it accurately describes the conduct and the results of the evaluation. The MA-Clinical Evaluator's signature also confirms their review and acceptance of any DOI disclosures provided by any approvers.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1 EXECUTIVE SUMMARY

This Clinical Evaluation Report (CER) has been written for Irrigation Sets and it complies with MEDDEV 2.7/1 Rev 4, Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 MDR regulations, and relevant MDCG guidance. Throughout this report, Irrigation Sets may be referred to as the Device(s) Under Evaluation or DUE.

For Irrigation Sets, the demonstration of conformity with general safety and performance requirements (GSPRs) based on clinical data was not deemed appropriate. Therefore, this clinical evaluation was based on the application of MDR Article 61(10) which relies on non-clinical data sets, including biocompatibility, design verification and validation studies, and simulated use studies that were performed on legacy MDD devices of the Irrigation Sets. In addition, the search and review of systematic scientific literature, supplemental internet literature, and Post Market Surveillance (PMS) data were also conducted to identify any potential safety concerns or performance issues.

The non-clinical studies established that Irrigation Sets comply with the applicable standards for safety and clinical performance. The results of biological and chemical characterization tests met all the requirements and current standards supporting the safety and biocompatibility of Irrigation Sets.

Irrigation Sets have been on the market since the early 1980s. The date of the first MDD CE mark for Irrigation Sets can be found detailed per code in **Table 4-2**, the current MDD CE mark was acquired on 18-NOV-2019. During the current data collection period analyzed in this CER, approximately 5,001,478 units of the DUE were sold worldwide. During this data collection period, the total global complaint incidents per million (CIPM) were 677.8 for the DUE. In addition, a detailed search within the external vigilance and recall databases of MHRA, BfArM, Swissmedic, and FDA (MAUDE and Recall) did not identify any risks or usability aspects for similar devices which could be considered applicable to the DUE, which have not already been assessed within the risk management file for the DUE.

Comprehensive systematic scientific literature searches and supplemental manual internet searches were conducted for State-of-the-art (SotA)-Clinical Landscape, SotA-Similar (Benchmark) Devices, and the DUE. The literature searches resulted in 14 relevant publications for the SotA, and one relevant non-clinical publication for the DUE. The overall quality of the identified publications was assessed to be sufficient. The identified literature was analyzed for safety, clinical performance, usability, hazards/risks, off-label use, etc. In addition, relevant publications were analyzed with a focus on comparing the DUE to medical alternatives (similar devices and alternate therapies). Irrigation Sets showed favorable outcomes in comparison with medical alternatives based on the identified SotA information.

No unknown side effects, emergent risks, or possible systematic misuse or off-label use of the device were identified.

In addition, the data analyzed during this data collection period confirms the information stated in the device's information materials, such as the intended purpose, indirect benefits, and the intended patient population is accurate.

The safety, clinical performance, and indirect benefit of Irrigation Sets were demonstrated with this clinical

evaluation. All identified safety-related complaints, potential risks, and usability aspects have been addressed in the DUE's risk management file. The overall residual risks were assessed as acceptable in the final risk management report for Irrigation Sets.

The benefits associated with the use of Irrigation Sets outweigh the residual risks when used as intended.

2 PURPOSE AND SCOPE

2.1 Purpose

Clinical evaluation is an essential element of the conformity assessment for CE marking of medical devices and is required for all risk classes. According to Regulation (EU) 2017/745, Article 61 and ANNEX XIV, a clinical evaluation is a systematic and planned process to continuously generate, collect, analyze, and assess the clinical data pertaining to a device in order to verify the safety and clinical performance, including clinical benefits, of the device when used as intended by the manufacturer. However, there are certain conditions when conformity with the General Safety and Performance Requirements (GSPRs) outlined in Regulation (EU) 2017/ 745, Annex I can be based on the results of non-clinical testing methods alone (Article 61[10]). This CER will be relying on non-clinical data to support the GSPRs.

The purpose of this CER is to document the assessment of the safety and clinical performance of Irrigation Sets, as described in the Clinical Evaluation Plan (CEP) [BXU601670_MDR_CEP]. The objective of the clinical evaluation process is to establish conformity with the relevant GSPRs set out in Annex I of MDR 2017/745. The planning and execution of the clinical evaluation is conducted in accordance with MDR 2017/745 Annex XIV Part A, Clinical Evaluation and MEDDEV 2.7/1 Rev 4, Guidelines on Medical Devices, "Clinical Evaluation: A Guide for Manufacturers and Notified Bodies Under Directives 93/42/EEC and 90/385/EEC".

This CER is written in compliance with the Baxter global procedure: GQP-09-31.

This clinical evaluation is carried out in accordance with the clinical evaluation plan, BXU601670_MDR_CEP/A.

2.2 Scope

The scope of this clinical evaluation is based upon the applicable GSPRs set out in Annex I and XIV as specified to MDR 2017/745. This analysis is performed from the clinical perspective, with consideration of the nature and history of Irrigation Sets. This clinical evaluation shall be thorough and objective and identify, appraise, and analyze both favorable and unfavorable data. Its depth and extent shall be proportionate and appropriate to the nature, classification, intended purpose, and risks/hazards of the DUE, as well as to Baxter's claims with respect to the device.

The following outlines the aspects considered in this CER:

- Device description
- Design features of the device, indications for its use, or target populations that require specific attention, including any safety or performance concerns, contraindications, and precautions, method of application and claims about the safety and performance of the device

- Risk management documents associated with the device, identifying the risks associated with the device and how these risks have been addressed. The significance of any clinical risks that remain after design risk mitigation strategies is conducted
- Current knowledge and state of the art in the field, including applicable standards and guidance documents, information relating to the medical condition managed by the device, the natural course of the condition, benchmark devices and other devices and alternatives available to the target population
- Introduction or planned introduction of any clinically relevant (non-administrative) design changes, changes to materials and/or manufacturing processes, and changes to informational materials such as the label, Instructions for Use (IFU), or promotional materials
- Information on any specific clinical concerns that have more recently emerged and should be addressed
- Post-market surveillance (PMS) aspects that require updates in this CER
- The complaint history of the subject device(s)
- Needs for planning PMS activities
- Published scientific literature relevant to the subject devices
- Assessment of benefit/risk ratio
- Any off-label usage of the device will also be evaluated, and any risk(s) identified will be evaluated

Table 2-1 provides the data collection periods (DCP) for the periodic data sets that will be analyzed during the clinical evaluation.

Table 2-1: Data Collection Periods (DCP) for Periodic Data Sets Analyzed in the Clinical Evaluation

Data Type	Search Period
Scientific Literature	DUE: 01-SEP-2004 to 31-AUG-2024 SotA: 01-SEP-2019 to 31-AUG-2024
Supplemental Internet Literature	No date range limit
Clinical Trial Registries	No date range limit
External Vigilance/Recall Databases	01-SEP-2019 to 31-AUG-2024
Internal PMS Data	01-SEP-2019 to 31-AUG-2024
Sales Data	01-SEP-2019 to 31-AUG-2024

2.3 Regulatory Requirements

This clinical evaluation report will assess the conformity with the relevant GSPRs 1, 2, 3e, and 8 in Annex I of EU MDR 2017/745 under normal conditions of the intended use of the device, and the evaluation of the undesirable side-effects, and the acceptability of the risk-benefit ratio. The clinical evaluation shall be based on non-clinical data per Article 61(10) providing sufficient evidence, including where applicable, relevant data as referred to in Annex III of EU MDR 2017/745).

2.4 Changes Since Last Clinical Evaluation

Since the last issued MDD CER [1248528_CER] for Irrigation Sets the following changes have occurred:

- This initial MDR CER will refer to MDR requirements according to article 61(10).
  - Essential Requirements were replaced with GSPRs. The CER refers to MDR article 61(10) requirements.
- Finished Goods Product Code EMC4002A has not been added to the scope of this clinical evaluation as the product is undergoing end of life per CC-2023-005849 / PR#2803507.
  - Several sections of the CER were revised to incorporate the new finished goods product codes
- The IFU of all included products were updated according to MDR requirements.
  - The updated labelling elements were addressed in **Section 5**.
- The wording of the indications was slightly changed. However, the content did not change.
  - The changed wording of the indications was addressed in **Section 5.2**.
- The cautions were aligned for the Irrigation Sets within MDR remediation.
  - The aligned cautions were addressed in **Section 5.10**.
- The method of application was updated.
  - The updated method of application was addressed in **Section 5.7**.
- The technical outcome parameter for the indirect benefit of the Irrigation Sets was changed to “No use-related risks or complaints that trigger a need for Human Factors validation.” what is reflected by the Irrigation Sets (Malta Access Codes) human factors/usability engineering evaluation report [BXU578606].
  - The updated technical outcome parameter were addressed in **Section 5.12**.
- The safety and clinical performance objectives as well as the respective safety and clinical performance acceptance criteria have been updated.
  - The updated safety and clinical performance objectives as well as the respective safety and clinical performance acceptance criteria were addressed in **Section 13**.
- The clinical hazards/ risks associated with the intended use of the medical device were updated.
  - The updated list of hazards/ risks will be addressed in **Section 8.2**.
- The intended users were updated [BXU574574].
  - The updated intended users were addressed in **Section 5.4**.
- The intended patient population were updated [BXU574574].
  - The updated patient population was addressed in **Section 5.3**.
- Applicable standards were updated.
  - The updated standards were addressed in **Section 7**.
- Reliance on non-clinical data in accordance with article 61(10) MDR.
  - The whole CER was updated (where required) to reflect the reliance on non-clinical data in accordance with article 61(10) MDR.
- The device description was updated [BXU574574].
  - The updated device description is addressed in **Section 4.2**.

2.5 Deviations from the CEP

No deviations occurred between the CEP and the CER.

3 MANUFACTURER CONTACT DETAILS

Table 3-1 presents the manufacturer information for Irrigation Sets.

Table 3-1: Manufacturer Information

Legal Manufacturer Information	
Name:	Baxter Healthcare SA
Address:	Thurgauerstrasse 130 8152 Glattpark (Opfikon) Switzerland
SRN:	CH-MF-000026124
Person Responsible for Regulatory Compliance (PRRC for Legal Manufacturer)	
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E-mail:	serkan_sezer@baxter.com
Phone:	+41 (79) 3762517
Authorized Representative (if applicable)	
Address:	Baxter Deutschland GmbH Edisontrasse 4 85716 Unterschleissheim Germany
Contact Person Name:	Serafeim Liapis
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SRN:	DE-AR-000010308

4 DEVICE UNDER EVALUATION (DUE) OVERVIEW

4.1 Identification of the EU MDR DUEs in Scope of the Clinical Evaluation

General information on the DUEs in scope of this CER is provided in **Table 4-1**. The devices and codes included in **Table 4-1** are intended to be included in the MDR certificate.

Table 4-1: MDR DUE General Device Information

Device Proprietary Name(s) for the DUE	Irrigation Sets					
Development Code(s) for the DUE	**#**	**Product Name**	**Finished Goods Product Code**	**EMDN Codes**	**EMDN Terms**	**Basic UDI-DI**
	1.	Set for Urological Irrigation	7400009A	A03040201	Bladder Irrigation Kits, Single Use	00854120000000000000153JC
	2.	Y Set for Urological Irrigation	7401010A	A03040201	Bladder Irrigation Kits, Single Use	00854120000000000000153JC
	3.	Single Lead Irrigation Set	E5MC4002	A030402	Irrigation Kits, Single- Use - Other	00854120000000000000153JC
	4.	Y-Type Irrigation Set	E5MC4007N	A030402	Irrigation Kits, Single- Use - Other	00854120000000000000153JC
	5.	Fast Flow Y-Type Irrigation Set	EMC4015N	A030402	Irrigation Kits, Single- Use – Other	00854120000000000000153JC
	6.	Single Lead Irrigation Set	EMC4042	A030402	Irrigation Kits, Single- Use - Other	00854120000000000000153JC
	7.	Y-Type Irrigation Set	EMC4047	A030402	Irrigation Kits, Single- Use - Other	00854120000000000000153JC
	8.	Y-Type Irrigation Set	EMC4055N	A030402	Irrigation Kits, Single- Use - Other	00854120000000000000153JC

Table 4-1: MDR DUE General Device Information

	9.	Irrigation Jet	RMC4916	A030402	Irrigation Kits, Single- Use - Other	00854120000000000000153JC
	10.	Y-Type Irrigation Set	VMC4005	A030402	Irrigation Kits, Single- Use - Other	00854120000000000000153JC

	#	Product Name	Finished Goods Product Code	Version/Model or Size (if applicable)
DUE Catalog Numbers(s) and Versions or Sizes	1.	Set for Urological Irrigation	7400009A	Set for Urological Irrigation
	2.	Y Set for Urological Irrigation	7401010A	Y Set for Urological Irrigation
	3.	Single Lead Irrigation Set	E5MC4002	Single Lead Irrigation Set
	4.	Y-Type Irrigation Set	E5MC4007N	Y-Type Irrigation Set
	5.	Fast Flow Y-Type Irrigation Set	EMC4015N	Fast Flow Y-Type Irrigation Set
	6.	Single Lead Irrigation Set	EMC4042	Single-lead Irrigation Set – Easy Flow Uni Set
	7.	Y-Type Irrigation Set	EMC4047	Y-Type Irrigation Set – Easy Flow Multi - Set
	8.	Y-Type Irrigation Set	EMC4055N	Y-Type Irrigation Set – Easy Flow Ultra Set
	9.	Irrigation Jet	RMC4916	Irrigation Jet
	10.	Y-Type Irrigation Set	VMC4005	Y-Type Irrigation Set
Registration Status	MDR: Not available yet – certificate to be done MDD legacy devices: see **Table 4-2** below			
CE Mark Certificate Number and the Date of First MDD CE Mark	G2S 062680 0146 Rev.00 Date: 2019-11-18 The date of the first MDD CE mark for Irrigation Sets can be found detailed per code in **Table 4-2**.			

Table 4-1: MDR DUE General Device Information

Certificate (if available)		
CE Mark Certificate Number and the Date of First MDR CE Mark Certificate (if available)	Medical Device Regulation (MDR) certificate is not yet available.	
Risk Class	**Risk Class**	**Additional Characteristics**
	Class I ☒	Reusable (r) ☐ Sterile (s) ☒ Measuring (m) ☐
	Class IIa ☐ Class IIb ☐ Class III ☐	Active ☐ Invasive ☐ Implantable ☐
Applicable MDR Device Classification Rule	Rule 2 of Annex VIII Regulation (EU) 2017/745 on Medical Devices All non-invasive devices intended for channelling or storing blood, body liquids, cells or tissues, liquids or gases for the purpose of eventual infusion, administration or introduction into the body are classified as class IIa: • if they may be connected to a class IIa, class IIb or class III active device; or • if they are intended for use for channelling or storing blood or other body liquids or for storing organs, parts of organs or body cells and tissues, except for blood bags; blood bags are classified as class IIb. In all other cases, such devices are classified as class I.	
Shelf Life	The Shelf life of the Irrigation Sets is 36 months (35 months Expiry), after release.	

Table 4-1: MDR DUE General Device Information

Expected Lifetime	The Irrigation Sets are single use devices which can be used up to 72 hours during urological procedures and up to 6 hours during surgical procedures. Note: The above information is not applicable to the product code RMC4916 since this is used as a jet-set rather than an irrigation set. This set is typically for one time use only and the clinical feedback does not demand for the specification of a period of use.
Novel Product	Yes ☐ No ☒ The Irrigation Sets qualify as well-established technology and the changes made to the product since the initial CE mark for MDD device are not considered significant changes per MDCG_2020-13, refer to **Sections 4.4** and **4.5**.
Device-Related Novelties, if applicable	Yes ☐ No ☒ N/A ☐ The Irrigation Sets do not include any device related novelties.
Clinical or Surgical Procedure Related Novelty, if applicable	Yes ☐ No ☒ N/A ☐ The Irrigation Sets do not include any clinical or surgical procedure related novelty.

Table 4-2 provides a list of additional Baxter devices which are not the EU MDR DUE. These Baxter MDD legacy devices will be included in the scope of this CER. Although these devices are not in scope of the EU MDR DUE's CE certificate, these devices provide historical data to support the MDR DUE as they are the same as the EU MDR DUE. These devices/codes will be included in the review of literature, internal complaints, FSCAs, CAPAs, etc. The Baxter similar devices codes will be included in the review of literature and external vigilance & recall database searches.

Additional non-Baxter similar devices are discussed in **Section 9.4** and they will also be included in the review of literature and external vigilance & recall database searches. The device categories in **Table 4-2** are listed in the order of the strength of their evidence (from high to low) to support the safety and clinical performance of the DUE.

Table 4-2: Other Baxter Devices Used in this Clinical Evaluation

#	Product Name	Finished Goods Product Code	Version/Model or Size, if applicable	In What Countries?	First MDD CE certificate[1]
DEVICES WHICH ARE EXACTLY THE SAME AS THE DUE					
Legacy Device This device category is used when the legacy device (CE-marked under MDD or AIMDD) and the MDR device are the exact same device* (same design, components, functionality, labelling, etc.). *may include non-clinically relevant label differences to address country requirements					
1.	Set for Urological Irrigation	7400009A	Set for Urological Irrigation	European countries	25-MAR-2009
				Non-European countries	N/A
2.	Y Set for Urological Irrigation	7401010A	Y Set for Urological Irrigation	European countries	25-MAR-2009
				Non-European countries	N/A
3.	Single Lead Irrigation Set	E5MC4002	Single Lead Irrigation Set	European countries	01-JAN-2009
				Non-European countries	N/A
4.	Y-Type Irrigation Set	E5MC4007N	Y-Type Irrigation Set	European countries	01-JAN-2009
				Non-European countries	N/A
5.	Fast Flow Y-Type Irrigation Set	EMC4015N	Fast Flow Y-Type Irrigation Set	European countries	14-APR-2011
				Non-European countries	N/A
6.	Single Lead Irrigation Set	EMC4042	Single-lead Irrigation Set – Easy Flow Uni Set	European countries	01-FEB-2009
				Non-European countries	N/A

[1] The date of the first MDD CE certificate is not relevant for the Non-European countries. However, the Irrigation Sets have been on the market since the early 1980s.

Table 4-2: Other Baxter Devices Used in this Clinical Evaluation

#	Product Name	Finished Goods Product Code	Version/Model or Size, if applicable	In What Countries?	First MDD CE certificate[1]
7.	Y-Type Irrigation Set	EMC4047	Y-Type Irrigation Set – Easy Flow Multi - Set	European countries	01-AUG-2008
				Non-European countries	N/A
8.	Y-Type Irrigation Set	EMC4055N	Y-Type Irrigation Set – Easy Flow Ultra Set	European countries	01-DEC-2008
				Non-European countries	N/A
9.	Irrigation Jet	RMC4916	Irrigation Jet	European countries	01-JUL-2008
				Non-European countries	N/A
10.	Y-Type Irrigation Set	VMC4005	Y-Type Irrigation Set	European countries	04-MAY-2012
				Non-European countries	N/A
Finished Goods Product Code EMC4002A has not been added to the scope of this clinical evaluation as the product is undergoing end of life per CC-2023-005849 / PR#2803507. EMC4002A contained DEHP and was replaced by an existing nDEHP code (E5MC4002).					
11.	Single-lead Irrigation Set	EMC4002A	Single-lead Irrigation Set	European countries	12-JUN-2012
				Non-European countries	N/A

4.2 Technical Device Description for all DUE in Scope of the CER

This section provides an overview of the Irrigation Sets, which reflects the scope of the clinical evaluation.

These sets are intended for the delivery of irrigation solutions from the fluid container to the irrigation site during continuous/intermittent bladder irrigation or surgical procedures including but not limited to arthroscopic, gynaecological, obstetrical, gastrointestinal and open wound procedures [BXU574574].

These sets come in various configurations including, but not limited to:

- Spike (Standard or Easyflow)
- Irrigation Chamber (with bubble trapper where applicable)
- Clamps
- Tubing
- Catheter Adaptor
- Silicone Tubing

A typical Irrigation Set consists of a spike, transparent tubing, on/off clamp, irrigation chamber (not essential), roller clamp, catheter adaptor, and silicone tube at the distal end. The spike is intended to perforate the irrigation solution container closure. The on/off clamp is intended to shut-off the flow completely per the therapy needs.

The chamber is intended to visualize drops and has no intent for counting the drops. A bubble trapper filter is part of some chambers (EMC4015N, EMC4055N) to minimize the entrainment of bubbles within the irrigated solution to mitigate air generated in the fluid due to the turbulence caused by the high flow rates. Roller clamps (flow regulators) are intended to adjust the flow rate per therapy needs. The silicone tube facilitates compatibility/interface with the surgical instrument (e.g. endoscopes, resectoscopes and cystoscopes), and it is manually detachable to allow for the catheter adaptor to be connected to the urinary drainage catheter (i.e. Foley catheter).

Irrigation sets have either a single-lead configuration or a double-lead configuration. Double-lead configuration sets are intended to ensure continuity of fluid flow during irrigation therapy. Whilst the first container is being depleted, the second container is spiked with the remaining lead and placed on a hanger by the clinician.

All tubes and chambers are translucent to allow for observation of the fluid and detect any potential air bubbles. The Irrigation Sets are not to be used in conjunction with an active medical device such as an infusion pump. They may be used together with a pressure cuff around the solution container (as allowed by the manufacturer). A schematic diagram representing a typical Irrigation Set is presented in **Figure 4-1**.

Figure 4-1: Schematic picture of a typical Irrigation Set [EMC4055N]

Based on the procedure performed, the total number of bags used vary from two “3-Litre” bags to twenty “3-Litre” bags. The flow rates of the Irrigation Sets vary and are dependent on the catheter used and the working element. Y-Type Sets are preferred in operating theaters, whereas single flow sets are used more often in the hospital wards. Sets containing a bubble trapper filter are suitable for most surgical procedures.

4.3 Previous Generations of the DUE

There are no previous generations of Irrigation Sets.

4.4 Well-Established Technology (WET)

The Irrigation Sets are considered to be well-established technology (WET) based on the criteria set forth in MDCG 2020-6 and the MDR. The Irrigation Sets fulfill the requirements listed below:

- Relatively simple, common, and stable designs with little evolution (see **Sections 4.2** and **9**)
- Their generic device group has well-known safety and has not been associated with safety issues in the past (see **Section 9.5**)

- Well-known clinical performance characteristics and their generic device group are standard of care devices where there is little evolution in indications and the state of the art (see **Sections 4.2** and **9**)
- A long history on the market (see **Section 9**)

Per MDCG 2020-6: Stable, well-established technologies that perform as intended and are not associated with safety concerns, and where there has been no innovation, are less likely to be the subject of research, and therefore literature data may be limited or non-existent. In exceptional cases, particularly for low-risk standard of care devices where there is little evolution in the state of the art, and the device is identified as belonging to the group of 'well-established technologies' a lower level of evidence may be justified to be sufficient for the confirmation of conformity with relevant GSPRs.

The demonstration of conformity with General Safety and Performance Requirements based on clinical data is not deemed appropriate for the Irrigation Sets in compliance with Regulation (EU) 2017/745 Article 61 Section 10 (see Section 10.5 of BXU601670_MDR_CEP/A). Details on the datasets that will contribute to the clinical evaluation of the Irrigation Sets can be found in Table 10-1 ("Planned Clinical Evaluation Data Sources") of BXU601670_MDR_CEP/A and a detailed justification for the level of evidence is included in Section 10.3 of BXU601670_MDR_CEP/A.

4.5 Device Change Identification

The technology used for Irrigation Sets is well established and there have been no recent changes to design, the principles of operation, or intended use.

Since the MDD CER [1248528_CER], there have been no changes in the intended purpose related to the devices under evaluation with impact to the current MDR CER. However, the intended users of the DUE were revised for MDR since these devices should not be used by Patients or Caregivers as mentioned in Design Input - Requirements for Access Products in scope of Medication Delivery EU MDR Compliance Change Controls [BXU574574]. The Irrigation Sets Risk Management Plan [1266804] and RACT [BXU600002] will be updated accordingly. Irrigation Sets such as Irrigation Set for Urology (EMC3263U, EMC3263L), Artroline (7A505A00A), Uni-Set Single-lead Irrigation Set (RMC4043) and TUR Cysto Irrigation Series Set (RMC4006) have been obsoleted from the European market and were excluded from DUE scope in the current MDD CER revision (see Section 2.4 of 1248528_CER/C). The product codes E5MC4002, EMC4042, EMC4015N, E5MC4007N, EMC4055N, and VMC4005 underwent non-DEHP conversion, which was already included in the previous MDD CER (rev B). Device changes are listed in **Table 4-3**.

Table 4-3: Device Revision History of MDD Legacy Devices

#	Product Code	Modification Date	Modification
1	7400009A	September 10, 2009	Transfer of Mould
		September 26, 2014	Revise Sterilization Category
		October 6, 2016	Remove Cap

Table 4-3: Device Revision History of MDD Legacy Devices

#	Product Code	Modification Date	Modification
		December 01, 2016	New Roller
		January 26, 2018	New Ink P/N 20002188
		March 31, 2020	New Carton Boxes P/N 30002723U and P/N 30002724U
		February 27, 2021	Update Silicone Tube P/N 20002733; Update Expiry Date
		July 5, 2022	Remove Sterilization Indicator
2	7401010A	September 10, 2009	Transfer of Mould (0M01137T)
		September 26, 2014	Revise Sterilization Category
		October 22, 2018	New Large Clamp 60023119 Instead of 60021043.
		April 1, 2020	New Carton Boxes P/N 30002723U and P/N 30002724U
		February 27, 2021	Update Silicone Tube P/N 20002733; Update Expiry Date
		July 5, 2022	Remove Sterilization Indicator
3	E5MC4002	October 21, 2014	Malta Alternate Manufacturing Plant
		June 06, 2016	Remove Cap
		January 19, 2017	Non-DEHP Conversion
		November 15, 2017	New Roller Clamp
		January 29, 2017	New Ink P/N 20002188
		May 10, 2018	Addition of Malta Alternate
		November 21, 2019	UDI Requirement: New Labelling
		April 20, 2020	New Carton Boxes P/N 30002718U and P/N 30002724U
		February 27, 2021	Update Silicone Tube P/N 20002733; Update Expiry Date; Remove Reference to Certification
		April 22, 2022	Update Label P/Ns; Remove Sterilization Indicator
4	E5MC4007N	October 21, 2014	Alternate Malta Manufacturing Plant
		May 25, 2015	Tube Quantity; Alternates for 60017430
		April 25, 2016	Jig Reference; Cert. for Malta
		January 25, 2017	New Ink P/N 20002188
		April 10, 2020	New Carton Boxes P/N 30002723U and P/N 30002724U

Table 4-3: Device Revision History of MDD Legacy Devices

#	Product Code	Modification Date	Modification
		October 21, 2020	Non-DEHP Conversion; Update Silicone Tube P/N; Update Clamp P/N; Update Label P/Ns
		April 28, 2021	Temporary Reduction of Expiry Date to 34 Months
5	EMC4015N	December 09, 2003	Upper Tube Length
		September 09, 2004	Chamber (Tap/Conical), Catheter
		November 16, 2005	New Chamber 60061580
		September 11, 2007	Starex Spike
		April 17, 2013	Tunisia Transfer
		July 09, 2014	Alternate Malta Production and Certificate Update
		October 28, 2016	Non-DEHP Conversion/Temporary Remove of Malta Production
		October 24, 2018	New Large Clamp 60023119
		April 9, 2020	New Carton Boxes P/N 30002718U and P/N 30002724U
		March 1, 2021	Update Silicone Tube P/N 20002733; Update Expiry Date; Remove Reference to Certification
		December 10, 2021	Remove 04.99.18.099; Remove Cert 2005-07 (for Malta)
		July 13, 2022	Remove Sterilization Indicator
6	EMC4042	May 07, 2005	Revert to Catheter ASBL 60061055
		September 24, 2007	Change Tube Tolerance
		February 12, 2008	Alternate Cut Tube (MACC100)
		October 21, 2014	Malta Alternate Manufacturing Plant
		September 20, 2016	Remove Cap
		October 28, 2016	Non-DEHP Conversion/Temporary Removal of Malta Manufacturing
		January 25, 2017	New Roller Clamp
		November 29, 2017	New Ink P/N 20002188
		April 3, 2018	Addition of Malta Alternate
		October 10, 2019	UDI Requirement: New Flexo P/N
		March 31, 2020	New Carton Boxes P/N 30002718U and P/N 30002724U

Table 4-3: Device Revision History of MDD Legacy Devices

#	Product Code	Modification Date	Modification
		February 27, 2021	Update Silicone Tube P/N 20002733; Update Expiry Date; Remove Reference to Certification
		July 13, 2022	Remove Sterilization Indicator
7	EMC4047	September 30, 2004	New Modified Catheter Adaptor
		January 05, 2005	Lustran Roller Clamp
		September 19, 2005	In-House Roberts; tube
		March 16, 2006	Welvic Tubing Material
		May 15, 2013	Tunisia Transfer
		June 13, 2016	Remove Cap
		October 22, 2018	New Large Clamp
		March 5, 2019	New Carton Boxes P/N 30002723U and P/N 30002724U
		February 27, 2021	Update Silicone Tube P/N 20002733; Update Expiry Date; Replace Traction Note
		July 13, 2022	Remove Sterilization Indicator
8	EMC4055N	January 20, 2016	Remove Cap
		October 14, 2016	Non-DEHP Conversion
		October 22, 2018	New Large Clamp 60023119 Instead of 60021043
		April 1, 2020	New Carton Boxes P/N 30002718U and P/N 30002724U
		March 1, 2021	Update Silicone Tube P/N 20002733; Update Expiry Date; Remove Reference to Certification
		December 10, 2021	Remove 04.99.18.099; Remove Cert 2005-07 & 2008-10 (for Malta)
9	RMC4916	August 07, 2013	Tunisia Transfer
		May 9, 2016	Malta Alternate; Addition of Notes for Malta
10	VMC4005	July 15, 2005	In-house Roberts Clamp; New Tube Part No. 9062
		April 10, 2013	Tunisia Production
		June 19, 2014	Alternate Malta Production and Certificate Update
		October 13, 2016	Non-DEHP Conversion/Temporary Removal of Malta Production
		May 04, 2017	Update Solvent App Method for Junction 5 to 6

Table 4-3: Device Revision History of MDD Legacy Devices

#	Product Code	Modification Date	Modification
		October 22, 2018	New Large Clamp 60023119 Instead of 60021043
		April 10, 2020	New Carton Boxes P/N 30002718U and P/N 30002724U
		March 1, 2021	Update Silicone Tube P/N 20002733; Update Expiry Date; Remove Reference to Certification
		November 22, 2021	Remove 04.99.18.100; Remove Cert 2005-07 (for Malta)
		April 22, 2022	Update Label P/Ns; Remove Sterilization Indicator
Finished Goods Product Code EMC4002A has not been added to the scope of this clinical evaluation as the product is undergoing end of life per CC-2023-005849 / PR#2803507 (see also **Table 4-2**)			
11	EMC4002A	October 12, 2004	Modified Catheter Sub-Assembly
		October 12, 2005	Tunisia Production
		September 24, 2007	Change Tube Tolerance-Starex
		October 21, 2014	Malta Alternate Manufacturing Plant
		April 22, 2016	Alternate for P/N 60017430; Jig Reference; Cert. for Malta
		April 4, 2018	New Ink P/N 20002188
		March 5, 2019	New Carton Boxes P/N 30002723U and P/N 30002724U
		February 27, 2021	Update Silicone Tube P/N 20002733; Update Expiry Date; Remove Reference to Certification
		July 13, 2022	Remove Sterilization Indicator

4.6 Accessories, Compatible Devices and Component Parts Not Considered to be the DUE

Irrigation Sets are used during and/or after surgery to channel irrigation solutions from the irrigation solution container (plastic bags) to the surgeon's tools (e.g., resectoscope) or urological catheter. Irrigation Sets are used in combination with a storage plastic container (containing sterile solutions for irrigation) and a surgical scope or a urological catheter. The storage container may be used together with a pressure cuff.

There are no components of the DUE that are sold independently or could be used as replacement parts.

4.7 Special Concerns

The DUE does not have design features that require specific attention. These features are incorporation of pharmaceutical/medicinal substances, non-viable animal or human tissues, blood products (human or animal),

substances which are carcinogenic, mutagenic or toxic to reproduction (CMR), endocrine-disrupting substances, radioactive materials, special mechanical and physicochemical characteristics or other design features of the device, or any indications or target populations, which require specific attention/ pose special performance or safety concerns such as sterile/ nonsterile, radioactivity, invasive, active, therapeutic/ diagnostic, etc.).

No specific clinical concerns have emerged for the DUE since the previous clinical evaluation [1248528_CER/C] which need to be addressed in the clinical evaluation.

5 DUE PRODUCT LABELING OVERVIEW

5.1 Intended Purpose [BXU574574, IFU for the DUE[2]]

For the delivery of irrigation solutions from the fluid container to the irrigation site.

5.2 Indications [IFU for the DUE2]

There is no indication stated for the Irrigation Sets in the IFU. However, **Table 5-1** provides a list of the indications and the reference citation(s) to non-clinical studies to support each indication. Refer to **Section 20** for the bibliography of any referenced citations.

Table 5-1: List of Indications for Irrigation Sets

Indication [BXU574574]	Reference Citation or Study	Evidence to Support Indication
These sets are intended for the delivery of irrigation solutions from the fluid container to the irrigation site during continuous/intermittent bladder irrigation or surgical procedures including but not limited to arthroscopic, gynaecological, obstetrical, gastrointestinal and open wound procedures.	Access Validation Study [63129FR] (**Section 11.1.3.2**)	All the 15 participants completed 100% of all the tasks in the scenario and met the acceptance criteria of the study. The study demonstrated Irrigation Sets could effectively be used for their intended uses in the intended use environments. Overall, all user needs and intended uses were successfully validated and no additional tests were required.

5.3 Intended Patient Populations [BXU574574]

These sets are used by healthcare professionals (nurses, physicians, technicians, and pharmacists) to irrigate drugs/solutions to stable patients and unstable/critically ill patients with comorbidities; as well as to patients of all age ranges (pediatric/adult/elderly).

[2] 07-19-00-4283, 07-19-00-4284, 07-19-00-4768, 07-19-00-4769, 07-19-00-4304, 07-19-00-4773, 07-19-00-3744, 07-19-00-7245, 07-19-00-3743, 07-19-00-4775, 07-19-00-3746, 07-19-00-5643, 07-19-00-3745, 07-36-00-4780, 07-36-00-4306, 07-19-00-5644, 07-19-00-4307; see **Section 21.3**

5.4 Intended Users [BXU574574]

These sets are intended to be used by healthcare professionals (nurses, physicians, technicians, and pharmacists).

5.5 Intended Environment [BXU574574]

These products are used in health care institutions, alternate sites including long term care facilities, skilled nursing facilities, and subacute care facilities, physician offices, free standing centers, home health and hospice, transport/ambulance, and free-standing specialty pharmacies.

5.6 Single Use or Reusable

The Irrigation Sets are intended for single use only.

5.7 Application Guidance

Directions for Use: Use Aseptic Technique [07-19-00-4283]

(1) Tip Protector - (2) Spike - (3) Chamber - (4) Roller clamp - (5) Catheter Adapter - (6) Silicone Tube

1. Close Roller Clamp (4).
2. Remove Protective Cap (1) from Spike (2).
3. Insert spike (2) into irrigation solution bag.
4. Squeeze and release the Chamber (3) until it is half-filled with solution.
5. Open roller clamp (4).
6. Fully prime the set to remove all air bubbles from set prior to use.
7. Close roller clamp (4).
8. For Surgical Application: Connect Silicone Tube (6) to the Resectoscope or Cystoscope.
   For Urological Application: Remove Silicone tube (6) from Catheter Adapter (5) and insert the Catheter Adapter (5) into the funnel of the urinary drainage catheter.
9. Open Roller clamp (4) and adjust the flow.

Directions for Use: Use Aseptic Technique [07-19-00-4284, 07-19-00-4769, 07-19-00-4304, 07-19-00-4773, 07-19-00-3744, 07-19-00-4775, 07-19-00-3746, 07-19-00-5643, 07-19-00-3745]

(1) Protective Cap - (2) Spike - (3) Shut-off Clamp - (4) Chamber - (5) Roller Clamp - (6) Catheter Adapter - (7) Silicone Tube

1. Close shut-off clamps (3) & roller clamp (5).
2. Remove Protective Cap (1) from Spike (2).
3. Insert spike (2) into the irrigation solution bag.
4. Open the shut-off clamp (3) under the Spike (2) which is connected to the irrigation solution bag.
5. Squeeze and release the Chamber (4) until it is half-filled with solution.
6. Open roller clamp (5) and lower shut-off clamp (3).
7. Fully prime to remove all air bubbles from set prior to use.
8. Close roller clamp (5).

9. For Surgical Application: Connect Silicone Tube (7) to the Resectoscope or Cystoscope.
   For Urological Application: Remove Silicone tube (7) from Catheter(s) Adapter (6) and insert the Catheter Adapter (6) into the funnel of the urinary drainage catheter.
10. Open Roller clamp (5) and adjust the flow.
11. Upon depletion of the irrigation solution bag, close the open shut-off clamp (3) and replace the empty bag.

Directions for Use: Use Aseptic Technique [07-19-00-4768, 07-19-00-7245, 07-19-00-3743]

(1) Protective Cap - (2) Spike - (3) Chamber - (4) Roller Clamp - (5) Catheter Adapter - (6) Silicone Tube

1. Close Roller Clamp (4).
2. Remove Protective Cap (1) from Spike (2).
3. Insert spike (2) into irrigation solution bag.
4. Squeeze and release the Chamber (3) until it is half-filled with solution.
5. Open roller clamp (4).
6. Fully prime the set to remove all air bubbles from set prior to use.
7. Close roller clamp (4).
8. For Surgical Application: Connect Silicone Tube (6) to the Resectoscope or Cystoscope.
   For Urological Application: Remove Silicone tube (6) from Catheter Adapter (5) and insert the Catheter Adapter into the funnel of the urinary drainage catheter.
9. Open Roller clamp (4) and adjust the flow.

Directions for Use: Use Aseptic Technique [07-36-00-4780, 07-36-00-4306]

(1) Protective Cap - (2) Spike

1. Remove Protective Cap (1) from Spike (2).
2. Insert spike (2) into irrigation solution bag.
3. Fully prime the set to remove all air bubbles from set prior to use.

Directions for Use: Use Aseptic Technique [07-19-00-5644, 07-19-00-4307]

(1) Protective Cap - (2) Spike - (3) Shut-off Clamp - (4) Catheter Adapter - (5) Silicone Tube

1. Close shut-off clamps (3).
2. Remove Protective Cap (1) from Spike (2).
3. Insert spike (2) into the irrigation solution bag.
4. Open the shut-off clamp (3) under the Spike (2) which is connected to the irrigation solution bag.
5. Open lower shut-off clamp (3).
6. Fully prime to remove all air bubbles from set prior to use.
7. Close lower shut-off clamp (3).
8. For Surgical Application: Connect Silicone Tube (5) to the Resectoscope or Cystoscope.
   For Urological Application: Remove Silicone tube (5) from Catheter Adapter (4) and insert the Catheter Adapter (4) into the funnel of the urinary drainage catheter.

9. Open lower shut-off clamp (3) to start the flow.
10. Upon depletion of the irrigation solution bag, close the open shut-off clamp (3) and replace the empty bag.

Notes [IFU for the DUE2]

- All incidents should be reported to the manufacturer as identified on the label. In case of incidents involving death or serious injury report them to the competent authority as well.
- Store at room temperature.
- Set to be replaced every 72 hours or as per institutional protocol, whichever comes first.
- Dispose as per healthcare provider's policy.
- *07-19-00-4283, 07-19-00-4284, 07-19-00-4768, 07-19-00-4769, 07-19-00-4304, 07-19-00-5644, 07-19-00-4307:* The fluid path of this product contains ABS, PVC, and Silicone Rubber. Ensure that the drug is compatible with these materials.
  07-19-00-4773, 07-19-00-3744, 07-19-00-3745, 07-19-00-5643: The fluid path of this product contains ABS, MABS, HDPE, PVC, and Silicone Rubber. Ensure that the drug is compatible with these materials.
  07-19-00-7245, 07-19-00-3743, 07-19-00-4775, 07-19-00-3746: The fluid path of this product contains ABS, MABS, PVC, and Silicone Rubber. Ensure that the drug is compatible with these materials.
  07-36-00-4780, 07-36-00-4306: The fluid path of this product contains ABS and PVC. Ensure that the drug is compatible with these materials.
- This product is not manufactured with natural rubber latex.
- Contains less than 0.1% w/w DEHP
- See the glossary for all symbols and definitions.[3]

5.8 Contraindications

There are no known specific situations that contraindicate the use of this device.

5.9 Warnings

There are no warnings applicable to the use of this device.

5.10 Cautions [IFU for the DUE2]

- Do not use if package has been opened or damaged or if tip protectors are loose or missing.[4]
- The set can be used under pressure to assist flow (max. 300mmHg).
- Do not allow air to be trapped in set.
- Do not remove from pouch until ready to use.

[3] 07-19-00-4283, 07-19-00-4284, 07-19-00-4768, 07-19-00-4773, 07-19-00-3744, 07-19-00-3743, 07-19-00-4775, 07-19-00-3746, 07-19-00-5643, 07-19-00-3745, 07-36-00-4780, 07-36-00-4306, 07-19-00-5644, 07-19-00-4307 only; see **Section 21.3**

[4] 07-19-00-4283, 07-19-00-4284, 07-19-00-4768, 07-19-00-4769, 07-19-00-4304, 07-19-00-4773, 07-19-00-3744, 07-19-00-4775, 07-19-00-3746, 07-19-00-5643, 07-19-00-3745, 07-36-00-4780, 07-36-00-4306, 07-19-00-5644, 07-19-00-4307 only; see **Section 21.3**

- Reuse or reprocessing of a single use device may lead to contamination and compromised device function or structural integrity.
- Single use only. Do not resterilize.
- Not I.V. compatible.

5.11 Residual Risks or Undesirable Side-Effects

There are no adverse events or undesirable effects applicable to the use of this device.

5.12 Indirect Benefits and Outcome Parameters

The clinical benefits of the Medication Delivery Access codes (including the Irrigation Sets) are attained indirectly based on the achievement of the intended purpose (see **Section 5.1**). That is, the medical device on its own does not have direct clinical benefits that are meaningful, measurable, patient-relevant clinical outcomes (as defined in Regulation (EU) 2017/745 Chapter I, Article 2), however the combination of the medical device and the therapy administration indirectly provide a positive impact on the health of the patient. Therefore, the intended purpose of the respective medical device is considered sufficient to indicate the indirect benefits of the device to the intended user. Thus, the Intended Purpose statement in the IFU will be considered sufficient to indicate the indirect benefits. Furthermore, the IFU will detail the safety precautions of the respective medical device, for safe and effective use. **Table 5-2** lists the indirect benefits and technical outcome parameters based on SotA for the Irrigation Sets. However, since the demonstration of conformity with General Safety and Performance Requirements based on clinical data is not deemed appropriate for the Irrigation Sets (see Justification in Section 10.5 of BXU601670_MDR_CEP/A), the acceptance criteria will be evaluated based on non-clinical data within this CER.

Table 5-2: Indirect Benefits and Technical Outcome Parameters Based on SotA

Indirect Benefits	Technical Outcome Parameters	SotA-Based Evidence to Justify the Outcome Parameters	Reference Citations Used to Demonstrate Whether the DUE Meets or Exceeds the Outcome Parameters
The indirect benefit for Irrigation Sets is described through the products intended purpose which states: For the delivery of irrigation solutions from the fluid container to the irrigation site.	No use-related risks or complaints that trigger a need for Human Factors validation [BXU578606].	IEC 62366-1:2015+AMD1:2020, Annex C	Between 01-JAN-2020 and 01-JAN-2022 there were 18 complaints written against the Irrigation Sets Product Family. None of the complaints were found to be associated Use / User Errors. The control measures are in place to mitigate the other failure modes found in the complaint search. It was concluded that Use Error complaints never crossed the threshold. Risk controls already implemented on the product are considered to be adequate. Residual risk as indicated by the risk assessment is considered to be at an acceptable level. (BXU578606, see **Section 11.1.3.3**)

6 SAFETY AND CLINICAL PERFORMANCE PROMOTIONAL CLAIMS

A key consideration in the clinical evaluation is the manufacturer`s clinical claims regarding the safety and clinical performance of the DUE(s). Irrigation Sets are applying Article 61(10); therefore, there are no Baxter-sponsored promotional materials or websites containing clinical claims for Irrigation Sets at the time when this clinical evaluation was conducted.

6.1 Promotional Materials Claims

There were no clinical claims related to the safety and clinical performance of Irrigation Sets included in the promotional materials at the time when this clinical evaluation was conducted. However, **Table 6-1** lists the safety and technical performance claims that are used in the promotion of the DUE and provides reference citations to support each claim, including a summary of each cited reference. All non-clinical claims (supported by non-clinical data) have been included and were validated using non-clinical studies, bench testing and HF testing.

Table 6-1: Safety and Technical Performance Claims

Claim	References and Data for the Claim	Actions Required (if any)
Technical Claims Supported by Non-Clinical Data		
Bubble trap helps to avoid bubbles in the scope view, providing clear visibility during surgery	Reference #1: Air Volume Test [BXU542284], **Section 11.1.3.1** Summary: The purpose of this test was to verify that the bubble trapper filter shall not allow more than 1mL of air after flushing 1.2L of irrigation solution at a flow rate of 600ml/min. A minimum of 298 samples per code to be tested. Requirement: The filter shall eliminate air bubbles. Result: passed	☒ Existing reference ☐ New reference from current DCP ☒ Supports the claim ☐ Refutes the claim
Large drip chamber allows the flow of the solution and potential air bubbles to be easily observed	Reference #1: Simulation of Use Test [BXU542284], **Section 11.1.3.1** Summary: The purpose of this test was to verify that the set and set components exhibit the expected functionality and maintain physical integrity during use while inspecting the set for any leaks, junction disconnections and damaged components. A minimum of 298 samples per code to be tested. Requirement: The drip chamber shall facilitate the priming procedure Result: passed	☒ Existing reference ☐ New reference from current DCP ☒ Supports the claim ☐ Refutes the claim
Safety cap helps prevent touch contamination	Reference #1: Particulate matter testing [BXU542284], **Section 11.1.3.1** Summary:	☒ Existing reference ☐ New reference from current DCP

Table 6-1: Safety and Technical Performance Claims

Claim	References and Data for the Claim	Actions Required (if any)
	The purpose of this test is to verify that the number of particles found inside the fluid path of each sample tested does not exceed the contamination index limit as specified in their respective ISO standard. A minimum of 10 samples (as per ISO standards) per code to be tested. Requirement: Set shall meet particulate matter limits Result: passed	☒ Supports the claim ☐ Refutes the claim
4.0-6.95mm wide bore tubing enables appropriate flow rates	Reference #1: Flow Rate Test [BXU542284], **Section 11.1.3.1** Summary: This test was performed to determine the volume of water that flows through the irrigation set at a determined height for a specific period of time. Such a test shows conformance to ISO 16391 (2002)[5]. A minimum of 30 samples per code are to be tested. Requirement: The set shall allow a flow rate of at least 200 mL water in 1 min under a static head of 0.6m. Result: passed	☒ Existing reference ☐ New reference from current DCP ☒ Supports the claim ☐ Refutes the claim
Clamps provide optimal flow regulation and bag changes when continuous administration is required	Reference #1: Simulation of Use Test [BXU542284], **Section 11.1.3.1** Summary: The purpose of this test was to verify that the set and set components exhibit the expected functionality and maintain physical integrity during use while inspecting the set for any leaks, junction disconnections and damaged components. A minimum of 298 samples per code to be tested. Requirements: • The clamp shall shut-off flow • The regulating clamp shall allow flow regulation Result: passed	☒ Existing reference ☐ New reference from current DCP ☒ Supports the claim ☐ Refutes the claim
Spike with finger guard assists in reducing the risk of touch contamination	Reference #1: Particulate matter testing [BXU542284], **Section 11.1.3.1** Summary: The purpose of this test is to verify that the number of particles found inside the fluid path of each sample tested does not exceed the	☒ Existing reference ☐ New reference from current DCP ☒ Supports the claim ☐ Refutes the claim

[5] ISO 16391 (2002) Aids for ostomy and incontinence - Irrigation sets - Requirements and test methods was withdrawn without any replacement in 2022. However, as there is no replacement, ISO 16391 (2002) still provides insight into the SotA requirements that could be applied to the Irrigation Sets.

Table 6-1: Safety and Technical Performance Claims

Claim	References and Data for the Claim	Actions Required (if any)
and 'needlestick' injuries, while allowing you fast, simple connectivity	contamination index limit as specified in their respective ISO standard. A minimum of 10 samples (as per ISO standards) per code to be tested. Requirement: Set shall meet particulate matter limits Result: passed	
	Reference #2: Simulation of Use Test [BXU542284], **Section 11.1.3.1** Summary: The purpose of this test was to verify that the set and set components exhibit the expected functionality and maintain physical integrity during use while inspecting the set for any leaks, junction disconnections and damaged components. A minimum of 298 samples per code to be tested. Requirements: The spike shall allow insertion into unused containers Result: passed	☒ Existing reference ☐ New reference from current DCP ☒ Supports the claim ☐ Refutes the claim

7 COMMON SPECIFICATIONS, HARMONIZED STANDARDS, AND OTHER SOLUTIONS RELEVANT TO THE DUE

Table 7-1 provides the relevant common specifications, harmonized standards, and other solutions (non-harmonized standards, etc.) which were used in the design and testing of the DUE to demonstrate conformity to the GSPRs that are used to specifically support this clinical evaluation. **Table 7-1** also indicates whether the latest revision of the common specifications, harmonized standards, etc. were fully, or partially applied to the DUE, as well as any exceptions or deviations from those standards. The applicable regulations (e.g., MDR) and guidance (e.g., MEDDEV and MDCG) that have been followed for this clinical evaluation are presented in **Table 7-2** below.

Table 7-1: Common Specifications, Harmonized Standards, and Other Solutions Relevant to the DUE

Relevant Common Specifications, Harmonized Standards, and Other Solutions	Title	Fully or Partially Applied to DUE?	Justification/ Conclusion
Common Specifications			
None			

Table 7-1: Common Specifications, Harmonized Standards, and Other Solutions Relevant to the DUE

Relevant Common Specifications, Harmonized Standards, and Other Solutions	Title	Fully or Partially Applied to DUE?	Justification/ Conclusion
Harmonized Standards			
ISO 15223-1:2021	Medical Devices – Symbols to be used with Medical Device Labels, Labeling and Information to be Supplied – Part 1: General Requirements	Fully applied	N/A
EN ISO 10993-12:2021	Biological Evaluation of Medical Devices – Part 12: Sample Preparation and Reference Materials	Fully applied	N/A
ISO 11135:2014/Amd 1:2018	Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices (ISO 11135-1:2014)	Fully applied	N/A
EN ISO 11607-1:2020+A11:2022	Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems	Fully applied	N/A
ISO 11607-2:2019/Amd 1:2023	Packaging for Terminally Sterilized Medical Devices – Part 2: Validation Requirements for Forming, Sealing and Assembly Processes	Fully applied	N/A
EN ISO 13485:2016	Quality Systems – Medical Devices – Particular Requirements for the Application of ISO 9001	Fully applied	N/A
EN ISO 14971:2019	Medical Devices – Application of Risk Management to Medical Devices	Fully applied	N/A
Other Solutions			
EN 556-1 2001/AC2006	Sterilization of Medical Devices – Requirements for Medical Devices to be Designated “Sterile” – Part 1: Requirements for Terminally Sterilized Medical Devices	Fully applied	N/A

Table 7-1: Common Specifications, Harmonized Standards, and Other Solutions Relevant to the DUE

Relevant Common Specifications, Harmonized Standards, and Other Solutions	Title	Fully or Partially Applied to DUE?	Justification/ Conclusion
ISO 20417:2021	Information Supplied by the Manufacturer of Medical Devices	Fully applied	N/A
EN ISO 10993-1: 2018	Biologic Evaluation of Medical Devices – Part 1: Evaluation and Testing Within a Risk Management Process	Fully applied	N/A
EN ISO 10993-5:2009	Biological Evaluation of Medical Devices, Part 5: Tests for in vitro Cytotoxicity	Fully applied	N/A
ISO 10993-7:2008/Amd 1:2019	Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals (ISO 10993-7:2008/AC:2009)	Fully applied	N/A
ISO 10993-7:2008/AC:2009	Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals (ISO 10993-7:2008/AC:2009)	Fully applied	N/A
EN ISO 11138-2:2017	Sterilization of Health Care Products – Biological Indicators – Part 2: Biological Indicators for Ethylene Oxide Sterilization Processes (ISO 11138-2:2006)	Fully applied	N/A
EN ISO 14644-1:2015	Cleanrooms and Associated Controlled Environments – Classification of Air Cleanliness	Fully applied	N/A
EN ISO 14644-2:2015	Clean Rooms and Associated Controlled Environments. Specifications for Testing and Monitoring to Prove Continued Compliance with ISO 14644-1	Fully applied	N/A
ISO 14644-3:2019	Cleanrooms and Associated Controlled Environments – Part 3: Test Methods	Fully applied	N/A
ISO 14644-4:2022	Cleanrooms and Associated Controlled Environments – Part 4: Design, Construction and Start-up	Fully applied	N/A

Table 7-1: Common Specifications, Harmonized Standards, and Other Solutions Relevant to the DUE

Relevant Common Specifications, Harmonized Standards, and Other Solutions	Title	Fully or Partially Applied to DUE?	Justification/ Conclusion
ISO 14644-5:2004	Cleanrooms and Associated Controlled Environments – Part 5: Operations	Fully applied	N/A
ISO 14004:2016	Environmental Management Systems and Supporting Techniques	Fully applied	N/A
ISO 16391:2002[5]	Aids for Ostomy and Incontinence – Irrigation Sets – Requirements and Test Methods	Fully applied	N/A
BS EN 15986:2011	Symbol for use in the labelling of medical devices. Requirements for labelling of medical devices containing phthalates	Fully applied	N/A
BS EN ISO 3166-1:2020	Codes for the representation of names of countries and their subdivisions - Part 1: Country code	Fully applied	N/A

Table 7-2: Regulations and Guidance Which Will be Applied to the Clinical Evaluation

Regulation or Guidance	Title
MEDDEV 2.12/1 Rev 8	European Commission (EC) Guidelines on a Medical Device Vigilance System
MEDDEV 2.7/1 Rev 4	Guidelines on Medical Device: Clinical Evaluation
Regulation (EU) 2017/745 April 2017	European Medical Device Regulations (MDR)
MDCG 2020-13 July 2020	Clinical evaluation assessment report template
MDCG 2020-6 April 2020	Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC. A guide for manufacturers and notified bodies
MDCG 2020-7	Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies

Table 7-2: Regulations and Guidance Which Will be Applied to the Clinical Evaluation

Regulation or Guidance	Title
April 2020	
MDCG_2021-24 October 2021	Guidance on classification of medical devices
MDCG_2020-3 Rev.1 May 2023	Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD
MDCG 2022-4 Rev 2 May 2024	Guidance on appropriate surveillance regarding the transitional provisions under Article 120 of the MDR with regard to devices covered by certificates according to the MDD or the AIMDD

8 RISK MANAGEMENT

The risk management process is implemented according to EN ISO 14971 and in accordance with the Baxter Risk Management Process GQR-10. Risks stemming from identified hazards and hazardous situations and their mitigations have been assessed in the device's risk management file and shall be used in evaluating clinical safety and performance.

Risk control measures were defined and implemented according to RACT [BXU600002]. The risk control options considered for the risk mitigation and associated clinical evaluation are one or more of the following in the priority order listed:

1) Inherent safety by design and by manufacture (safe design and safe manufacture)
2) Protective measures in the product or the manufacturing process
3) Information for safety

The effects of these risk control measures are then analyzed to avoid the introduction of new hazards or hazardous situations and to determine the impact on previously identified risks.

The review of (non-)clinical data during the clinical evaluation was used to provide further supporting evidence that the benefits outweigh the risks of the product.

8.1 Risks Associated with the Device or Treatment Population

Clinical hazards (risks) identified and analyzed in the Risk Management files based on the intended use of Irrigation Sets are summarized in the Risk Assessment and Control Table (RACT) [BXU600002]. The RACT also includes the evaluation of the controls that are in place to mitigate the identified hazards.

8.2 Clinical Hazards and Risks

Clinical hazards/ risks associated with the intended use of the medical device are:

- Air in system
- Allergens
- Contaminants of animal origins
- Delay in therapy
- Electrical, thermal, electromechanical energy
- Endotoxins / pyrogens
- Excessive therapy
- Foreign body
- Impurities
- Incorrect application of product
- Incorrect product
- Incorrect route of administration
- Insufficient therapy
- Interruption of therapy
- Leachables
- Microbial contamination
- Particulate matter
- Unintended exposure to product
- Blood loss
- Mechanical stress

8.3 Residual Risks

A risk analysis has been performed for Irrigation Sets in accordance with EN ISO 14971 and the result of the analysis is documented in the DUE's RACT [BXU600002].

After successful implementation of the risk control measures, all residual risks have been reduced to "as far as possible" and are acceptable when weighed against the benefits.

The overall residual risks were assessed as acceptable [1277312]. The analysis of the risks/benefits of the device under evaluation compared to the risks/benefits of alternative treatments and therapies is documented in the device's Clinical Risk-Benefit Analysis (cRBA) [1277308].

9 CLINICAL BACKGROUND, CURRENT KNOWLEDGE, STATE-OF-THE-ART

9.1 State-of-the-Art (SotA) Literature Search

The objective of this systematic SotA literature search was to identify applicable clinical standards, clinical practice guidelines, and information related to the medical condition managed with the DUE, and its natural

course, benchmark devices, or other similar devices and medical alternatives available to the target population.

The information obtained from this review of SotA literature was used to confirm the safety and clinical performance objectives and acceptance criteria which are provided in **Section 13**.

Refer to Section 3.1 and Section 3.2 of the Literature Search Protocol (LSP, **APPENDIX A**) for detailed objectives for the systematic scientific literature searches for SotA-Clinical Landscape and SotA-Similar (Benchmark) Devices respectively. In addition to the systematic scientific literature searches, supplemental manual and grey literature searches were performed to enhance the sensitivity of systematic literature searches. See Section 10 of the LSP (**APPENDIX A**) for details.

This SotA literature search was conducted in accordance with **GQP-05-16**. Refer to LSP (**APPENDIX A**) for information related to the search strategy, process, and including literature exclusion criteria, appraisal and grading, and Level of Evidence. **APPENDIX B** provides flowcharts for scientific and supplemental internet literature search results and review process. Total number of included/excluded articles for SotA-Clinical Landscape and SotA-Similar (Benchmark) Devices are provided in Section 7 of LSR (**APPENDIX B**).

After a comprehensive appraisal of all the SotA literature search results, 14 publications obtained from the current systematic and supplemental internet literature search were considered relevant for the SotA literature discussion in this CER. The content obtained from these SotA publications is incorporated in **Section 9.2** through **Section 9.7**.

9.2 Clinical Condition(s) to be Managed

9.2.1 Bladder Cancer

Bladder cancer is common, with almost 500,000 new diagnoses globally in 2018. [1, 2] Bladder cancer is the seventh most commonly diagnosed cancer in the male population worldwide.[3] Approximately 70-75% of these present as low-grade non-muscle invasive bladder cancers (NMIBC), which have a low risk of progression and are rarely lethal.[1-5] Among them, most of NMIBC are papillary tumors under the microscope.[5] The initial clinical manifestation of most bladder cancer is hematuria, usually manifested as painless, intermittent, gross macroscopic hematuria.[4] The 5-year survival for NMIBC tumors is >90%.[3] Nonetheless, these tumors can be associated with a significant risk of recurrence, and hence require periodic invasive procedures for cystoscopic surveillance and appropriate treatment by transurethral resection of bladder tumor (TURBT)[1, 3-5] combined with individualized intravesical chemotherapy or immunotherapy that is tailored to tumor risk stratification is recommended as the routine treatment model by the major international guidelines[2].

The risk of recurrence varies, ranging between 15% and 60% at 12 months, and is definable on the basis of well-established risk factors.[1] Recurrence can result from a number of underlying pathogenetic mechanisms: a precancerous ‘field change’ affecting the entire urothelium, incomplete resection of identified tumors as well as missed tumors too small or subtle in appearance and reimplantation of tumor cells exfoliated during TURBT.[1, 3, 5] Immediate instillation of intravesical chemotherapy (IC) following TURBT can be effective against all three modes of recurrence.[1, 3-5] However, immediate instillation of chemotherapy is associated to many drawbacks, from the selection of patients, the perioperative identification of contraindications (bladder perforation) and

potential morbidity.[3, 5]

Initially, after transurethral tumor resection, continuous saline bladder irrigation (CBI) was used to prevent the formation of blood clots and achieve excellent hemostasis.[1, 2, 4] Meanwhile, in theory, CBI can flush out exfoliated tumor cells effectively and prevent them from implanting in the bladder mucosa, thereby reducing the risk of tumor recurrence after conventional resection.[1, 2] However, CBI has no therapeutic effect on the residual tumors at the initial resection site, so it is necessary to perform high-quality and complete tumor resection to make sure that the tumor specimens contain the lamina propria and superficial muscular layer.[2] CBI has been proposed as a simple, cheap and safe alternative to IC.[1, 5]

In the past decade, *en bloc* resection of bladder tumor (ERBT) served as a valuable alternative technique that has obtained increasing interest among urologists worldwide.[2] As a “no touch” surgical technique for the treatment of NMIBC, ERBT shows the potential to minimize the number of exfoliated tumor cells and reduce the risk of tumor cell reimplantation. The use of thulium laser as the energy source for ERBT does not generate high-frequency current and has excellent hemostatic effect.[2]

9.2.2 Hemorrhagic Cystitis (HC)

Chronic hemorrhagic cystitis (HC) occurs in up to 5% of patients after pelvic radiotherapy. Although the advent of intensity-modulated radiation therapy may decrease radiation-induced bladder toxicity, robust data on long-term outcomes are limited. The response of the urinary bladder to radiation treatment can be classified into acute or subacute reactions that typically occur within 3-6 months of radiation treatment and late reactions that occur after 6 months. Delayed radiation-induced endothelial cell damage and perivascular fibrosis result in ischemia and obliterative end arteritis, leading to a range of symptoms including urinary frequency, urgency, pelvic pain and haematuria. Complications associated with radiotherapy account for up to 7% of emergency urology admissions. Initial management of radiation cystitis with hemorrhage frequently involves a sequential algorithm consisting of initial resuscitation and reversal of anticoagulation, as clinically appropriate, copious bladder washouts with clot evacuation, followed by continuous bladder irrigation and blood transfusions as required. Characteristic cystoscopy findings are telangiectasia with friable erythematous mucosa. Intractable HC severely affects a patient’s quality of life, with persistent bleeding resulting in life-threatening hypovolemic shock. The management of complex patients on anticoagulation requires balanced clinical decisions regarding the risks and benefits of blood transfusions and cessation of anticoagulation by the treating physician; however, often short periods without anticoagulation may be required to interrupt the pathological cycle. Urinary diversion and cystectomy for end-stage HC is associated with a 44% mortality rate. Alternative less invasive management options for nonemergent HC include systemic medical therapies, hyperbaric oxygen, intravesical therapies and laser ablation. These treatment strategies have several limitations including difficulty obtaining and administering some of the more historical treatments, such as formalin and alum, in the contemporary clinical setting.[6]

HC after allogeneic hematopoietic stem cell transplantation (HSCT) is characterized by diffuse inflammation and hemorrhage of the bladder mucosa.[7] HC is responsible for the bleeding from the bladder mucosa and a widespread symptomatology including burning, bladder pain, and severe haematuria with clots retention with possible renal failure.[8] Moreover, HC has been documented to increase the in-hospital length of stay and the risk of mortality.[8] Its clinical manifestation, severity, and prognosis vary greatly.[7] Infectious and/or non-

infectious factors contribute to HC occurrences, such as adenovirus or BK polyomavirus reactivation, conditioning regimens, graft-versus-host disease, and the stem cell sources or donor-recipient incompatibility.[8] It has been reported that the incidence of HC, as one of the major complications in allogeneic HSCT, is 14-30%.[7, 8] Referred to the Droller's HC classification, grade I means only microscopic haematuria, and gross hematuria means grade II or higher.[7] Urine alkalinization, hyperhydration and forced diuresis have been the most recommended preventive HC measures; however, conflicting data have been reported regarding the effectiveness of the preventive application of the CBI.[8] Regarding the HC treatment, no gold standard has been established to date.[8] Conservative observation, hydration, alkalization of urine, diuretics, and antiviral therapy were efficient for most HC patients with grade I or II, while CBI was required for some grade II, III, and IV patients to avoid urinary tract obstruction caused by blood clots in the bladder.[7] Patients with this allogeneic HSCT have abnormal immunity, coagulopathy, and graft-versus-host disease.[7] For urinary tract obstruction of HSCT patients, surgical treatment is associated with mortality and effects were minimal.[7]

9.2.3 Benign Prostatic Hyperplasia (BPH)

Benign prostatic hyperplasia (BPH) has long been recognized as a common disease affecting the health of elderly individuals. Accompanying BPH development, blockage of the bladder outlet may deteriorate, resulting in urine retention, repeated haematuria, bladder stones, recurrent urinary tract infections, and possibly other relevant severe problems, such as hydrops of the upper urinary tract and renal insufficiency. Transurethral surgery is the most commonly performed procedure for BPH surgery, including transurethral resection of the prostate (TURP), holmium laser enucleation of the prostate (HoLEP), thulium laser enucleation of the prostate (ThuLEP), greenlight laser enucleation of the prostate (GreenLEP), and greenlight laser vaporization of the prostate (photoselective vaporization of the prostate [PVP]). The TURP technique has several drawbacks, e.g., insufficient excision of the prostate tissue, TUR syndrome, excessive bleeding, and limited prostate volume. In contrast, the HoLEP technique has become one of the most effective alternatives to BPH surgery because of the shorter catheterization and hospital stay, effective hemostasis, and fewer complications. Research has shown that HoLEP is superior to conventional transurethral prostate enucleation techniques. Additionally, it is thought to have the best chance of becoming the gold standard for the treatment of BPH. In terms of BPH surgery, postoperative bleeding is the most significant complication independent of open surgery, TURP and the HoLEP procedure. To overcome this, the main strategy for postoperative bleeding is CBI to avoid the formation of clots that can block the urinary catheter. At the same time, the urinary catheter can be pulled, and the untreated blood vessel hemorrhage can be squeezed using the urine catheter balloon. With the development of minimally invasive surgery, the blood loss associated with HoLEP surgery has been decreasing. Meanwhile, the prostatic fossa wound may be bloodless after the surgery. Related studies have also shown that the time required after bladder irrigation is decreasing, and in some cases, daytime surgery has been implemented for BPH surgery. Therefore, the time of CBI postoperative has been decreasing and it may not be considered an essential step after HoLEP for BPH surgery.[9]

9.2.4 Septic Arthritis

Septic arthritis in children is relatively uncommon in developed countries, with a stable incidence of 1-5 in 100,000. The hip and knee are the most commonly involved joints. Septic arthritis in children has been reported

to cause chondrolysis, impaired ambulation, joint stiffness, deformity and osteonecrosis. Repeated aspiration of the joint can be employed; however, surgical joint irrigation is commonly used as it allows simultaneous debridement of loculations and joint visualization, unachievable by needle aspiration alone, and has a lower failure rate.[10]

Pediatric septic arthritis of the hip joint is a bacterial infection of the synovium and subsequently of all the structures within the joint, with the potential to cause an intense inflammatory reaction, articular cartilage degradation and eventual joint destruction. Although septic arthritis of the hip is second in frequency to that of the knee, adverse outcomes are more common in the hip. Delayed treatment of septic arthritis of the hip can result in damage to the physis or articular cartilage, osteonecrosis of the proximal femur, femoral osteomyelitis, and sepsis. The incidence of pediatric septic hip arthritis is low and the presentation is quite variable making accurate and prompt diagnosis challenging. In order to streamline the diagnosis of pediatric septic hip arthritis, a series of presenting variables have been identified and applied as a clinical prediction algorithm, which, despite some controversy over widespread validity, has aided clinicians in making an accurate and prompt diagnosis. In addition, many academic children's hospitals have adopted reproducible clinical practice guidelines in order to streamline treatment and improve outcomes. By standardizing care delivery using a clinical treatment algorithm, most cases of pediatric septic hip arthritis are relatively uncomplicated and resolve without sequelae. Occasionally, patients fail to improve clinically and undergo further workup, imaging and treatment in the form of repeat surgical irrigation and debridement in an effort to help clear their infection.[11]

9.2.5 Wounds

There are many factors that are out of the surgeon's control when dealing with trauma injuries, but initial surgical wound management may be the most important single factor within the provider's control. Wound irrigation serves a vital role in the management of open fractures and is critical in decreasing the bacterial load, which can ultimately have major impacts on patient outcomes. Studies show the important of early antibiotic administration; however, the importance of irrigation and debridement cannot be discarded. Surgeon preference as to what they choose to irrigate wounds may vary from provider to provider. Different factors to consider such as type of irrigation solution, tubing, height of bag solution, staff availability to exchange bags, all become pertinent in the efficiency of care in open traumatic orthopedic wounds.[12]

9.3 Therapy Related to the DUE

Irrigation is a process used with the intention of cleansing areas such as body surfaces, body cavities or wounds using a stream of irrigation fluid generated by hydraulic forces.[6] Irrigation can be a part of endoscopic, arthroscopic, and other surgical procedures. Effective fluid irrigation systems are essential for improved visualization. Although the properties (e.g., stickiness and transparency), performance, safety and price play a role in the selection of the irrigation solution to be used during a procedure, it is largely governed by tradition.

[6] George T. Rodeheaver- Wound Cleansing, Wound Irrigation, Wound Disinfection.

Irrigation Sets are used during and/or after surgery to channel irrigation solutions from the container (plastic bags) to the surgeon's tools (e.g., resectoscope) or urological catheters. During urological endoscopic procedures, irrigation is used to improve visualization, maintain urinary tract patency by dilating the ureter and collecting tubes.[7,8] Furthermore, during ureteroscopy (URS), where accessory instruments (baskets, laser fibers, etc.) are passed through a narrow-shared irrigation and working channel making visualization difficult, pressurized irrigation is necessary to compensate for the restricted flow and maintain sufficient distension of the lumen for a clear image.[7,8] Sufficient pressure is required to facilitate visualization, generate a stream of fluid that is strong enough to clear the procedural field and maintain adequate dilation of the ureter to facilitate the passage of tools through the scope. [7,9,10]

To control the pressure, flow and temperature of the irrigation solution, several types of Irrigation Sets (that are coupled with systems which regulate pressure, flow and temperature) are currently available in the market. Pressure and fluid flow can be generated and controlled with the use of gravity, manual force, pressure sleeves, motorized pumps, hand- or foot-operated pump devices or pressure bags that use gravity and pressure valves to promote continuous flow. [7,10,11] At times, Irrigation Sets are coupled with systems that allow for the temperature control of the irrigation solution.[10] Currently, the choice of irrigation system is based on the surgeon's preference, procedure type, availability and specific hospital stocking preferences.[7]

A brief description of the procedures that use irrigation solutions is provided in the following paragraphs.

9.3.1 Cystoscopy

Cystoscopy is an endoscopic technique used to examine the internal aspect of the bladder. It is the principal approach to visualize and diagnose bladder conditions.[12] There are two main types of cystoscopies categorized on the basis of flexibility: flexible cystoscopy and rigid cystoscopy. Flexible fiberoptic cystoscopes are associated with reduced pain and postoperative morbidity compared to rigid cystoscopes.[13] However, the flow rate of the irrigation fluid in a flexible fiberoptic cystoscope is lower than that in a rigid fiberoptic cystoscope. Also, the visualization of the operative site from a flexible cystoscope is not as clear as that from a rigid cystoscope. Irrigating fluids are instilled to distend the bladder and improve visualization. Different distending media, including conductive fluids (e.g., lactated Ringer's solution and normal saline), non-conductive or non-electrolyte fluids (e.g., sterile water, 5% glycine, 3% sorbitol, and 5% mannitol), and gas are available for use. Isotonic saline and sterile water are the most frequently used distending mediums for diagnostic procedures, primarily because they provide better visualization. Use of any distending medium requires monitoring of fluid absorption to avoid volume overload. Because non-conductive fluids (glycine) may cause hyponatremia, they are reserved for

[7] Tarplin, S., et al., Endoscopic Valves and Irrigation Devices for Flexible Ureteroscopy: Is There a Difference? J Endourol, 2015. 29(9): p. 983-92.
[8] Hendlin K, Weiland D, Monga M. Impact of irrigation systems on stone migration. J Endourol. 2008;22(3):453-458.
[9] Blew, B.D., et al., Comparison of Peditrol irrigation device and common methods of irrigation. J Endourol, 2005. 19(5): p. 562-5.
[10] De, S., et al., Evaluating the automated Thermedx Fluid Management System in a ureteroscopy model. J Endourol, 2014. 28(5): p. 549-53.
[11] Molina, W.R., et al., Influence of saline on temperature profile of laser lithotripsy activation. J Endourol, 2015. 29(2): p. 235-9.
[12] Stoller Marshall L, "Chapter 10. Retrograde Instrumentation of the Urinary Tract" (Chapter). Tanagho EA, McAninch JW: Smith's General Urology, 17e.
[13] Denholm, S.W., et al., Morbidity following cystoscopy: comparison of flexible and rigid techniques. Br J Urol, 1990. 66(2): p. 152-4.

operative procedures.

9.3.2 Transurethral resection of the prostate (TURP)

Although, several surgical procedures are available for the treatment of BPH, TURP is the most frequently preferred procedure.[14] In a TURP, the surgeon approaches the enlarged prostate gland via the penile urethra and seeks to excise the excess prostate tissue compressing the lumen of the urethra by using an electrocautery blade. To reach the prostatic tissue, the surgeon cuts through the wall of the urethral lumen leading to bleeding from the tissues being resected. To maintain clear visualization of the operating field, a continuous flow of irrigation solution across the operating field is needed. Compared to open prostatectomy, which is more appropriate for larger prostates, TURP is associated with one-fourth of the mortality and morbidity including a reduction in the postoperative hospital stay from an average of 9 days to 5 days. The catheter can be removed 2 days after the TURP, as opposed to 5 days after open prostatectomy. The amount of irrigation solution used varies by procedure.[15]

9.3.3 Laparoscopy

Laparoscopy is an endoscopic procedure that allows the visualization of the abdominal and pelvic structures. Laparoscopy is commonly used for removal of the appendix or gallbladder. It allows the visualization of organs, biopsy of tissues and management of gynecologic and urologic conditions at the same time. It is performed with the patient under general anesthesia, usually by a surgeon or a gynecologist. During laparoscopy (also known as peritoneoscopy), a small incision is made in the abdomen and a thin tube containing a light and camera known as a laparoscope is inserted to observe the abdominal and pelvic structures. The abdominal cavity is inflated with gas for adequate visualization of the organs. One or more small incisions are made for insertion of other small instruments if needed. Irrigation is used to improve visibility of the operative field and remove surgical debris.

9.3.4 Hysteroscopy

Hysteroscopic procedures are an alternative to hysterectomy for the surgical treatment of menorrhagia, uterine fibroids, and ablation of the uterine lining. Irrigation is required for diathermic resection to distend the uterine cavity (particularly the fundus), to facilitate good visibility and provide lavage for the removal of debris. As with urologic procedures, the use of diathermy requires a non-electrolyte irrigation solution such as 1.5% glycine irrigation solution. The quantity of the solution used depends on individual patient characteristics and the surgeon’s skills, although about 8 L of the solution is typically used. An alternative technique to diathermy is the use of a Neodymium-doped Yttrium Aluminum Garnet (YAG) laser to destroy endometrial cells. Compared to a diathermic resection, this technique may double or triple the surgical time and requires using more irrigation solution (≈12L) which poses a greater risk of complications from irrigation solution absorption. Because electric

[14] American Urological Association Education and Research, Inc. Guideline on the management of benign prostatic hyperplasia (BPH). Linthicum (MD): American Urological Association Education and Research, Inc.; 2010. 34 p. National Guide-lines Clearinghouse.
[15] Research, Inc. Guideline on the management of benign prostatic hyperplasia (BPH). Linthicum (MD): American Urological Association Education and Research, Inc.; 2010. 34 p. National Guide-lines Clearinghouse.

current is not used, an electrolyte-free solution is not required. Therefore, more physiologic irrigation solutions such as saline or Ringer's Lactate are commonly used for this procedure.

9.3.5 Arthroscopy

Irrigation is also required for arthroscopic procedures, which involve observing a closed joint through a fiberoptic scope called an arthroscope. The arthroscope permits the definition and assessment of the exact anatomical site of the injury in a joint. The use of irrigation solutions allows atraumatic joint entry, visualization within the joint, lavage to remove debris, and the conduction of electrodiathermy. The irrigant needs to be isotonic and the solution that is typically used is Ringer's Lactate, normal saline, or 5% dextrose. Electrodiathermy, a procedure not frequently used in arthroscopy, requires the use of an electrolyte-free solution such as glycine, mannitol, sorbitol, or a combination of sorbitol and mannitol.

9.3.6 Bladder Irrigation in General

Continuous bladder irrigation (CBI) is a common procedure after transurethral surgery, open prostatectomy, and is also performed in cases of spontaneous gross hematuria, e.g., due to bleeding from a malignancy in the urinary tract.[13] CBI is used to maintain the patency of indwelling catheters, minimize clot formation, and provide additional comfort to the patient.[13-15] It is indicated in the setting of a urinary catheter outflow obstruction, typically the result of a blood clot.[14, 15] Continuous irrigation with normal saline allows the restoration of urinary free flow and will maintain catheter patency.[14] Furthermore, infection is always a concern with indwelling catheters.[14] Using CBI to maintain catheter patency helps minimize the incidence of urinary tract infections (UTIs).[14] CBI is usually carried out using normal saline and a three-way Foley catheter over two days.[13] The goal of bladder irrigation is to produce rose-colored urine that is completely free of clot.[14] The rate of irrigation should be adjusted to obtain the aforementioned goal and does not need to run at a set rate throughout irrigation.[13, 14] It should be continued to empty and hang new bags of normal saline until consistent rose-colored urine free of clot is seen.[14] The inflow must be continuously calibrated to the blood concentration of the outflow drainage in order to sufficiently prevent intravesical blood clot formation.[13] In addition, an obstruction in the outflow can quickly cause the bladder to fill uncontrollably, thus raising the risk of bladder perforation and causing the patient pain and discomfort.[13] Resulting complications often require surgical interventions such as transurethral clot evacuation or even open surgical repair of a bladder perforation.[13] It is therefore imperative to closely monitor CBI to prevent such complications and avoid unnecessary surgical interventions.[13] CBI is therefore part of nursing training in urology to identify and solve technical problems (e.g., tube obstruction) without delay.[13] Bladder irrigation is not indicated when a catheter is blocked by sediment; instead, the catheter should be replaced.[15] In addition to causing discomfort for the patient, a blocked catheter can lead to bladder overdistension and injury, including perforation of the bladder wall in severe cases.[15] There are two types of bladder irrigation:

- **Manual or intermittent irrigation:** When the catheter is blocked, manual irrigation can restore patency by using a syringe to flush, aspirate, and remove the blockage. It can be performed through a standard urinary catheter or a triple-lumen urinary catheter. If the obstruction cannot be cleared, the catheter may have to be replaced.[15]

- **Continuous bladder irrigation:** This procedure is indicated to maintain catheter patency and prevent blockages in patients with significant hematuria. Fluid is continuously administered into the bladder via a triple-lumen urinary catheter or a “3-way catheter” and allowed to drain. CBI by itself will not clear a blocked catheter. Patients undergoing CBI require close monitoring and frequent intervention. The infusion runs by gravity and the rate is determined by urine color.[15]

If hematuria does not resolve with manual and CBI, the patient may need a urologic procedure.[15] Both manual and continuous irrigation are associated with a high risk of infection because they involve opening the system and manipulating the catheter.[15] Even though they are not true sterile procedures, sterile products help prevent the introduction of a pathogen during manipulation.[15]

9.4 Unmet Medical Needs

According to Appendix 8 of MEDDEV 2.7/1, Rev 4, June 2016, “medical devices for unmet medical needs” refers to the devices that deliver clinical benefits to patients for medical conditions that are life-threatening or cause permanent impairment of a body function, and for which current medical alternatives are insufficient or carry significant risks. Corresponding medical devices are referred to as “breakthrough products”.

Irrigation Sets are indicated for the delivery of irrigation solutions from the fluid container to the irrigation site. Irrigation Sets are not considered breakthrough products and there are also alternative therapies that exist for conditions where Irrigation Sets are indicated and, therefore, it does not meet the criteria of “medical devices for unmet medical needs”.

9.5 Similar Devices

Table 9-1 provides the list of identified similar devices with their length of time on the market and estimated sales volumes, when known.

Table 9-1: Similar Device Information

#	Name of Similar Device	Manufacturer of Similar Device	Length of Time on the EU Market	Estimated Sales Volume for the EU Market	Length of Time on the non-EU Market	Estimated Sales Volume for the Non-EU Market
1.	Urology Set	B. Braun	Not available	Not available	Not available	Not available
2.	Irrigation Sets	Vital Concepts, Inc.	Not available	Not available	Not available	Not available
3.	Irrigation Sets	International Medsurg Connections, Inc.	Not available	Not available	Not available	Not available
4.	Urological Connector	ICU Medical	Not available	Not available	Not available	Not available

Table 9-1: Similar Device Information

#	Name of Similar Device	Manufacturer of Similar Device	Length of Time on the EU Market	Estimated Sales Volume for the EU Market	Length of Time on the non-EU Market	Estimated Sales Volume for the Non-EU Market
5.	Urological Connector	Hospira	Not available	Not available	Not available	Not available
6.	Eziflow	Fairmont Medical	Not available	Not available	Not available	Not available
7.	Quickflow	Fairmont Medical	Not available	Not available	Not available	Not available
8.	TUR/Cystoscopy Sets	Fairmont Medical	Not available	Not available	Not available	Not available
9.	Irrigation Set Disposable Urology Set, Single bag	Fairmont Medical	Not available	Not available	Not available	Not available
10	Irrigation Set Disposable Urology Set, Double bag	Fairmont Medical	Not available	Not available	Not available	Not available
11	Irrigation Set Single bottle set wide bore urological flowfusor cystoscopy	Fresenius Kabi	Not available	Not available	Not available	Not available
12	Irrigation Set Two bottle universal set for TUR post-operative wide bore	Fresenius Kabi	Not available	Not available	Not available	Not available

Table 9-2 provides an assessment of the indirect benefits and indirect risks of the DUE compared to the identified relevant similar devices based on the cRBA. No additional information was included in the SotA literature.

Table 9-2: Indirect Risks and Indirect Benefits of the DUE compared to Similar Devices

#	Name of Similar Device	Indirect Benefits of DUE Compared to Similar Device	Indirect Risks of DUE Compared to Similar Device
1.	Urology Set (B. Braun)	Increased	Equal
2.	Irrigation Sets (Vital Concepts, Inc.)	Equal	Equal
3.	Irrigation Sets (International Medsurg Connections, Inc.)	Equal	Equal
4.	Urological Connector (ICU	Equal	Equal

Table 9-2: Indirect Risks and Indirect Benefits of the DUE compared to Similar Devices

#	Name of Similar Device	Indirect Benefits of DUE Compared to Similar Device	Indirect Risks of DUE Compared to Similar Device
	Medical)		
5.	Urological Connector (Hospira)	Equal	Equal
6.	Eziflow (Fairmont Medical)	Equal	Equal
7.	Quickflow (Fairmont Medical)	Equal	Equal
8.	TUR/Cystoscopy Sets (Fairmont Medical)	Equal	Equal
9.	Irrigation Set Disposable Urology Set, Single bag (Fairmont Medical)	Equal	Equal
10.	Irrigation Set Disposable Urology Set, Double bag (Fairmont Medical)	Equal	Equal
11.	Irrigation Set Single bottle set wide bore urological flowfusor cystoscopy (Fresenius Kabi)	Equal	Equal
12.	Irrigation Set Two bottle universal set for TUR post-operative wide bore (Fresenius Kabi)	Equal	Equal

Note: the assessment of DUE indirect benefits and indirect risks compared to the similar devices is based on the review of available scientific literature/public data and clinical judgement.

Alternate product manufactures available in the market, such as B. Braun, Hospira, Vital Concepts, International Medsurg Connections, Orion Life Systems, ICU Medical, Fairmont Medical and Fresenius Kabi, collectively offer similar Irrigations Sets, that can differentiate in some features.

A typical Irrigation Set consists of a spike, transparent tubing, on/off clamp, irrigation chamber (not essential), roller clamp, catheter adaptor, and silicone tube at the distal end.

Irrigation sets have either a single-lead configuration, double-lead configuration or 4-lead configuration.

9.5.1 Irrigation Sets single-lead configuration [1277308]

Irrigation/Urology Set for Plastic Irrigation Containers (B. Braun) is a line of irrigation and urology solutions and sets for cystoscopy, Trans-Ureteral Resection (TUR), general and arthroscopic surgical procedures. Baxter Irrigation Sets have a drip chamber which enables visualization of drops during therapy and roller clamp/s to regulate flow rate in accordance with therapy needs. The Irrigation/Urology Set for Plastic Irrigation Containers

(B. Braun) does not have either of these components therefore the benefit of Baxter Irrigation Sets is considered to be increased. Despite these compositional differences, the risk associated with each are considered equal.

Urological Connector (Hospira), Urology Irrigation Set (Vital Medical Supplies, Inc.), Single-lead Irrigation Sets (International Medsurg Connections, Inc.), Irrigation Set Disposable Urology Set, Single bag (Fairmont Medical) and Irrigation Set Single bottle set wide bore urological flowfusor cystoscopy (Fresenius Kabi) are typical irrigation sets with single-lead configuration, thus the benefit and risk compared to Baxter irrigation Set single-lead configuration is considered equal, given their similarities.

9.5.2 Irrigation Sets double-lead configuration [1277308]

Doble Spike Irrigation Set (Vital Medical Supplies, Inc.), Irrigation Set Disposable Urology Set, Double bag (Fairmont Medical) and Irrigation Set Two bottle universal set for TUR post-operative wide bore (Fresenius Kabi) include doble-lead configuration that allow continuously flow rate with less manipulation. Since Baxter irrigation Set is available in double-lead configuration, with similar features, the benefit and risk are considered equal.

9.5.3 Irrigation Sets single and double-lead configuration [1277308]

The following Irrigation Sets have single and doble-lead configuration presentation: Eziflow (Fairmont Medical), Quickflow (Fairmont Medical), and TUR/Cystoscopy Sets (Fairmont Medical). Baxter Irrigation Set is available in single and doble-lead configuration, with similar characteristics with the sets mentioned above, hence the benefits and risks are considered to be equal.

9.5.4 Irrigation Set 4-lead configuration [1277308]

Multiple leads Irrigation Sets (International Medsurg Connections, Inc.) and Urological Connector (ICU Medical) are ideal/preferred sets to perform long procedures, in order to minimize bag manipulations. When we compare these sets with a Baxter Irrigation Set 4-lead configuration, the benefits and risks are considered equal.

9.6 Alternative Treatment Options

Table 9-3 provides a summary of the indirect risks and indirect benefits associated with the alternative therapies.

Table 9-3: Indirect Risks and Indirect Benefits of the DUE Compared to Alternative Therapies

Name of Alternative Therapy	Indirect Benefits of DUE Compared to Alternative Therapy	Indirect Risks of DUE Compared to Alternative Therapy
Manual irrigation systems	Increased	Decreased
Gravity flow irrigation systems	Equal	Equal
Hand-held devices	Increased	Decreased
Foot-controlled irrigation devices	Equal	Equal
Thermedx Fluid Management System	Equal	Decreased

Table 9-3: Indirect Risks and Indirect Benefits of the DUE Compared to Alternative Therapies

Name of Alternative Therapy	Indirect Benefits of DUE Compared to Alternative Therapy	Indirect Risks of DUE Compared to Alternative Therapy

Note: The assessment of DUE indirect benefits and indirect risks compared to the alternative therapies is based on the review of available scientific literature/public data and clinical judgement.

The effectiveness of cleaning and irrigation is influenced by the type of irrigation device used to deliver the solution to the surgical site. It is essential that the method used provides sufficient flow for clear visualization and effective removal of debris. Irrigation can be accomplished with a variety of medical tools and specially made devices. Commercially available devices used for irrigation include gravity flow irrigation systems, manual irrigation systems, and Thermedx Fluid Management System (TFMS). Description of currently available irrigation systems is provided in the following paragraphs.

9.6.1 Manual Irrigation Systems [1277308]

Manual irrigation methods include using solution delivered via bulb syringe, piston syringe and plastic containers with a sterile bowl. These methods of irrigation are not appropriate for all procedures such as continuous bladder irrigation to keep a Foley catheter clear of blood and debris after some urinary surgeries. Also, manual irrigation may not deliver the amount of fluid required to provide a clear surgical field or provide sufficient wound irrigation to promote healing. With the Baxter Irrigation Set attached to one or two fluid filled containers, more volume can be delivered in a controlled manner and/or continuously. Baxter Irrigation Set can provide these large volumes (as compared to manual irrigation techniques) when attached to one or more bag solution containers.

Because manual irrigation may not provide the intended therapy as desired, Baxter Irrigation Sets offer an increased benefit over manual irrigation. Baxter Irrigation Sets also present reduced risks over manual irrigation because they achieve the irrigation purpose by a closed system, reducing the possibility of microbial contamination.

9.6.2 Gravity Flow Irrigation Systems [1277308]

Adequate maintenance of an optimal surgical field during operative procedures is one of the most important factors to ensure safe performance of the procedure. Gravity-based irrigation system is natural irrigation based on the height from tip of the reteroscope to the surface of saline. This system leverages the natural force of gravity to facilitate a steady flow rate, minimizing the need for complex mechanical pumps or dependent devices. Since, Baxter Irrigation Sets may be used for gravity flow irrigation, the gravity flow irrigation system benefits and risks are considered equal to the Baxter Irrigation Sets.

9.6.3 Hand-held Devices [1277308]

Hand-operated pumps use manual force to control flow as necessary during the procedure. It is possible that active, hand-operated irrigation pumps need an assistant during the procedure, but some surgeons routinely

operate the device alone. Within hand-operated pumps, some may provide better ergonomics with less fatigue, and this is especially important for physicians who operate without the use of an assistant. In high volume operating rooms, cumulative fatigue from using manual irrigation devices can become significant. As a result, the benefit of Baxter Irrigation Sets is considered increased. The variation in flow rate, due to manual handling or inadvertent pressure changes, can potentially compromise treatment outcomes. Thus, the risk of Baxter Irrigation Sets is considered decreased.

9.6.4 Foot-Controlled Irrigation Devices [1277308]

Foot-controlled irrigation devices provide hands-free operation, allowing the surgeon to control irrigation flow while maintaining the use of both hands for surgical instruments, particularly during endoscopic surgeries, when higher pressured flow is needed. When no weight is placed on the spring-loaded foot pedal, fluid will not flow. Active foot-pump systems provide sufficient control of irrigation flow and require labor to effectively maintain endoscopic visualization. Blew et al. demonstrated that the intrarenal pressures using gravity irrigation were lower compared with foot-controlled irrigation device. However, considering the Foot-controlled irrigation devices a complement to the irrigation therapy to achieve higher pressure, and Baxter Irrigation Sets allow increase pressure in the irrigation therapy with external devices when it is needed, the benefit of Baxter Irrigation Sets over foot-controlled irrigation devices is considered to be equal. Since using foot-controlled irrigation devices carries no additional risks, the risk is considered to be equal.

9.6.5 Thermedx Fluid Management System [1277308]

The Thermedx Fluid Smart Management System (TMFS) is an automated pressurized irrigation system that offers concurrent temperature control. It provides consistent flow and pressure, which can be adjusted according to the surgical requirements. Thus, considering the TMFS a complement to the irrigation therapy, and Baxter Irrigation Sets can archive higher pressure or temperature control with external device when it is needed during irrigation therapy, the benefit is considered to be equal. However, Thermedx Fluid Smart Management System may underestimate pressures at the tip of the endoscope and overestimate flow rates and temperature, thus the risk of Baxter Irrigation Sets is considered to be decreased compared to TMFS.

9.7 Conclusion

No changes were required to the safety & clinical performance objectives and acceptance criteria as a result of the review of the SotA literature.

10 DEMONSTRATION OF EQUIVALENCE

Equivalence is not being claimed with any other device; therefore, this section is not applicable.

11 PERTINENT DATA TO DEMONSTRATE CONFORMITY WITH THE RELEVANT GSPRS

11.1 Non-Clinical Data

The non-clinical review will focus on three major elements: The biocompatibility of Irrigation Sets as tested according to ISO 10993, the safety and clinical performance testing of the final product conducted by Baxter, and the summaries of performance tests with predecessor variants of the Irrigation Sets.

In addition, any safety and clinical performance data as detailed in the peer-reviewed publications identified and selected during the non-clinical literature search for Irrigation Sets are summarized in **Section 11.1.4**.

11.1.1 ISO 10993 Biocompatibility Testing

Based on the intended clinical use, nature, and duration of contact, the Irrigation Sets have dual classification. The device is classified as noted in **Table 11-1**.

Table 11-1: ISO 10993 Classification

Product	Category	Contact Location	Contact Duration
Irrigation Sets	For surgical procedures: External communicating devices	Tissue/Bone/Dentin	Limited (≤24 h) contact duration
	For urological procedures: Surface contacting devices	Mucosal membrane	Prolonged (>24 h to 30 d) contact duration

The potential risk associated with patient-contacting components, raw materials, the device manufacturing process, processing aids/cleaning agents, sterilization, and the packaging of the final, finished device has been evaluated. Biocompatibility testing was conducted on the representative device EMC4055N. The representative code was selected based on the complexity of the device in terms of containing the same materials/componentry, worse case sterilization, similar geometry/configurations, and similar assembly/manufacturing process. Testing was performed on the finished device post ethylene oxide (EO) sterilization to meet a dual ISO 10993-1 category of surface device, mucosal membrane prolonged contact duration and external communicating device, tissue/bone/dentin for a limited contact duration. The results of the pre-clinical testing are summarized in the Biological Evaluation Report for Irrigation Sets [BXU586239]. The devices were found to be biocompatible for their intended use. **Table 11-2** (Full Device) summarizes the biocompatibility studies that were conducted on representative code EMC4055N.

Table 11-2: Full Device Biocompatibility Testing Performed on code EMC4055N as the representative code

Series No	Study Type	Applicable Standard	Results	Disposition	Document/ Report #
1.	Cytotoxicity (L929 Neutral Red Uptake Test)	ISO 10993-5:2009	Acceptance criteria: If the cell viability is less than 70% at the highest tested concentration, the test article is considered to have a cytotoxic potential. Results: The cell viability at 100%, 50%, 25%, and 12.5% concentrations of test article extract	Cytotoxic (see risk evaluation below)	21-03630-G1 Amended

Table 11-2: Full Device Biocompatibility Testing Performed on code EMC4055N as the representative code

Series No	Study Type	Applicable Standard	Results	Disposition	Document/ Report #
			were 37%, 91%, 97%, and 100%, respectively.		
2.	Cytotoxicity (L929 Neutral Red Uptake Test)	ISO 10993-5:2009	Acceptance criteria: If the cell viability is less than 70% at the highest tested concentration, the test article is considered to have a cytotoxic potential. Results: The cell viability at 100%, 90%, 80%, 75%, and 65% concentrations of test article extract were 75%, 76%, 100%, 103%, and 100%, respectively.	Non-cytotoxic	21-04204-G1
3.	Intra-cutaneous reactivity test	ISO 10993-10:2010, ISO 10993-23:2021	Acceptance criteria: The requirements of the test are met if the difference between the test article mean score and the vehicle control mean score (based on Erythema and Edema score) is 1.0 or less. Results: The difference in the overall mean score between the test article extracts (polar and non-polar) and the control article was 0.0.	Non-irritant (Pass)	21-03630-G2
4.	Sensitization (Kligman Maximization Test)	ISO 10993-10:2010, USP-NF <1184> :2021	Acceptance criteria: Magnusson and Kligman grades greater than or equal to 1 (Discrete or patchy erythema) indicate a positive response. A sensitizer is a test article in which a positive response is observed in at least 10% of test animals. Results: Grade 0 (No visible changes) and 0% sensitized.	Non-sensitizer (Pass)	21-03630-G3
5.	Pyrogenicity (Rabbit Pyrogen Test-Material-Mediated)	ISO 10993-11:2017, USP-NF <151>:2021	Acceptance criteria: If no rabbits show an individual rise in temperature of 0.5°C or more above baseline temperature, the test article extract meets the requirements for the absence of pyrogens. Results: The temperature increases for the three test animals were 0.0°C, 0.0°C, and 0.0°C.	Non-pyrogenic (Pass)	21-03630-G6
6.	Acute Systemic Toxicity (Systemic	ISO 10993-11:2017	Acceptance criteria: The test article extract met the requirements if none of the mice treated with the test article exhibited a significantly greater biological reactivity than the control mice. If two	No acute systemic toxicity	21-03630-G4

Table 11-2: Full Device Biocompatibility Testing Performed on code EMC4055N as the representative code

Series No	Study Type	Applicable Standard	Results	Disposition	Document/ Report #
	Injection Test)		or more mice died or if abnormal behavior such as convulsions or prostration occurred in two or more mice, or if the body weight loss greater than 10% occurred in three or more animals, the test article did not meet the test requirements. Results: None of the treated animals showed toxicologically significant changes in clinical signs, weight loss, or mortality when compared to control animals.	(Pass)	
7.	Sub-chronic dual route toxicity (30 days, IV/IP)	ISO 10993-11:2017	Acceptance criteria: No statistical significance or biological difference in the clinical signs, morbidity/mortality, ophthalmological examination, body weights, food consumption, clinical pathology (blood collection, hematology, coagulation, clinical chemistry, and urinalysis), organ weight, gross and histopathologic al evaluation of test item treated animals and control animals. Results: No test items-related effects on the clinical signs, mortality, ocular changes, growth and no systemic toxicity in Sprague-Dawley rats under the test conditions.	No systemic toxic effects (Pass)	G23933
8.	*In vitro* Hemolysis Assay (Direct method)	ISO 10993-4:2017, ASTM F756-17:2017	Acceptance criteria: The results of the test sample should be compared to the results of the negative control, using the following hemolytic index: Hemolytic Index above the negative control: <2% (non-hemolytic); ≥2 and <5% (slightly hemolytic); ≥5% (hemolytic). Results: Hemolytic index was below 2% (0.29%).	Non-hemolytic (Pass)	AD-G0401
9.	*In vitro* Hemolysis Assay (Indirect method)		Acceptance criteria: The results of the test sample should be compared to the results of the negative control, using the following hemolytic index: Hemolytic Index above the negative control: <2% (non-hemolytic); ≥2 and <5% (slightly hemolytic); ≥5% (hemolytic). Results: Hemolytic index was below 2%		

Table 11-2: Full Device Biocompatibility Testing Performed on code EMC4055N as the representative code

Series No	Study Type	Applicable Standard	Results	Disposition	Document/ Report #
			(0.48%).		

Risk evaluation

The Irrigation Sets were evaluated for biological safety based on ISO 10993-1:2018. The raw materials used in the manufacture of Irrigation Sets do not contain any known chemicals of concern. CMR (carcinogenic, mutagenic, or toxic to reproduction) and EDs (endocrine-disrupting substances) assessment was conducted on Irrigation Sets. Based on the assessment, Irrigation Sets do not contain nanomaterials, and CMR or ED substances >0.1% w/w in accordance with the MDR regulation, and the particulate matter were within the acceptable limits. The processing aids and cleaning agents used during the manufacturing process have not shown any safety concerns in the final, finished devices. The primary packaging material and printing ink has been evaluated and pose no significant toxicological concern. Also, EO sterilization of the Irrigation Sets does not impact the biological safety of the device.

The biological testing strategy was defined based on Annex A of ISO 10993-1:2018, and testing was performed on the representative device, EMC4055N. All biological tests conducted on the representative device met their assay-specific criteria. The results of cytotoxicity test performed on the device EMC4055N was cytotoxic at 100% concentration and non-cytotoxic at the lower concentrations (50%, 25%, and 12.5%). The reason for failure was unknown, therefore, to confirm the cytotoxic results, the test was repeated using the same device at different dilutions. The results of the retest showed the device is non-cytotoxic at 100% concentration. Despite the difference in the cytotoxicity test results, the results of additional *in vivo* testing including the repeated dose systemic toxicity and the toxicological risk assessment of the extractable profile indicate the device is not anticipated to pose a toxicological risk to patients.

Cytotoxicity testing was performed to support the shelf-life requirements of the final, finished sterilized device EMC4055N. Accelerated aged samples to simulate a 3-year expiry were tested. The samples were conditioned at 45°C for 225 days and 52°C for 146 days to simulate the 3-year shelf-life. The test results failed at 100%, 75%, and 50% concentrations with a cell viability of less than 70% and passed at 25% concentration with a cell viability of >70%. The cytotoxicity test was repeated using the modified test method by filling the device internal fluid path area with Dulbeccos Modified Eagle Medium (DMEM), and the extracts were tested following incubation at 37°C for 72 hours for both accelerated and real-time test articles.

The samples are conditioned at:

- Accelerated aged at 52°C for 146 days to simulate 3-year or 36 months shelf-life
- Real-time aged samples equivalent to 22 months

The results of the accelerated aged sample indicate the device failed at 100% and 75% dilutions but had passing results at 50% and 25% dilutions with a cell viability of >70%. The results of the real-time aged samples indicate

the device failed at 100% but has a cell viability of more than 90% at 75%, 50%, and 25% concentrations. The results of the real-time aged study indicate the devices naturally aged at room temperature have increased cell viability compared to the devices heat-aged at 52°C or 45°C. Further, to investigate the failure rate cytotoxicity test was repeated using clinically relevant solvent. Cytotoxicity test was performed on the accelerated aged sample of the representative device EMC4055N subjected to 2 × EO sterilization where test articles were stored at 45°C for 101 days, equivalent to 3-year shelf-life using clinical simulated conditions. The test was performed using saline extract and the results were non-cytotoxic at all the concentration levels (100%, 75%, 50%, and 25%) and met the requirements of the assay. Therefore, the data presented demonstrates the device is safe for its intended use. Hence, it is concluded that shelf-life is not expected to influence the device's biocompatibility.

An extractable assessment and associated toxicological risk assessment on the representative device, EMC4055N concluded that the extractables identified above the reporting limits were not anticipated to be a risk to the patient's safety. Collectively, the data support the conclusion that the likelihood that the final, finished Irrigation Sets under their clinical use condition will pose a biological or toxicological risk is negligible.

Conclusion

The potential risk associated with patient-contacting components, raw materials, the device manufacturing process, processing aids/cleaning agents, sterilization, and the packaging of the final, finished device has been evaluated and determined to have no potential toxicity. Hence, they do not pose any safety risk to patients. The raw materials do not contain any known chemicals of concern >0.1% w/w per Regulation (EU MDR) 2017/745.

All the biological tests met their assay-specific criteria. Chemical characterization was established through exaggerated and simulated extractable studies performed on the representative code EMC4055N. The toxicological risk assessment performed on the extractable datasets concluded that clinical exposure to these extractables is not anticipated to pose a toxicological risk to the patient's safety. Irrigation Sets are sterilized with a validated process of Ethylene Oxide (EO) sterilization, and the residual EO and Ethylene Chlorohydrin (ECH) levels were within acceptable limits. The final, finished device has a shelf-life of 3 years. Collectively, the data support the conclusion that the Irrigation Sets are safe for clinical use, and no additional risks were identified that would require further testing.

11.1.2 Device Pre-Clinical (Animal) Testing

This Section is not applicable, no device pre-clinical (animal) testing was performed.

11.1.3 Non-Clinical Design Verification and Validation Studies

Refer to the Traceability Matrix Design Inputs Requirements to Verification [BXU542284] and the Access Validation Study [63129FR] for the full details of the design verification and validation (V&V) studies that were conducted on the DUE.

11.1.3.1 Verification and Validation Studies[16] [BXU542284]

Since Irrigation Sets are subjected to pressures for a period of time, they are designed to meet certain requirements ensuring that no leaks are present during the stipulated period. Irrigation Sets are designed to meet certain requirements whereby they can withstand a tensile force for a period of time ensuring that junctions can withstand certain loads and will not separate under the conditions stipulated. The design of Irrigation sets is optimized to reduce the likelihood of the presence of particulate matter. Functionality of the Irrigation Sets is verified to ensure that the set and its constituents serve their purpose well. The components of the Irrigation Sets are verified to requirements. **Table 11-3** provides a summary of the V&V studies that were conducted to support the safety and technical performance of the Irrigation Sets. The V&V studies included in this section provide non-clinical data. Below the table, the Access Validation Study [63129FR] is summarized.

Table 11-3: Summary of Verification and Validation Studies

Series No	Document Name / Report #	Test	Test Method and Acceptance Criteria	Summary of Results	Disposition (e.g., Passed/ Failed)
1.	Traceability Matrix Design Inputs Requirements to Verification [BXU542284]	Leak Requirements – Freedom from Leakage Test	The scope of this test was to verify that the set does not leak. A positive result in this test shows conformance to ISO 16391 (2002)[5]. A minimum of 298 samples per code to be tested. Requirement: Set shall not Leak when subjected to a pressure cuff.	Passed	Passed
2.		Leak Requirements – Pressure Cuff Test	The scope of this test was to verify the junction integrity of the set when used in conjunction with a pressure cuff, pressurized to 300 mmHg, while delivering the required volume of solution. A minimum of 298 samples per code to be tested. Requirement: Set shall not Leak when subjected to a pressure cuff.	Passed	Passed
3.		Tensile Requirement – The sets were subjected to	The purpose of this test was to verify the integrity of sample sets at junctions when subjected to a tensile force for a stipulated period of time or tested to failure. A minimum of 30 samples per code to be	Passed	Passed

[16] This CER is referencing the existing verification and validation studies currently traceable in the design history file 81548-DHF-ERD. New verification is being generated as per the execution activities of PR#2190026 (Change Control-2021-004222) - EU MDR Compliance for Medication Delivery - Irrigation Sets. The new verification will be documented in a future revision of this CER.

Table 11-3: Summary of Verification and Validation Studies

Series No	Document Name / Report #	Test	Test Method and Acceptance Criteria	Summary of Results	Disposition (e.g., Passed/ Failed)
		tensile forces for a stipulated period of time or tested to failure.	tested. Requirement: Set can withstand tensile force testing		
4.		Particulate Matter – Particulate matter testing	The purpose of this test is to verify that the number of particles found inside the fluid path of each sample tested does not exceed the contamination index limit as specified in their respective ISO standard. A minimum of 10 samples (as per ISO standards) per code to be tested. Requirement: Set shall meet particulate matter limits.	Passed	Passed
5.		Functionality Requirements – Simulation of Use Test	The purpose of this test was to verify that the set and set components exhibit the expected functionality and maintain physical integrity during use while inspecting the set for any leaks, junction disconnections and damaged components. A minimum of 298 samples per code to be tested. Requirements: The spike shall allow insertion into unused containers The drip chamber shall facilitate the priming procedure The clamp shall shut-off flow The regulating clamp shall allow flow regulation The silicone tube shall allow attachment to and detachment from the catheter adaptor.	Passed	Passed
6.		Functionality Requirements – Air Volume Test	The purpose of this test was to verify that the bubble trapper filter shall not allow more than 1mL of air after flushing 1.2L of irrigation solution at a flow rate of 600ml/min.	Passed	Passed

Table 11-3: Summary of Verification and Validation Studies

Series No	Document Name / Report #	Test	Test Method and Acceptance Criteria	Summary of Results	Disposition (e.g., Passed/ Failed)
			A minimum of 298 samples per code to be tested. Requirement: The filter shall eliminate air bubbles.		
7.		Functionality Requirements – Flow Rate Test	This test was performed to determine the volume of water that flows through the irrigation set at a determined height for a specific period of time. Such a test shows conformance to ISO 16391 (2002)[5]. A minimum of 30 samples per code are to be tested. Requirement: The set shall allow a flow rate of at least 200 mL water in 1 min under a static head of 0.6m.	Passed	Passed
8.		Leak Requirements – Freedom from Leakage Test	The scope of this test was to verify that the set does not leak. A positive result in this test shows conformance to ISO 16391 (2002)[5]. A minimum of 298 samples per code to be tested. Requirement: Set shall not Leak when subjected to a pressure cuff.	Passed	Passed

All tests were conducted following a validated protocol in accordance with the relevant harmonized standards. The Irrigation Sets maintained their physical integrity during the maximum intended period of use (72 hours for urological procedures). The Irrigation Sets withstood a dynamic tensile force of not less than 25 N. The Irrigation Sets had a visible fluid path to allow visualization of air in the set's line. The Irrigation Sets packaging conformed to BS EN ISO 8536-4:2013+A1:2013. The Irrigation Sets maintained their physical integrity after being subjected to 2 ethylene oxide sterilization cycles (subsequent cycles). The volume of air allowed to pass through the Irrigation Sets and into the patient during surgical procedures was not greater than 50 mL. The Irrigation Sets had a vented system to allow the ingress/egress of ethylene oxide sterilization gas in order to have a sterilized fluid path. All test results were reported to be conforming and complete.

Shelf-life testing for the functionality of the devices was performed using a representative code strategy. Code EMC4055N was used as a representative code for real-time and accelerated aging studies in parallel. The shelf

life of 5 years[17] was confirmed by the accelerated aging protocol, whereas the real-time studies are currently ongoing for confirmation.

Traceability of the shelf-life studies performed and ongoing on the irrigation sets in scope is available in Stability Testing Tracker [1269720], where lifecycle changes of the product and associated shelf-life verification studies are also traced.

11.1.3.2 Human Factors Study [63129FR]

The Access Validation Study [63129FR] was executed 15-OCT-2012 till 23-OCT-2012 to perform the simulated use test to validate Irrigation Sets along with other access product families to ensure that the final products conform to the user needs and the intended uses and also to ensure that the devices have mitigated potential use errors and abnormal use, identified in the risk document.

Irrigation sets product codes 2C4005 and 2C4040 were used in this study and these serve as representative codes of the Irrigation Sets in scope of this CER as explained in Design Validation of Irrigation Sets [BXU542980].

Study Design Overview

Three major components of the device user system were tested: (1) device users, (2) device use environments, and (3) device user interfaces. This was done by evaluating the residual risk post-mitigation per the Risk Assessment and Control (RACT) [1227341].

The risk method that was used to determine the probability and severity of risks associated with the access products is defined in Analysis of Access Products Hazardous Situations [1236658] and RACT [1227341]. There are no hazards categorized as ‘Unacceptable’ after application of risk mitigations.

In total, 15 registered nurses with experience in handling infusion products were included in the study. Prior to performing the usability validation study, training was conducted using the direction inserts to educate clinicians about the access products. The training comprised of the medical affairs clinician reading out loud the current direction inserts used with the products involved in the study. The simulated use study consisted of a minimum of 15 individual evaluation sessions, each session comprised a single participant completing the tasks in two clinical scenarios. The clinical scenarios represented the device use environment.

Acceptance Criteria

The acceptance criterion for this study was the completion of the validation study by all the 15 participants. In addition, 90% of all tasks in the scenario shall be completed by each of the participants.

Results and Conclusion

All the 15 participants completed 100% of all the tasks in the scenario and met the acceptance criteria of the study. The study demonstrated Irrigation Sets could safely and effectively be used for their intended uses in the intended use environments. All use errors observed during this validation study were analyzed against risks. A sound rationale was documented for each task failure as to why safety was or was not impacted. New issues

[17] The shelf life of Irrigation Sets is being reduced to 3 years. This CER is referencing data which covers a total shelf life of 5 years.

discovered during the study that impacted safety were reviewed by the core team and the respective risk files were updated. Overall, all user needs and intended uses were successfully validated and no additional tests were required.

11.1.3.3 Irrigation Sets (Malta Access Codes) Human Factors/Usability Engineering Evaluation [BXU578606]

The report summarizes the Human Factors (HF) assessment of the Irrigation Sets (Malta Access Codes) product family. Human Factors reviewed the complaints opened between 1-JAN-2020 to 1-JAN-2022 for the Irrigation Sets product family to assess whether any new or unmitigated use errors have been identified and if any further risk mitigation should be implemented from the findings. The codes within this group are operating within the expected risk profile established for use-related complaints. Adequate risk controls have been implemented on the device as indicated by the Irrigation Sets Risk Assessment and Control Table (RACT) and the use-related risk is reduced to an acceptable level. Based on the assessment, no Human Factor testing is needed.

Between 01-JAN-2020 and 01-JAN-2022 there were 18 complaints written against the Irrigation Sets Product Family. None of the complaints were found to be associated Use / User Errors. The control measures are in place to mitigate the other failure modes found in the complaint search. Based on this information, these complaints do not represent atypical events or unexpected 'near miss events. These complaints were communicated to involved personnel and will be kept under the trending records that are followed during quality reviews for awareness. Therefore, it was concluded that Use Error complaints never crossed the threshold.

The Irrigation Sets family are legacy products established in the market prior to the publication of IEC 62366-1:2015+AMD1:2020 and is currently being used by intended users. The use-related hazards or hazardous situations for the Irrigation Sets were reviewed as part of this assessment. Risk controls already implemented on the product are considered to be adequate. Residual risk as indicated by the risk assessment is considered to be at an acceptable level.

11.1.4 Non-Clinical Data from Literature

The scientific literature search identified one publication of non-clinical data for the DUE. This section provides a summary of this non-clinical publication from the current DCP.

In a non-clinical study [12], Hyland et al. (2023) to compare three different apparatuses with varying quantities of irrigation fluid to assess efficiency of administration and evaluate overall time for fluid administration. This *ex-vivo* study was designed to compare flow time for commonly available methods of gravity irrigation in an experimental setup, mimicking their typical clinical application. Fluid flow time was measured for three different types of tubing:

- Single-lumen cystoscopy tubing (Baxter International),
- Y-type double-lumen cystoscopy tubing (Baxter International), and
- Nonconductive suction tubing (Cardinal Health).

Cystoscopy tubing with standard 4.95mm internal diameter and 2.1m length in both single lumen and Y-type

TUR/bladder irrigation double lumen (Baxter International) was used. The third delivery method consisted of 6.0mm internal diameter and standard 3.7m length, nonconductive suction tubing (Cardinal Health). This type of tubing typically is used for suction. Fluid reservoirs consisted of 3L bags of normal saline solution (Baxter International). Cystoscopy tubing include a plastic spike to allow connection with fluid bags. A bag decanter (Advance Medical Design) was utilized to connect suction tubing to saline bag reservoirs. Bag height has been shown to affect fluid flow rates; therefore, both bag height and fluid delivery height were standardized in the study. Stryker Neptune 3 (Stryker) suction devices include an intravenous pole, which can be raised to a maximum height of approximately 259cm. This height was utilized for all fluid bags. The delivery height of tubing apparatuses was set at 81.2cm (32inches) from the ground as to approximate the height of a typical OSI Jackson table at its lowest setting, resulting in 178cm between the base of the saline bag and the fluid delivery location. The Neptune IV pole was positioned at 91.4cm (36inches) from the fluid delivery point to mimic a typical clinical scenario (see **Figure 11-1**).

Figure 11-1: Simulation setup for irrigation trials consisting of canisters set at appropriate height to simulate patient height on flat top operating table and Stryker Neptune IV pole at a set height and distance from the canister (from Hyland et al. (2023) [12])

Irrigation times were assessed for varying volumes of 3, 6, and 9L to investigate the relationship between bag changes and irrigation time. Bag changes were not conducted for the 3L trial, but were for 6 and 9L trials. Seven trials were performed for each variable, creating a 3×3 design (three volumes for single lumen cystoscopy tubing, Y-type cystoscopy tubing, and suction tubing) for a total of 63 data points. New bags of fluid were utilized for

each trial. Refilling of bags was avoided to eliminate concern for inequitable fluid volumes. Statistical analysis was performed using Microsoft Excel software (Microsoft). The flow times were summarized for each irrigation method and volume using means and 95% confidence intervals. Standard deviations were calculated. Analysis of variance (ANOVA) tests were performed to compare the mean flow times between irrigation methods for each volume. Independent sample student's t tests were utilized for comparisons across continuous variables. Significance was set at P<0.050 a prior.

Table 11-4 lists the flow times and flow rate with the timing for bag change removed. The mean flow time for suction tubing was significantly faster than the cystoscopy tubing for the 3 and 9L trials (P<0.001). At 6L, flow time for the suction tubing and the double lumen cystoscopy tubing were similar, 264 versus 260s, respectively. At 9L, the mean flow time for the suction tubing was 80s faster (410 vs. 491s) compared with single-lumen cystoscopy and was nearly 30s faster compared with Y-type cystoscopy tubing.

Table 11-4: Mean Flow Times and Flow Rates for each of the Seven Trials (from Hyland et al. (2023) [12])

Parameter	3L	6L	9L
Single-lumen cystoscopy tubing			
Flow Time [s]	140.14	285.83	426.14
Flow rate [ml/min]*	1284.43	1259.49	1267.19
Double-lumen cystoscopy			
Flow Time [s]	131.57	260.86	403.72
Flow rate [ml/min]*	1368.09	1380.05	1337.56
Nonconductive suction tubing			
Flow Time [s]	115.43	228.86	343.71
Flow rate [ml/min]*	1559.39	1573.01	1571.09

*The flow rates have been calculated for the purpose of the clinical evaluation of the Irrigations Sets

The authors concluded that gravity irrigation is known to be the safest and most efficient method of irrigation in open fracture management. They added that the study demonstrates the use of nonconducting suction tubing as an alternative to cystoscopy tubing for irrigation and debridement procedures can be beneficial. It can lead to a reduction in operating room times and can also be cost-effective. Overall, the authors recommend to use of nonconducting suction tubing as the primary tubing in irrigation procedures for open fractures to provide a faster, widely available, and more cost-efficient alternative to commonly used cystoscopy tubing.

However, the study has several limitations. Trials were conducted in a simulated environment and did not include clinical wounds on patients, but instead were simulated using approximate heights and distances. Bag changes in this study were performed immediately and in an efficient manner, which may not always be the case in a busy operating room. Additionally, the tubing was held in the same place and there was no movement, while throughout an actual irrigation and debridement procedure the lumen of the tube will be moved over the wound.

Lastly, there is the nature of human error in relation to the timing; however, this is likely reduced by multiple trials with very little difference between times. Human interobserver effect is one of greatest limitations as described in conjunction with variability of institution resource availability, protocols. Clinical relevance may be criticized as multiple factors could ultimately lead to longer procedural times such as wound size, degree of wound contamination, and extent of debridement. The analysis attempts to provide an objective comparison between irrigation alternatives to negate these variables. The choice of tubing may also be seen as clinically irrelevant as long as the saline bags are elevated to maximum height on IV pole, the number of needed bags are readily available in the operating room suite, and staff is nearby for quick and efficient bag changes.

11.1.5 Summary and Conclusion of Non-Clinical Data

All biocompatibility test results meet the acceptance criteria identified for the Irrigation Sets. The results indicate that the device materials are safe and biocompatible with no negative effect on the safety of the device. The Irrigation Sets are considered biocompatible in accordance with ISO 10993.

The design verification studies showed that the Irrigation Sets design outputs meet all the design inputs identified in the system requirements. The system requirements establish the integrity, functionality, and shelf-life criteria for the sets; meeting these criteria demonstrates that the DUE meets all performance expectations.

The non-clinical testing results (biocompatibility and design verification), in tandem with manufacturing process controls, support the safety and performance of the DUE. In summary, the non-clinical data revealed supporting outcomes for the tests performed for the verification of the functionality of the Irrigation Sets. Furthermore, the human factors study demonstrated Irrigation Sets could safely and effectively be used for their intended uses in the intended use environments. Overall, all user needs and intended uses were successfully validated.

All the results of non-clinical (design verification and validation, biocompatibility, shelf-life) tests conducted on Irrigation Sets met their acceptance criteria and comply with the requirements for biological safety.

11.2 Clinical Data

Although complaints and other PMS data are considered clinical data under the MDR, they are not generally considered a high-quality source of data due to limitations in reporting. Since these data sets would only be considered supportive data, they have been summarized in **Section 11.3**.

11.2.1 Baxter-Sponsored Pre-Market or Post-Market Clinical Investigation Data

No clinical investigations for the DUE were carried out by or on behalf of the manufacturer. The clinical evaluation identified sufficient non-clinical data to conclude that the medical devices comply with the relevant GSPRs 1, 2, 3e and 8 of ANNEX I, Regulation (EU) 2017/745. The DUEs have been introduced to the market in the early 1980s and obtained their MDD CE-mark on 18-NOV-2019. Therefore, the analysis of literature (**Section 11.2.6)** and market experience data (**Section 11.3**) are determined as appropriate methods to evaluate the safety and clinical performance.

The identified data are in line with current knowledge/state of the art, are scientifically sound, cover all aspects of the intended purpose for the DUE (including the devices' models, sizes, and settings). Based on the findings

of the literature, non-clinical data as well as the risk analysis, it can be inferred that the probability of a patient experiencing a substantial benefit when using the DUE outweighs the probability of suffering harm due to a residual risk of the device (**Section 12.3**).

Furthermore, PMCF activities are planned to confirm the safety and clinical performance, to assess for any new risks and/or side-effects, and to ensure the continued acceptability of the risk-benefit ratio. Therefore, according to the Regulation (EU) 2017/745, further clinical investigations are not required.

11.2.2 Baxter-Sponsored Clinical User Surveys

No clinical user surveys have been conducted for the DUE.

11.2.3 Investigator-Initiated Research

No investigator-initiated research has been conducted or is planned/in-progress for the DUE.

11.2.4 Clinical Trial Registries

An internet search of clinical trial registries was conducted for the DUE. This information provides real-world, objective information and prevents selective publication or selective reporting of clinical trial data related to the DUE.

This search was conducted using the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) website with the purpose of obtaining information on any in-progress or completed clinical trials related to the DUE.

The search strategy is developed based on the DUE names. Alternate spellings of device names and common variations in punctuation and spacing as well as common abbreviations, acronyms, etc., were also searched.

Date of the search: 18-SEP-2024

DCP covered by the search: There are no date limits for this search

Device names to be searched: DUE name

Name of person who created the search strategy: Lori Delaney, Research Analyst

Name of person who conducted the search: Lori Delaney, Research Analyst

Clinical Trial Registry Database(s) Searched: WHO International Clinical Trials Registry Platform (WHO ICTRP)

The clinical trials registry search was conducted in accordance with GQP-05-16. The search of clinical trial registries did not result in any clinical studies relevant to the DUE.

11.2.5 Summary of PMCF Activities for the Current Data Collection Period

As this is the initial MDR submission CER, there is no previous MDR PMCFP already in place; therefore, the summary of the MDR PMCF activities will be summarized in the first MDR PMCFER will be due at the time of

the next MDR CER periodic update.

11.2.6 Analysis of Clinical Data from Literature for Current Data Collection Period

11.2.6.1 Review of Scientific Literature

The scientific literature searches were conducted according to the Literature Search Protocol (LSP) in **APPENDIX A.** The summary of the scientific literature search results, screening, appraisal, level of evidence along with the total number of included/excluded articles from the current DCP are summarized in the LSP and Literature Search Report (LSR, **APPENDIX B**). The included articles are critically analyzed as per Section 13 of LSP and are summarized in **Section 11.2.6.3**.

11.2.6.2 Review of Supplemental Internet Literature (Supplemental Internet Searches)

The supplemental internet literature search was conducted according to the Literature Search Protocol (LSP) in **APPENDIX A**. The summary of the supplemental internet literature search results, screening, appraisal, level of evidence along with the total number of included articles from the supplemental manual internet literature search from the current DCP are summarized in the LSP and Literature Search Report (LSR, **APPENDIX B**). The number of relevant supplemental grey literature will also be provided in the LSR. The included articles are critically analyzed as per Section 13 of LSP and are summarized in **Section 11.2.6.3**.

11.2.6.3 Summary of Scientific and Supplemental Literature for Current Data Collection Period

This section includes a summary of each included scientific and supplemental manual publication from the current DCP. It also includes a comparison of key aspects of the included clinical publications in **Table 11-5** and a summary of the results of the comparison (both in **Section 11.2.6.3.1**).

It should be noted that clinical publications on intermittent/continuous irrigation usually do not focus on details of the irrigation sets used. Therefore, the clinical data included are more related to the irrigation procedure itself than to any type of irrigation device (similar devices, DUE). As a result, the data obtained on the procedure cannot be used directly as any kind of clinical evidence for the Irrigation Sets. However, the information is included in the subsections of **Section 12** (if applicable) as it is considered to provide supportive and indirect input to the clinical evaluation of the DUE.

In the current DCP, one non-clinical publication reporting on the device under evaluation was retrieved [12]. This publication is considered as LoE 5 as it contains only non-clinical data. The publication is detailed in **Section 11.1.4**.

In addition,14 publications reported on the usage of irrigation in general, without specifying a particular device, which is considered to represent the SotA. These publications included one systematic review [4] with a LoE of 1, one systematic review and meta-analysis [5] and five retrospective comparative studies [2, 3, 9-11] with a LoE of 3, one case series [7], one prospective study [13] and two systematic reviews [1, 6] with a LoE of 4, and two articles [14, 15] and one survey [8] with a LoE of 5. However, the studies had some limitations, such as limited/small sample size [1, 2, 6, 7, 9, 11], retrospective nature [2, 3, 7, 9-11], study design [5], lack of power

[1], heterogenous patient groups [5, 6], variable follow up periods [5, 6, 10, 13], varying causative organisms [10], patients were not operated on concurrently [9], generalizability of the results [3, 5, 9, 11, 13], missing randomization [10], surgeon selection bias [11], optimistic bias [11], information bias [4, 13], interviewing bias [13], selection bias [5], and a low level of evidence [8, 14, 15]. These publications are detailed in **Sections 0** to **11.2.6.3.5**. The reported indications for irrigation included:

- Bladder cancer: [1-5] (**Section 11.2.6.3.1**)
- Hemorrhagic cystitis: [6-8] (**Section 11.2.6.3.2**)
- Benign prostatic hyperplasia: [9] (**Section 11.2.6.3.3**)
- Septic arthritis: [11] (**Section 11.2.6.3.5**)

Furthermore, three (3) publications [13-15] reported on bladder irrigation in general (**Section 11.2.6.3.4**). Included 14 publications for SotA have been added to **Section 9.2** to describe in detail the clinical conditions to be managed by the DUE. A comparison of key aspects of the included 14 clinical publications is in **Table 11-5**.

11.2.6.3.1 Bladder Cancer

A total of 5 publications [1-5] reported on continuous bladder irrigation in relation to bladder cancer.

Li et al. (2021) performed a systematic review [1] to assess the effect of CBI on NMIBC recurrence. Following PRISMA guidelines, relevant publications were identified by online search of databases, including Ovid Medline and EMBASE (1980-2019). All published prospective randomized controlled trials comparing CBI post-TURBT to a control group were included. The primary end-point was recurrence. The search yielded 514 studies, of which six met inclusion criteria. Two studies (935 participants), albeit without peer-reviewed publication, comparing CBI to no CBI both showed a reduction in recurrence at 2 years. Four publications from three trials (331 participants) compared CBI to IC, showing similar recurrence rates at 1 year (odds ratio 1.29, 95% confidence interval 0.78-2.13) but a lower risk of adverse events (6-34% versus 27-48%). The authors concluded that CBI post-TURBT appears to yield 1-year recurrence rates of NMIBC comparable to immediate IC. They added that existing studies are small and of heterogenous design, precluding definitive conclusions. Therefore, further trials are required to determine if CBI can be implemented routinely to reduce NMIBC recurrence, as well as the optimal irrigant, volume and duration.

In a retrospective comparative study [2], Yang et al. (2021) evaluated the safety and efficacy of overnight continuous saline bladder irrigation for patients who have received thulium laser *en bloc* resection of bladder tumor (TmLRBT) combined with immediate intravesical chemotherapy previously. From October 2014 to June 2018, 235 patients with newly diagnosed NMIBC were included in the study. The patients were divided into two groups according to the duration of postoperative bladder irrigation with normal saline. After immediate intravesical chemotherapy, patients in group 1 received overnight CBI, while patients in group 2 did not receive overnight CBI. Data on the time of initial tumor recurrence, recurrence-free survival (RFS) and progression-free survival (PFS) rates, and perioperative complications were collected and analyzed. Of 235 included patients (129 in group 1 and 106 in group 2), the median follow-up periods were 42 and 38 months, respectively. There were no significant differences in patients' baseline characteristics between the two groups. The RFS rates of patients in group 1 were 90.7, 82.7, and 76.8% at the end of the first, third, and fifth years, while the

corresponding RFS rates of patients in group 2 were 87.7, 78.9, and 73.3%, respectively. Four patients in group 1 and five patients in group 2 experienced tumor progression. No significant differences between the two groups were observed in the time of initial tumor recurrence, RFS, and PFS rates. Only Grade I complications occurred in the two groups, and no significant difference was reached between the two groups. The authors concluded that for patients with NMIBC who have previously received TmLRBT combined with immediate intravesical chemotherapy, overnight CBI may not improve oncological outcomes and reduce perioperative complications. Therefore, TmLRBT may be performed as day-surgery operation for well selected patients. However, limitations of the study are the retrospective nature and the small sample size. Therefore, further prospective randomized controlled trials with more patients are needed to confirm the results.

Gondran-Tellier et al. (2021) performed a retrospective comparative study [3] to evaluate the efficacy of continuous saline bladder irrigation after blue light TURBT to prevent recurrence of low- to intermediate-risk NMIBC. The authors conducted a retrospective study including patients with low- to intermediate-risk NMIBC who underwent TURBT in two urological centers between January 2017 and December 2018. The experimental group included patients who received CBI while the control group included patients without CBI. CBI was started after the surgery in absence of bladder perforation, using physiological saline solution at a rate of 500-1000 mL/h, for a duration of 24 hours. Low-risk NMIBC had a surveillance while intermediate NMIBC had 8 adjuvant endovesical instillations of Mitomycin (MMC). The primary endpoint was bladder tumor recurrence-free survival which was defined as the time between the initial TURBT and the date of TURBT for bladder recurrence. A total of 167 patients were included. CBI was performed in 95 cases (57%). No complication related to irrigation was reported. Bladder recurrence was observed in 55 cases (32.9%): 22 (23.1%) in the CBI group vs. 33 (45.8%) in the control group (P=0.002). Multivariate stepwise logistic regression analysis with backward selection revealed that CBI (HR 0.47 [0.27-0.81]; P=0.006) and MMC (HR 0.55 [0.31-0.95]; P=0.034) were significantly associated with reduced risk of bladder recurrence. The authors concluded that CBI reduced the risk of bladder recurrence after blue light TURBT in patients with low- to intermediate-risk NMIBC while being safe. The study has several limitations, such as its retrospective nature, CBI was performed without standardization of flow, volume and duration, short follow-up, selection bias, no generalizability of the results, the value of *en bloc* resection of the bladder tumor to reduce bladder recurrence is still highly debated and some patients in the study were operated on with an *en-bloc* technique. Therefore, a prospective randomized study is needed to confirm the results.

In a meta-analysis [4], Zhou et al. (2019) aimed to confirm the efficacy and safety of continuous saline bladder irrigation compared with intravesical chemotherapy after transurethral resection for the treatment of non-muscle invasive bladder cancer. Randomized controlled trials of continuous saline bladder irrigation compared with intravesical chemotherapy were searched using MEDLINE, EMBASE, and the Cochrane Controlled Trials Register. The data were evaluated and statistically analyzed using RevMan version 5.3.0. Four studies including 861 participants which compared continuous saline bladder irrigation with intravesical chemotherapy were considered. One-year recurrence-free survival [odds ratio (OR)=0.76, 95% CI=0.55-1.05, P=0.09]; 2-year recurrence-free survival (OR=0.94, 95% CI=0.71-1.25, P=0.68); the median period to first recurrence (OR=-1.01, 95% CI=-2.96 to 0.94, P=0.31); the number of tumor progression (OR=0.80, 95% CI=0.54-1.17, P=0.25); and the number of recurrence during follow-up (OR=1.12, 95% CI=0.84-1.50, P=0.43) suggested that two methods of postoperative perfusion had no significant differences. In terms of safety, including macrohematuria, frequency

of urination and bladder irritation symptoms, continuous saline bladder irrigation showed better tolerance than intravesical chemotherapy. The authors concluded that continuous saline bladder irrigation seems to provide a better balance between prevention of recurrence and local toxicities than intravesical chemotherapy after transurethral resection of bladder tumors. However, the study could only obtain the parameter of the short term of efficacy, safety and tolerance of CSBI and intravesical chemotherapy. In addition, the diagnostic methods and transurethral resection techniques have developed recently, which could lead to a decrease in incomplete resections, which could explain the lower recurrence rates in the studies. Moreover, the study does not include data acquired from unpublished studies. Therefore, more high-quality controlled trials with suitable data should have been further studied for the purpose of investigating the efficacy and tolerance of CSBI and intravesical chemotherapy for NMIBC after TURBT.

Wang et al. (2023) performed a systematic review and meta-analysis [5] to explore the prognosis and safety of continuous saline bladder irrigation after TURBT. The authors searched PubMed, EMBASE, Cochrane Library databases and original references of the included articles. PRISMA checklists were followed. The authors used the GRADEpro GDT to assess the certainty of evidence from the results of the meta-analysis. A total of eight articles including 1600 patients were studied. The results indicated that patients received CBI after TURBT had no statistical differences compared to the control group in the recurrence-free survival and progression-free survival. However, the CBI group showed significant improvements compared to the control group in terms of the number of recurrences during follow-up and the period to first recurrence except for the number of tumor progression during follow-up. Furthermore, patients treated with CBI did not show an inferior effect than those treated with immediate IC in respects of recurrence-free survival, progression-free survival, the number of recurrences during follow-up, the number of tumor progression during follow-up and the period to first recurrence. But the immediate IC group had a higher incidence than the CBI group in terms of macrohematuria, micturition pain, frequency of urination, dysuria, retention and local toxicities. The authors concluded that patients treated with CBI after TURBT showed a significant improvement compared to the control group in terms of the number of recurrences during follow-up and the period to first recurrence. However, compared to immediate IC, CBI did not show an inferior effect except for lower incidence of adverse reactions. The study has several limitations, such as that the quality of the selected studies was flawed, primarily in terms of study design, patient selection, tumor number (single/multiple), tumor size (<3cm/ ≥3cm), tumor stage (Ta/T1), different lengths of follow-up, different intravesical chemotherapeutic agents and outcome data. Therefore, the results of the should be interpreted with caution. Bias regarding selection and subjective factors may also affect the final results of the study. More high-quality randomized control trials with sufficient sample size and statistics are required to confirm the effect of CSBI for bladder cancer patients after TURBT. It's also important to note that this systematic review and meta-analysis included the data from Yang et al. (2021) [2] and Gondran-Tellier et al. (2021) [3] described above.

11.2.6.3.2 Hemorrhagic Cystitis

A total of 3 publications [6-8] reported on continuous bladder irrigation in relation to hemorrhagic cystitis.

In a systematic review [6], Pascoe et al. (2019) aimed summarize the available therapies for treating chronic radiation-induced HC and to propose a practical management algorithm. A literature search was performed using

MEDLINE, Embase, PubMed and Google Scholar. Results were limited to publications in the English language involving adult human patients and published after 1990. Reviews and case reports were excluded. A total of 23 studies were included in the review with 2 studies reviewing systemic therapy, 7 studies evaluating hyperbaric oxygen therapy, 10 studies investigating a variety of intravesical therapies and the remaining 4 were relating to ablative therapies. Across these studies, the patient groups were heterogenous with small numbers and variable follow up periods. A variety of treatment options are described for radiation induced hemorrhagic cystitis. Initial management of radiation cystitis with hemorrhage frequently involves a sequential algorithm including continuous bladder irrigation with normal saline (0.9%).

Yang et al. (2020) performed a retrospective case series [7] to evaluate factors for failed CBI in hemorrhagic cystitis patients after HSCT. The general information, clinical characteristics, and consultation records of HC patients in 1,380 patients with hematopoietic stem cell transplantation in the author's center from 2017 to 2019 were analyzed retrospectively. The receiver operating characteristic (ROC) curve was used to calculate the cutoff point of the continuous variable, and multivariate logistic regression was used to analyze the risk factors affecting CBI failure in HC patients. The incidence of HC after HSCT was 23%. A total of 227 patients with HC above grade 2 were included. Univariate analysis showed that CRP, age, platelet counts, onset time after transplantation, albumin, and hemoglobin were associated with CBI failure in the short-term ($P<0.05$). ROC curve and multivariate logistic regression analysis showed that CRP >8.89ng/ml (RR=7.828, 95% CI 2.885-21.244), age <14.5 years (RR=9.940, 95% CI 3.219-30.697), and onset time of HC>37d after transplantation (RR=7.021, 95% CI 2.204-22.364), were independent risk factors for failure of CBI ($P<0.05$). The authors concluded that CRP >8.89ng/ml, age <14.5 years, and onset time of HC after HSCT>37d are independent factors for failure of CBI, which could be combined to allow stratification of HC after HSCT patients into low-, intermediate- and high-risk subgroups of CBI failure. However, limitations of the study are the retrospective nature and the small sample size. Therefore, further prospective studies with more patients would be beneficial to confirm the results.

Visintini et al. (2019) performed a multicenter survey [8] to describe HC preventive and treatment interventions in patients undergoing HSCT as performed by Italian nurses in their daily practice. A multicenter survey was conducted in 2018 by inviting all 110 Italian HSCT centers belonging to the Italian Group for Bone Marrow Transplantation (GITMO). Data collection was performed with an online questionnaire submitted to GITMO reference nurses working in each HSCT center. Descriptive statistics were performed. A total of 38 Italian centers participated. Preventive CBI was performed in 13 centers (34.2%). Transfusions of blood products (n=32; 84.2%), CBI (n=31; 81.6%) and intravenous hydration (n=28; 73.7%) were the most applied treatments, beyond the administration of analgesics (n=38; 100.0%) and antispasmodics (n=26; 68.4%). Most centers reported using as infusing solution the normal saline (10 of 31; 32.2%) or water for injectable solutions (3 of 31; 9.7%) in CBI. One center out of 31 (3.2%) administered CBI using a volumetric pump, and 3 (9.7%) reported using solutions prepared at a lower temperature than that of the environment. Moreover, three centers of 31 (9.7%) started the administration at the onset of microhematuria or large clots, while one center (3.2%) reported stopping it at hematuria's resolution. Other centers did not report data regarding the timing of CBI use. The authors detailed that supportive therapies as hyperhydration, bladder irrigation, platelet transfusions and pain treatment are

recommended by the ECIL 6 Guidelines (AIII)[18] according to the evidence from opinions of respected authorities, thus strongly recommended for the clinical use. The authors concluded that there was a large variability in both the prevention and treatment of HC used in daily practice between centers, suggesting that no strong recommendations in this area are yet available. They added that there is therefore a need to increase the evidence available in this field by providing methodological studies of higher quality, multicenter and prospective.

11.2.6.3.3 Benign Prostatic Hyperplasia (BPH)

One (1) publication [9] reported on continuous bladder irrigation in relation to benign prostatic hyperplasia.

Hao et al (2023) performed a retrospective comparative study [9] to assess the feasibility of a no bladder irrigation strategy after transurethral HoLEP for the treatment of BPH. From August 2021 to December 2021, the clinical data of 62 patients who received no bladder irrigation after HoLEP (Group A) were studied. The control group contained the clinical data of 150 patients in the same therapy group (from January 2021 to July 2021) who received continuous bladder irrigation after HoLEP (Group B). The baseline was consistent after using the propensity score matching method (PSM), and the differences between groups were compared. The pre- and postoperative complications, international prostate symptom score (IPSS), quality of life (QOL), maximum urinary flow rate (Qmax), and postvoid residual urine (PVR) of the two groups were compared, accompanied by a follow-up evaluation of surgical effects. In total, 47 pairs of patients were successfully matched by PSM. Postoperatively, no bladder irrigation was applied in Group A, and continuous saline bladder irrigation was applied in Group B. There was no statistically significant difference in the intraoperative conditions and the incidence of early postoperative complications between the two groups (P>0.05). Before and one month after the surgery, significant differences were also found in the IPSS, QOL, Qmax, and PVR of both groups (P=0.05). Within one month after the surgery, no statistically significant difference was found in IPSS, QOL, Qmax, PVR, or the incidence of early postoperative complications between the two groups (P>0.05). The authors concluded that for appropriately selected patients according to the exclusion criteria, the no bladder irrigation strategy after HoLEP for BPH is safe and effective. The study has several limitations, including its retrospective nature and small sample size. Two groups of patients were not operated on concurrently, and additional prospective randomized comparative studies with long-term follow-up and larger cohorts are necessary to validate the findings. In addition, the study was not performed with other transurethral enucleations of the prostate to evaluate the effect of no-bladder irrigation. A large-sample prospective randomized controlled study would be beneficial to verify the safety of no bladder irrigation after HoLEP.

11.2.6.3.4 Bladder Irrigation in General

A total of 3 publications [13-15] reported on bladder irrigation in general.

Jones et al. (2019) conducted an article [14] to provide fundamental knowledge on several key procedural interventions in genitourinary procedures. Among others, the authors described CBI. CBI is used to maintain the

[18] Cesaro, S., Dalianis, T., Hanssen Rinaldo, C., Koskenvuo, M., Pegoraro, A., Einsele, H., ... & Hirsch, H. H. (2018). ECIL guidelines for the prevention, diagnosis and treatment of BK polyomavirus-associated haemorrhagic cystitis in haematopoietic stem cell transplant recipients. Journal of Antimicrobial Chemotherapy, 73(1), 12-21.

patency of indwelling catheters, minimize clot formation, and provide additional comfort to the patient. It is indicated in the setting of a urinary catheter outflow obstruction, typically the result of a blood clot. Continuous irrigation with normal saline allows the restoration of urinary free flow and will maintain catheter patency. Furthermore, infection is always a concern with indwelling catheters. Using CBI to maintain catheter patency helps minimize the incidence of urinary tract infections (UTIs). The authors added that the goal of bladder irrigation is to produce rose-colored urine that is completely free of clot. The rate of irrigation should be adjusted to obtain the aforementioned goal and does not need to run at a set rate throughout irrigation. It should be continued to empty and hang new bags of normal saline until consistent rose-colored urine free of clot is seen. However, due to its nature, the article has an inherently low level of evidence.

In another article [15], Lucas at el. (2022) outlined the best practices to perform bladder irrigation and prevent adverse events. The authors described that bladder irrigation involves the instillation of fluid into the bladder to clear an obstruction or maintain the patency of an indwelling urinary catheter. This is typically done because of hematuria or blood clots and may be indicated following interventions such as surgery, a traumatic urinary catheter insertion, or complex radiation cystitis. Bladder irrigation is not indicated when a catheter is blocked by sediment; instead, the catheter should be replaced. In addition to causing discomfort for the patient, a blocked catheter can lead to bladder overdistension and injury, including perforation of the bladder wall in severe cases. There are two types of bladder irrigation:

- **Manual or intermittent irrigation:** When the catheter is blocked, manual irrigation can restore patency by using a syringe to flush, aspirate, and remove the blockage. It can be performed through a standard urinary catheter or a triple-lumen urinary catheter. If the obstruction cannot be cleared, the catheter may have to be replaced.
- **Continuous bladder irrigation:** It is indicated to maintain catheter patency and prevent blockages in patients with significant hematuria. Fluid is continuously administered into the bladder via a triple-lumen urinary catheter or a “3-way catheter” and allowed to drain. CBI by itself will not clear a blocked catheter. Patients undergoing CBI require close monitoring and frequent intervention. The infusion runs by gravity and the rate is determined by urine color.

If hematuria does not resolve with manual and CBI, the patient may need a urologic procedure. Both manual and continuous irrigation are associated with a high risk of infection because they involve opening the system and manipulating the catheter. Even though they are not true sterile procedures, sterile products help prevent the introduction of a pathogen during manipulation. The authors concluded that an understanding of the irrigation procedure allows nurses to anticipate needs and to be prepared with supplies and resources to ensure catheter patency while avoiding complications such as infection and bladder damage. However, due to its nature, the article has an inherently low level of evidence.

In a prospective study [13], Reichelt et al. (2021) aimed to gather data on parameters of continuous saline bladder irrigation, medical staff's work load associated with CBI monitoring, patients' feeling of safety and of patients' impairments during CBI. The authors observed CBI taking place after transurethral surgery for a 2-9-hour period. Patients were asked to rank how safe they felt, general impairments and impaired mobility. Irrigation parameters and complications were documented at least every 30 minutes. The staff's workload was evaluated through the frequency of visits and presence time. The patients' mobility was notably reduced with an average

of 10.5%±16.7% of time spent outside of bed, pain was low (mean 0.60±1.15). Patients felt very safe with CBI (8.8±1.9), hardly impaired overall (3.8±3.0), but restricted in mobility (5.9±2.8). Pain was associated with general impairment and impaired mobility. Clot retention occurred in 5 patients. Average irrigation speed was 9.46±8.69 mL/min (0 to 86.7 mL/min). Urine bags were emptied on average every 2.2±1.2 hours. Patients were visited by medical personnel 1 to 11 times. The authors concluded that CBI remains an improvable procedure in terms of the irrigation process itself to prevent complications, the patients' feeling of safety and comfort during CBI and the amount of work associated with its monitoring. However, the study has several limitations such as different time intervals (most 1 day), no comparison of different catheter diameter sizes, only men were included, bias brought about by the interviewer, and information bias. Therefore, further studies would be beneficial to confirm the results.

11.2.6.3.5 Septic Arthritis

Two (2) publications [10, 11] reported on intermittent irrigation in relation to septic arthritis.

In a retrospective comparative study [11], Livingston et al. aimed to identify risk factors associated with repeat surgical irrigation in pediatric septic hip arthritis. Patients who underwent ≥2 washouts (cases) were compared with those who had only 1 washout (controls). Demographic, clinical, laboratory, microbial, and magnetic resonance imaging data were compared between cases and controls and a prediction model was developed using logistic regression. A risk score was then constructed by counting the number of risk factors from the model that were present in each patient. In total, 26 patients were identified between 1994 and 2015 who underwent ≥2 washouts for septic hip arthritis, and 63 control patients who had only a single washout. The most common reason for repeat washout was persistent fever (n=21), followed by persistently elevated laboratory values (n=13), abnormal magnetic resonance imaging findings (n=12), and continued pain (n=12). Repeat washout cases demonstrated higher temperature preoperatively (P<0.001), had more frequent initial misdiagnosis (P=0.002), and had a longer time from symptom onset to surgery (P=0.02). Laboratory values in these cases showed higher C-reactive protein (P=0.003), and more frequent left shift (P=0.03) at presentation, with a greater proportion of positive cultures (P<0.001). Postoperatively, repeat washout cases had higher temperatures (P<0.001), more frequent wound drainage (P=0.02), and complications (P=0.001). A risk score for predicting the likelihood of undergoing repeat washout was constructed by counting the number of the following factors present: presence of left shift in CBC, positive blood or synovial fluid cultures, and postoperative temperature over 39°C. Seventy percent of cases had ≥2 of these risk factors and 80% of controls had ≤1 risk factor. The authors concluded that cases of pediatric septic arthritis which undergo repeat washout are associated with left shift, high postoperative temperatures, and positive cultures. Furthermore, they have more frequent misdiagnosis leading to delayed treatment and subsequent medical complications. However, the study has several limitations, such as its retrospective nature, the small sample size, limited generalizability of the results, surgeon selection bias, and optimistic bias. Therefore, further studies would be beneficial to confirm the results.

Johns et al. (2017) performed a retrospective comparative study [10] to compare outcomes after arthroscopic versus open surgery for acute pediatric septic knee arthritis. Pediatric patients with acute knee septic arthritis treated at the author's institution from 1996 to 2016 were retrospectively assessed. The clinical presentations, operations, microorganisms, laboratory results, knee radiologic findings and antibiotics administered were

compared. Patients' long-term outcomes were assessed at mean 6.9 (range 1.1-20.3) years. In total, 24 patients met the inclusion criteria. Eleven patients received arthroscopic irrigation and 13 had open irrigation. For arthroscopic irrigation, a standard anterolateral portal was made; an anteromedial portal was also utilized in some cases. A 4mm or, in the smallest children, a 2.7mm arthroscope was used. For open irrigation, a partial lateral or medial parapatellar arthrotomy was made. Joints were lavaged with 1 to 6 liters of normal saline. Five patients in the open group (38.5%) required a second irrigation compared with none in the arthroscopic group [95% confidence interval (CI): 12%-65%; P=0.041]. Time to range the knee occurred earlier in the arthroscopic group (5.0 days; arthroscopic vs. 10.6 days; open, difference 5.6 days: 95% CI: 0.84-10.3, P=0.023), as well as weight-bearing (2.7 days; arthroscopic vs. 10.3 days; open, difference 7.6 days: 95% CI: 2.3-12.9, P=0.008). Eighty-three percent of patients attended follow-up. No infections recurred. No significant differences were found in knee injury and Osteoarthritis Outcome Scores for children, Lysholm scores, range-of-motion, leg length, gait and radiologic findings. The authors concluded that for acute pediatric septic knee arthritis, arthroscopic irrigation is associated with less repeat surgical irrigations and allows earlier knee ranging and weight-bearing compared with open irrigation. At long-term follow-up, no significant difference was found between groups. The study has several limitations, such as no randomization, retrospective nature, varying causative organisms, and different follow-up times. Therefore, further studies would be beneficial to confirm the results.

11.2.6.3.1 Comparison of Key Aspects of Literature

Table 11-5 provides a comparison of key aspects of the 14 clinical publications included, and a summary of the results of the comparison is added below **Table 11-5**.

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
Irrigation In General (No Device Stated)										
Bladder Cancer (see Section 11.2.6.3.1)										
[1]	To assess the effect of continuous bladder irrigation on non-muscle invasive bladder cancer recurrence.	Continuous bladder irrigation / bladder cancer	No CBI, intravesical chemotherapy	1,266 (CBI / no CBI: 935, CBI / IC: 331)	Not included	2-10 years	Haematuria, pain, frequency, self-limiting hyperkalemia	The search yielded 514 studies, of which six met inclusion criteria. Two studies (935 participants), albeit without peer-reviewed publication, comparing CBI to no CBI both showed a reduction in recurrence at 2 years. Four	CBI post-TURBT appears to yield 1-year recurrence rates of NMIBC comparable to immediate IC. However, existing studies are small and of heterogenous design, precluding definitive	Limited sample size, lack of power

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								publications from three trials (331 participants) compared CBI to IC, showing similar recurrence rates at 1 year but a lower risk of adverse events.	conclusions. Further trials are required to determine if CBI can be implemented routinely to reduce NMIBC recurrence, as well as the optimal irrigant, volume and duration.	
[2]	To evaluate the safety and efficacy of overnight continuous saline bladder irrigation for patients who	Continuous bladder irrigation / bladder cancer	Overnight CBI	235 (Overnight CBI: 129, CBI: 106)	Overnight CBI: mean age: 66 (24-84) years, 26 (20.16%) females, 103 (79.84%) males CBI: mean	Median follow-up: Overnight CBI: 42 months CBI: 38 months	Only Grade I complications occurred	The RFS rates of patients in group 1 were 90.7, 82.7, and 76.8% at the end of the first, third, and fifth years, while the	For patients with NMIBC who have previously received TmLRBT combined with immediate	Retrospective nature, small sample size

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
	have received thulium laser *en bloc* resection of bladder tumor combined with immediate intravesical chemotherapy previously.				age: 65.5 (38-82) years, 23 (21.70%) females, 83 (78.30%) males			corresponding RFS rates of patients in group 2 were 87.7, 78.9, and 73.3%, respectively. Four patients in group 1 and five patients in group 2 experienced tumor progression. No significant differences between the two groups were observed in the time of initial tumor recurrence, RFS, and PFS	intravesical chemotherapy, overnight CBI may not improve oncological outcomes and reduce perioperative complications.	

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								rates. Only Grade I complications occurred in the two groups, and no significant difference was reached between the two groups.		
[3]	To evaluate the efficacy of continuous saline bladder irrigation after blue light transurethral resection of bladder tumor to prevent	Continuous bladder irrigation / bladder cancer	No CBI	167 (No CBI: 72, CBI: 95)	No CBI: median age: 70 (64-76) years, 14 (19%) females, 56 (81%) males CBI: median age: 72 (64-78) years, 19 (20%) females, 43 (80%) males	Median follow-up: 14 months in both groups	No complication related to irrigation was reported.	Bladder recurrence was observed in 55 cases: 22 in the CBI group vs. 33 in the control group. Multivariate stepwise logistic regression analysis with	CBI reduced the risk of bladder recurrence after blue light TURBT in patients with low- to intermediate-risk NMIBC while being safe. A prospective	Retrospective nature, CBI was performed without standardization of flow, volume and duration, short follow-up, selection bias, no generalizability of the results, the value of *en*

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
	recurrence of low- to intermediate-risk non-muscle invasive bladder cancer.							backward selection revealed that CBI and MMC were significantly associated with reduced risk of bladder recurrence.	randomized study is needed to confirm the results.	*bloc* resection of the bladder tumor to reduce bladder recurrence is still highly debated and some patients in the study were operated on with an *en-bloc* technique
[4]	To confirm the efficacy and safety of continuous saline bladder irrigation compared with intravesical chemotherapy after	Continuous bladder irrigation / bladder cancer	Intravesical chemotherapy	861	N/A	Median follow-up: 3-5 years	Macrohematuria, frequency of urination, bladder irritation symptoms	One-year recurrence-free survival; 2-year recurrence-free survival; the median period to first recurrence; the number of tumor progression;	Continuous saline bladder irrigation seems to provide a better balance between prevention of recurrence and local toxicities than	The study could only obtain the parameter of the short term of efficacy, safety and tolerance of CSBI and intravesical chemotherapy. Also, the

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
	transurethral resection for the treatment of non-muscle invasive bladder cancer.							and the number of recurrence during follow-up suggested that two methods of postoperative perfusion had no significant differences. In terms of safety, including macrohematuria, frequency of urination and bladder irritation symptoms, continuous saline bladder irrigation showed better	intravesical chemotherapy after transurethral resection of bladder tumors.	diagnostic methods and transurethral resection techniques have developed recently, which may lead to decrease of incomplete resections, possibly explaining the lower recurrence rates in the studies. Moreover, the study does not include data acquired from unpublished studies.

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								tolerance than intravesical chemotherapy.		
[5]	To explore the prognosis and safety of continuous saline bladder irrigation after transurethral resection of bladder tumor.	Continuous bladder irrigation / bladder cancer	Placebo, immediate intravesical chemotherapy	1,600	N/A	1-5 years	Macrohematuria, frequency of urination, micturition pain, dysuria, retention, local toxicities	The results indicated that patients received CBI after TURBT had no statistical differences compared to the control group in the recurrence-free survival and progression-free survival. However, the CBI group showed significant	Patients treated with CBI after TURBT showed a significant improvement compared to the control group in terms of the number of recurrences during follow-up and the period to first recurrence. However, compared to immediate IC,	Quality of the selected studies was flawed, primarily in terms of study design, patient selection, tumor number (single/multiple), tumor size (<3cm/ ≥3cm), tumor stage (Ta/T1), different lengths of follow-up, different intravesical chemotherape

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								improvements compared to the control group in terms of the number of recurrences during follow-up and the period to first recurrence except for the number of tumor progression during follow-up. Furthermore, patients treated with CBI did not show an inferior effect than those treated with	CBI did not show an inferior effect except for lower incidence of adverse reactions.	utic agents and outcome data. Therefore, the results of the present analysis should be interpreted with caution. Bias regarding selection and subjective factors may also affect the final results of this study. More high-quality randomized control trials with sufficient sample size and statistics are required to confirm the

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								immediate intravesical chemotherapy in respects of recurrence-free survival, progression-free survival, the number of recurrences during follow-up, the number of tumor progression during follow-up and the period to first recurrence. But the immediate IC group had a higher incidence than		effect of CSBI for bladder cancer patients after TURBT.

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								the CBI group in terms of macrohematuria, micturition pain, frequency of urination, dysuria, retention and local toxicities.		
Hemorrhagic Cystitis (see Section 11.2.6.3.2)										
[6]	To summarize the available therapies for treating chronic radiation-induced hemorrhagic cystitis and to propose a practical	Continuous bladder irrigation / hemorrhagic cystitis	Not included	Not included	Not included	2-142 months	Not included	In total, 23 studies were included in this review with 2 studies reviewing systemic therapy, 7 studies evaluating hyperbaric oxygen	A variety of treatment options are described for radiation induced hemorrhagic cystitis. Initial management of radiation cystitis with hemorrhage	Heterogenous patient groups, small sample size, variable follow up periods

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
	management algorithm.							therapy, 10 studies investigating a variety of intravesical therapies and the remaining 4 were relating to ablative therapies. Across these studies, the patient groups were heterogenous with small numbers and variable follow up periods.	frequently involves a sequential algorithm including continuous bladder irrigation with normal saline (0.9%).	
[7]	To evaluate factors for failed continuous bladder	Continuous bladder irrigation / hemorrhagic cystitis	Not included	227	Mean age ± SD: 27.0±14.5 years, females: 104	Not included	Not included	Univariate analysis showed that CRP, age, platelet	CRP >8.89ng/ml, age <14.5 years, and onset time of	Retrospective nature, small sample size

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
	irrigation in hemorrhagic cystitis patients after hematopoietic stem cell transplantation.				(45.8%), males: 123 (54.2%)			counts, onset time after transplantation, albumin, and hemoglobin were associated with CBI failure in the short-term. ROC curve and multivariate logistic regression analysis showed that CRP >8.89ng/ml, age <14.5 years, and onset time of HC>37d after	HC after HSCT>37d are independent factors for failure of CBI, which could be combined to allow stratification of HC after HSCT patients into low-, intermediate- and high-risk subgroups of CBI failure.	

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								transplantation, were independent risk factors for failure of CBI.		
[8]	To describe hemorrhagic cystitis preventive and treatment interventions in patients undergoing hematopoietic stem cell transplantation as performed by Italian nurses in their daily practice.	Continuous bladder irrigation / hemorrhagic cystitis	Not included	N/A	N/A	N/A	N/A	N/A	A total of 38 Italian centers participated. Preventive continuous bladder irrigation was performed in 13 centers. Transfusions of blood products , CBI and intravenous hydration were the most applied treatments, beyond the	A great variability both in the HC prevention and treatment interventions applied in daily practice across centers have emerged suggesting that no strong recommendations in the field are available to date. Therefore, there is a need to increase the

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
									administration of analgesics and antispasmodics.	evidence available in the field by providing methodological studies of higher quality, multicenter and prospective.
Benign Prostatic Hyperplasia (BPH, see Section 11.2.6.3.3)										
[9]	To study the feasibility of a no bladder irrigation strategy after transurethral holmium laser enucleation of the prostate for the treatment of benign	Continuous bladder irrigation / benign prostatic hyperplasia	No CBI	94 (No CBI: 47, CBI: 47)	No CBI: mean age: 71.7±6.4 years, males CBI: mean age: 72.3±6.8 years, males	6 months	Urine retention, gross haematuria, hemorrhage, transitory urinary incontinence, urinary tract infection, testicular epididymitis,	Before and one month after the surgery, significant differences were also found in the IPSS, QOL, Qmax, and PVR of both groups. Within one month	For appropriately selected patients according to the exclusion criteria, the no bladder irrigation strategy after HoLEP for BPH is safe and effective.	Retrospective nature, small sample size, patients were not operated on concurrently, the study was not performed with other transurethral enucleations of the prostate to evaluate the

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
	prostatic hyperplasia.						urethral stricture	after the surgery, no statistically significant difference was found in IPSS, QOL, Qmax, PVR, or the incidence of early postoperative complications between the two groups.		effect of no-bladder irrigation
Bladder Irrigation In General (see Section 11.2.6.3.4)										
[14]	To provide fundamental knowledge on several key procedural interventions in	Bladder irrigation in general	Not included	Not included	Not included	Not included	Not included	Not included	Not included	Low level of evidence

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
	genitourinary procedures									
[15]	To outlined the best practices to perform bladder irrigation and prevent adverse events.	Bladder irrigation in general	Not included	N/A	N/A	N/A	Infection	Bladder irrigation involves the instillation of fluid into the bladder to clear an obstruction or maintain the patency of an indwelling urinary catheter. Bladder irrigation is not indicated when a catheter is blocked by sediment; instead, the catheter	An understanding of the irrigation procedure allows nurses to anticipate needs and to be prepared with supplies and resources to ensure catheter patency while avoiding complications such as infection and bladder damage.	Low level of evidence

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								should be replaced. In addition to causing discomfort for the patient, a blocked catheter can lead to bladder overdistension and injury, including perforation of the bladder wall in severe cases. There are two types of bladder irrigation: manual or intermittent, and continuous.		

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
[13]	To gather data on parameters of continuous saline bladder irrigation, medical staff's work load associated with CBI monitoring, patients' feeling of safety and of patients' impairments during CBI.	Bladder irrigation in general	Not included	90 (TUR-B: 29, TUR-P: 36, HoLEP: 25)	TUR-B: mean age: 69.4±11.4 (40-82) years, males TUR-P: mean age: 71.2±9.3 (52-90) years, males HoLEP: mean age: 72.4±9.4 (42-80) years, males	Not included	Bleeding, diarrhea, constipation, moderate edema of the genitals, genital discomfort, bladder spasm, clot retention with need for catheter based evacuation, surgical revision	The patients' mobility was notably reduced with an average of 10.5%±16.7% of time spent outside of bed, pain was low. Patients felt very safe with CBI, hardly impaired overall, but restricted in mobility. Pain was associated with general impairment and impaired mobility. Clot retention occurred in 5	CBI remains an improvable procedure in terms of the irrigation process itself to prevent complications, the patients' feeling of safety and comfort during CBI and the amount of work associated with its monitoring.	Different time intervals (most 1 day), no comparison of different catheter diameter sizes, only men were included, bias brought about by the interviewer, information bias

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								patients. Average irrigation speed was 9.46±8.69 mL/min (0 to 86.7 mL/min). Urine bags were emptied on average every 2.2±1.2 hours. Patients were visited by medical personnel 1 to 11 times.		
Septic Arthritis (see Section 11.2.6.3.5)										
[11]	To identify risk factors associated with repeat surgical	Intermittent irrigation / septic arthritis	Repeat surgical irrigation	89 (Surgical irrigation >1: 26,	Surgical irrigation >1: mean age: 7.9 (±5.4) years, 7	Not included	Complications Surgical irrigation >1: 10 (38%) Surgical	Laboratory values in these cases showed higher C-reactive	Cases of pediatric septic arthritis which undergo	Retrospective nature, small sample size, surgeon selection bias,

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
	irrigation in pediatric septic hip arthritis.			Surgical irrigation =1: 63)	(27%) females, 19 (73%) males Surgical irrigation =1: mean age: 6.3 (±4.4) years, 33 (52%) females, 30 (48%) males		irrigation =1: 5 (8%)	protein, and more frequent left shift at presentation, with a greater proportion of positive cultures. Postoperatively, repeat washout cases had higher temperatures, more frequent wound drainage, and complications. A risk score for predicting the likelihood of undergoing repeat washout was	repeat washout are associated with left shift, high postoperative temperatures, and positive cultures. They have more frequent misdiagnosis leading to delayed treatment and subsequent medical complications.	limited generalizability of the results, optimistic bias

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								constructed by counting the number of the following factors present: presence of left shift in CBC, positive blood or synovial fluid cultures, and postoperative temperature over 39°C. Seventy percent of cases had ≥2 of these risk factors and 80% of controls had ≤1 risk factor.		

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
[10]	To compare outcomes after arthroscopic versus open surgery for acute pediatric septic knee arthritis.	Intermittent irrigation / septic arthritis	Arthroscopic versus open irrigation	24 (Arthroscopic irrigation: 11, Open irrigation: 13)	Arthroscopic irrigation: median age: 2.2 (0.6–9.9) years, 5 males, 6 females Open irrigation: median age: 1.49 (0.2–10.0) years, 7 males, 6 females	Arthroscopic irrigation: 6.9 years Open irrigation: 5.2 years Mean follow-up: 6.9 years	Fever, tachycardic patients, pain/refusal to use lower limb, knee swelling, knee warmth	Five patients in the open group required a second irrigation compared with none in the arthroscopic group. Time to range the knee occurred earlier in the arthroscopic group, as well as weight-bearing. Eighty-three percent of patients attended follow-up. No infections recurred. No significant	For acute pediatric septic knee arthritis, arthroscopic irrigation is associated with less repeat surgical irrigations and allows earlier knee ranging and weight-bearing compared with open irrigation. At long-term follow-up, no significant difference was found	No randomization, retrospective nature, varying causative organisms, different follow-up times

Table 11-5: Comparison of Key Aspects of Scientific and Supplemental Manual Literature from Current DCP

Ref	Objective	Application/ Indication	Comparator Name	Sample Size	Demographics	Follow-up	Adverse Events/ complications	Results	Conclusion	Limitations
								differences were found in knee injury and Osteoarthritis Outcome Scores for children, Lysholm scores, range-of-motion, leg length, gait and radiologic findings.	between groups.	

Bladder Cancer

A total of 5 publications [1-5] reported on continuous bladder irrigation in relation to bladder cancer. These publications included one systematic review [4] with a LoE of 1, one systematic review and meta-analysis [5] and two retrospective comparative studies [2, 3] with a LoE of 3, and one systematic review [1] with a LoE of 4.

In summary, CBI has been shown to be safe in patients with low to intermediate risk NMIBC.[3] In addition, CBI reduced the risk of bladder recurrence after (blue light) TURBT.[3, 5] After TURBT, CBI was reported to result in 1-year NMIBC recurrence rates comparable to immediate IC [1, 4, 5] with a lower incidence of adverse events.[4, 5] However, in patients with NMIBC who have previously received TmLRBT combined with immediate intravesical chemotherapy, overnight CBI may not improve oncological outcomes and reduce perioperative complications.[2] Therefore, TmLRBT can be performed as a day surgery procedure in well-selected patients.[2]

However, the studies had some limitations, such as limited/small sample size [1, 2], retrospective nature [2, 3], study design [5], lack of power [1], heterogenous patient groups [5], variable follow up periods [5], generalizability of the results [3, 5], information bias [4], and selection bias [5]. It's also important to note that this systematic review and meta-analysis included the data from Yang et al. (2021) [2] and Gondran-Tellier et al. (2021) [3]. Therefore, further prospective studies with more patients would be beneficial to confirm the results.

Hemorrhagic Cystitis

A total of 3 publications [6-8] reported on continuous bladder irrigation in relation to hemorrhagic cystitis. These publications included one case series [7], one systematic review [6] with a LoE of 4, and one survey [8] with a LoE of 5.

In conclusion, the initial management of radiation cystitis with hemorrhage often involves a sequential algorithm that includes continuous bladder irrigation with normal saline (0.9%).[6, 7] However, there is a large variability in both the prevention and treatment of HC used in daily practice between centers, suggesting that no strong recommendations are yet available in this area.[8] Independent factors for failure of CBI are CRP >8.89ng/ml, age <14.5 years, and time of onset of HC after HSCT>37d.[7]

However, the studies had some limitations, such as limited/small sample size [7], retrospective nature [7], heterogenous patient groups [6], variable follow up periods [6], and a low level of evidence [8, 14, 15]. Therefore, further prospective studies with more patients would be beneficial to confirm the results.

Benign Prostatic Hyperplasia (BPH)

One (1) retrospective comparative study [9] reported on continuous bladder irrigation in relation to benign prostatic hyperplasia.

The strategy of no bladder irrigation after HoLEP for BPH has been reported to be safe and effective in appropriately selected patients.[9]

However, the study had some limitations, such as limited/small sample size, retrospective nature, patients were not operated on concurrently, and generalizability of the results. Therefore, further prospective studies with more patients would be beneficial to confirm the results.

Bladder Irrigation in General

A total of 3 publications [13-15] reported on bladder irrigation in general. These publications included one prospective study [13], and two articles [14, 15] with a LoE of 5.

In summary, CBI is reported to be used to maintain the patency of indwelling catheters, minimize clot formation, and provide additional comfort to the patient.[14, 15] It is typically performed for hematuria or blood clots and may be indicated after procedures such as surgery, a traumatic urinary catheter insertion, or complex radiation cystitis.[15] Usually, CBI taking place after transurethral surgery for a 2-9-hour period.[13]. Bladder irrigation is not indicated if a catheter is blocked by sediment; instead, the catheter should be replaced.[15] There are two types of bladder irrigation: manual or intermittent irrigation and continuous bladder irrigation.[15] Both manual and continuous irrigation are associated with a high risk of infection.[15] However, one article detailed that the use of CBI to maintain catheter patency helps minimize the incidence of urinary tract infections (UTIs).[14] CBI remains an area for improvement in terms of the irrigation process itself to prevent complications, the patient's sense of safety and comfort during CBI, and the amount of work associated with its monitoring.[13]

However, the studies had some limitations, such as variable follow up periods [13], generalizability of the results [13], information bias [13], interviewing bias [13], and a low level of evidence [8, 14, 15]. Therefore, further prospective studies with more patients would be beneficial to confirm the results.

Septic Arthritis

Two (2) retrospective comparative studies [10, 11] reported on intermittent irrigation in relation to septic arthritis.

In conclusion, cases of pediatric septic arthritis requiring repeat washout are associated with left shift, high postoperative temperatures and positive cultures, and are more likely to be misdiagnosed, leading to delayed treatment and subsequent medical complications.[11] In acute pediatric septic knee osteoarthritis, arthroscopic lavage is associated with fewer repeat surgical lavages and allows earlier knee range of motion and weight bearing compared with open lavage.[10]

However, the studies had some limitations, such as limited/small sample size [11], retrospective nature [10, 11], variable follow up periods [10], varying causative organisms [10], generalizability of the results [11], missing randomization [10], surgeon selection bias [11], and optimistic bias [11]. Therefore, further prospective studies with more patients would be beneficial to confirm the results.

11.3 Market Experience Data

Baxter has defined and implemented a PMS system to ensure that any new risks or increased rates in known risks are detected and appropriate corrective actions and preventive actions will be taken. This process is described in detail in **GQP-09-35**.

The PMSP [1248528PMSP] was designed for Irrigation Sets to maintain post product monitoring activities. The PMSP defines the process for gathering and analyzing active and passive PMS inputs from the PMS system to maintain safe and effective products in the field.

The purpose of this section in the CER is to provide a summary of the available internal and external market experience data and outline its relevance to the safety and clinical performance of Irrigation Sets.

11.3.1 Internal Market Experience Data

This section summarizes the market experience data obtained from internal Baxter databases. All devices listed in **Table 4-1** and **Table 4-2** will be considered in the analysis in this section.

Complaints related to the MDD legacy devices are included in this section as the risks identified for these devices would be applicable to the DUE.

The Sales, Number of Exposures and Complaint Incident (CI) data are presented per calendar year, and split regionally into European Economic Area, Turkey, and Northern Ireland (hereafter referred to as EEA+TR+XI) and Worldwide (which represents the total worldwide, including EEA+TR+XI). For the full list of countries contained within the EEA+TR+XI grouping, please refer to the Abbreviations and Definitions Table in **Section 22.**

11.3.1.1 Sales Data

The sales data for the MDD legacy devices, can be found in **Table 11-6**.

Table 11-6: Sales Data of MDD Legacy Devices

Region of Complaint Origin	Total	2024 (ending 31-AUG)	2023	2022	2021	2020	2019 (starting 01-SEP)
1. Set for Urological Irrigation (7400009A)							
EEA+TR+XI	116,297	11,750	23,750	21,397	23,750	26,700	8,950
Worldwide	125,247	11,750	23,750	21,397	23,750	26,700	17,900
2. Y Set for Urological Irrigation (7401010A)							
EEA+TR+XI	218,243	35,350	36,475	47,394	46,699	36,575	15,750
Worldwide	389,168	58,700	67,850	58,269	64,974	53,875	85,500
3. Single Lead Irrigation Set (E5MC4002)							
EEA+TR+XI	840,428	124,050	175,890	171,864	157,425	151,249	59,950

Table 11-6: Sales Data of MDD Legacy Devices

Region of Complaint Origin	Total	2024 (ending 31-AUG)	2023	2022	2021	2020	2019 (starting 01-SEP)
Worldwide	1,058,919	168,962	230,568	225,615	157,425	151,249	125,100
4. Y-Type Irrigation Set (E5MC4007N)							
EEA+TR+XI	467,016	62,475	80,125	92,378	102,663	92,350	37,025
Worldwide	1,098,381	135,645	192,344	207,554	216,380	189,054	157,404
5. Fast Flow Y-Type Irrigation Set (EMC4015N)							
EEA+TR+XI	173,989	29,625	40,305	30,246	35,293	28,590	9,930
Worldwide	199,272	31,530	41,970	32,991	36,951	30,510	25,320
6. Single Lead Irrigation Set (EMC4042)							
EEA+TR+XI	641,943	98,450	119,700	130,500	124,642	115,551	53,100
Worldwide	695,043	98,450	119,700	130,500	124,642	115,551	106,200
7. Y-Type Irrigation Set (EMC4047)							
EEA+TR+XI	132,580	16,475	25,800	29,800	25,080	25,050	10,375
Worldwide	142,955	16,475	25,800	29,800	25,080	25,050	20,750
8. Y-Type Irrigation Set (EMC4055N)							
EEA+TR+XI	365,124	58,500	91,065	61,984	69,560	56,640	27,375
Worldwide	392,499	58,500	91,065	61,984	69,560	56,640	54,750
9. Irrigation Jet (RMC4916)							
EEA+TR+XI	257,600	37,275	59,175	52,339	49,411	40,650	18,750
Worldwide	276,350	37,275	59,175	52,339	49,411	40,650	37,500
10. Y-Type Irrigation Set (VMC4005)							
EEA+TR+XI	153,926	19,900	34,125	30,136	30,415	27,900	11,450
Worldwide	623,644	135,990	250,906	155,533	30,415	27,900	22,900
Total							
EEA+TR+XI	3,367,146	493,850	686,410	668,038	664,938	601,255	252,655
Worldwide	5,001,478	753,277	1,103,128	975,982	798,588	717,179	653,324

11.3.1.2 Number of Exposures

To allow a comparison between different periods, the Number of Exposures will be used as a denominator to normalize the data. The method used will be consistent throughout the CER to allow a comparison between different periods. The Number of Exposures is the number of times customers, healthcare professionals, or other people can potentially come in contact with the products in scope of this document. A potential number of exposures will be used, as Baxter has only information about number of sold devices, and no information about the number of products still at the customer's warehouses or in their storage versus what was already used. As the DUE is a 'Single-Use Device', the sales data will be equal to the Number of Exposures, and the units distributed within each time period will be used for the calculations below.

11.3.1.3 Calculation of Complaint Incidents Per Million

The complaint incident rate will be presented as Complaint Incidents Per Million (CIPM) which is calculated as follows:

$$\text{CIPM} = \frac{\text{Number of Complaint Incidents}}{\text{Number of Exposures}} \times 1{,}000{,}000$$

CIPM is a metric used to measure the frequency or rate of complaint incidents within a given population or context. Baxter uses it as a performance indicator for product quality management.

The calculation of CIPM involves determining the number of complaint incidents received or recorded within a specific period and dividing it by the total population size or the total number of exposures (e.g., interactions with patients, healthcare professionals).

11.3.1.4 General Notes

To analyses the complaint incidents received for the of MDD legacy devices in scope of the internal market experience data analysis, the investigation results are used as starting point. This Medical Device Problem is determined by the Subject Matter Experts in the manufacturing sites and will describe the issue in the most accurate way for the purpose of analysis.

11.3.1.5 Complaint Incident Analysis

This section presents a summary of the complaints received for the devices in scope of the internal market experience data analysis, that are documented in Baxter's Complaint Management System.

Information, including feedback and incidents, are provided to Baxter by users, distributors, importers, and/or agencies. Complaints can also be identified during a review of literature and/or active market data collection. The collected incidents are entered into the Complaint Management System (CMS) by the PMS department as per GQP-05-01 (Post-Market Surveillance System - Intake Process) and investigated as per GQP-05-02 (Post-Market Surveillance Complaint Handling and Investigation).

Vigilance reporting is performed according to the applicable regulatory requirements as documented in GQP-05-03 (US Medical Device Reporting) and GQP-05-13 (Vigilance Reporting).

11.3.1.5.1 Complaint Incidents and CIPM

A general analysis of all incidents received by Baxter will be presented in this section (i.e., any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effects).

The total number of Complaint Incidents (CI) which is the quantity of units involved in all complaints received by Baxter, and the CIPM for the MDD legacy devices and the current DCP are presented in **Table 11-7**.

Table 11-7: Global Complaint Incidents (CI) and CIPM for the MDD Legacy Devices (Serious and Non-Serious Incidents)

Region of Complaint Origin	Total		2024 (ending 31-AUG)		2023		2022		2021		2020		2019 (starting 01-SEP)	
	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM
EEA+TR+XI	52	154.4	1	20.2	39	568.2	7	104.8	4	60.2	1	16.6	0	0.0
Worldwide	339	677.8	103	1367.4	133	1205.7	66	676.2	19	237.9	7	97.6	11	168.4

11.3.1.5.2 Complaint Incidents and CIPM per Medical Device Problem

A summary of the total complaint incidents per Medical Device Problem as well as the CIPM of the MDD legacy devices is provided in **Table 11-8.**

The top three Medical Device Problems reported during the current clinical evaluation are:

(1) Damaged set - collapsed or kinked (226)

(2) Leaks – separated (30)

(3) No Flow (10)

Table 11-8: Complaint Incidents and CIPM per Medical Device Problem for the MDD Legacy Devices

Region of Complaint Origin	Total		2024 (ending 31-AUG)		2023		2022		2021		2020		2019 (starting 01-SEP)	
	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM
Damaged Set - Collapsed or Kinked														
EEA+TR+XI	21	180.6	1	85.1	20	842.1	0	N/A	0	N/A	0	N/A	0	N/A
Worldwide	226	1,804.4	94	8,000.0	103	4,336.8	29	1,355.3	0	N/A	0	N/A	0	N/A
Leaks - Separated														
EEA+TR+XI	6	51.6	0	N/A	1	42.1	3	140.2	2	84.2	0	N/A	0	N/A
Worldwide	30	239.5	1	85.1	5	210.5	3	140.2	11	463.2	2	74.9	8	446.9
No Flow														
Worldwide	11	87.8	0	N/A	0	N/A	11	514.1	0	N/A	0	N/A	0	N/A
Under Infusion														
Worldwide	10	79.8	0	N/A	0	N/A	10	467.4	0	N/A	0	N/A	0	N/A
Improper Packaging - Packaging Wrong Quantity														
Worldwide	10	79.8	2	170.2	7	294.7	1	46.7	0	N/A	0	N/A	0	N/A
Contamination - PM Outside Fluid Path														
Worldwide	8	63.9	2	170.2	2	84.2	4	186.9	0	N/A	0	N/A	0	N/A
Contamination - PM Fluid Path														
Worldwide	6	47.9	0	N/A	1	42.1	1	46.7	2	84.2	1	37.5	1	55.9

Table 11-8: Complaint Incidents and CIPM per Medical Device Problem for the MDD Legacy Devices

Region of Complaint Origin	Total		2024 (ending 31-AUG)		2023		2022		2021		2020		2019 (starting 01-SEP)	
	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM
Leaks - Non Specific														
EEA+TR+XI	2	17.2	0	N/A	0	N/A	2	93.5	0	N/A	0	N/A	0	N/A
Worldwide	6	47.9	0	N/A	1	42.1	2	93.5	2	84.2	1	37.5	0	N/A
Leaks - Disconnection														
EEA+TR+XI	1	8.6	0	N/A	0	N/A	1	46.7	0	N/A	0	N/A	0	N/A
Worldwide	5	39.9	0	N/A	1	42.1	1	46.7	3	126.3	0	N/A	0	N/A
Missing Component														
EEA+TR+XI	3	25.8	0	N/A	3	126.3	0	N/A	0	N/A	0	N/A	0	N/A
Worldwide	4	31.9	0	N/A	3	126.3	0	N/A	1	42.1	0	N/A	0	N/A
Customer Feedback														
Worldwide	4	31.9	1	85.1	3	126.3	0	N/A	0	N/A	0	N/A	0	N/A
Damaged Set - Cracked Broken														
Worldwide	4	31.9	0	N/A	4	168.4	0	N/A	0	N/A	0	N/A	0	N/A
Packaging - Damaged Sterile Packaging														
EEA+TR+XI	1	8.6	0	N/A	0	N/A	0	N/A	0	N/A	1	37.5	0	N/A

Table 11-8: Complaint Incidents and CIPM per Medical Device Problem for the MDD Legacy Devices

Region of Complaint Origin	Total		2024 (ending 31-AUG)		2023		2022		2021		2020		2019 (starting 01-SEP)	
	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM
Worldwide	3	24.0	2	170.2	0	N/A	0	N/A	0	N/A	1	37.5	0	N/A
Leaks - Spike														
Worldwide	3	24.0	1	85.1	0	N/A	0	N/A	0	N/A	1	37.5	1	55.9
Backflow - Solution														
Worldwide	3	24.0	0	N/A	2	84.2	0	N/A	0	N/A	1	37.5	0	N/A
Overflow - Irrigation or Transfer														
Worldwide	2	16.0	0	N/A	2	84.2	0	N/A	0	N/A	0	N/A	0	N/A
Use - Difficult to Use														
Worldwide	2	16.0	0	N/A	0	N/A	2	93.5	0	N/A	0	N/A	0	N/A
Unable to Prime														
Worldwide	2	16.0	0	N/A	0	N/A	2	93.5	0	N/A	0	N/A	0	N/A
Leaks - Cut Slice Hole														
Worldwide	1	8.0	0	N/A	0	N/A	0	N/A	0	N/A	0	N/A	1	55.9
Leaks - Cracked Broken														
Worldwide	1	8.0	0	N/A	1	42.1	0	N/A	0	N/A	0	N/A	0	N/A

Table 11-8: Complaint Incidents and CIPM per Medical Device Problem for the MDD Legacy Devices

Region of Complaint Origin	Total		2024 (ending 31-AUG)		2023		2022		2021		2020		2019 (starting 01-SEP)	
	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM
Labeling - Missing Lot Info														
Worldwide	1	8.0	0	N/A	1	42.1	0	N/A	0	N/A	0	N/A	0	N/A
Connection - Difficult to Spike														
Worldwide	1	8.0	1	85.1	0	N/A	0	N/A	0	N/A	0	N/A	0	N/A

11.3.1.5.3 Serious Incidents

A Serious Incident is any incident that directly or indirectly led, might have led or might lead to any of the following:

1) the death of a patient, user, or other person,
2) the temporary or permanent serious deterioration of a patient's, user's, or other person's state of health,
3) a serious public health threat.

In the context of this analysis, the following definitions are used:

- **Malfunction:** a Serious Incident that did not lead to a Death or a Serious Injury, however, have the potential to lead to a Death or Serious Injury if to reoccur.
- **Serious Injury:** a Serious Incident that led to a Serious Injury, which is attributable to a Baxter Device (or where the cause association with the Baxter Device is unknown).
- **Death:** a Serious Incident that led to a Death, which is attributable to a Baxter Device (or where the cause association with the Baxter Device is unknown).
- **Serious Public Health Threat**: means an event which could result in imminent risk of death, serious deterioration in a person's state of health, or serious illness, that may require prompt remedial action, and that may cause significant morbidity or mortality in humans, or that is unusual or unexpected for the given place and time;

Table 11-9 provides the number of reports submitted for the type of serious incident and medical device problem code for the MDD legacy devices. There were no reportable serious injuries and deaths for the current DCP for the MDD legacy devices.

Table 11-9: Number Reports submitted for type of Serious Incident and Medical Device Problem Code for the MDD Legacy Devices

Region of Complaint Origin	Total		2024 (ending 31-AUG)		2023		2022		2021		2020		2019 (starting 01-SEP)	
	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM	CI	CIPM
Malfunction														
EEA+TR+XI	5	43.0	0	N/A	1	42.1	3	140.2	0	N/A	1	37.5	0	N/A
Worldwide	38	303.4	3	255.3	11	463.2	10	467.4	6	N/A	5	187.3	3	167.6

11.3.1.5.4 Use Errors and Abnormal Use

Baxter has received no complaint incidents that involved a use error and/or an abnormal use for the MDD legacy devices.

11.3.1.5.5 Customer Feedback

Customer Feedback is used in the Baxter CMS for product suggestion events without an allegation of a deficiency related to the identity, quality, durability, reliability, usability, safety, effectiveness, or performance of a product. This customer feedback is provided in **Table 11-10**.

Table 11-10: Customer Feedback Events for the MDD Legacy Devices for the Current DCP

Complaint PR#	Country of Origin	Narrative
4190094	Ecuador	This was a case report received via email on 09 February 2023 from a pharmacist at International Clinic regarding UROMATIC TUR.ADMIN.SET (Product code VMC4005 and Lot number: 22F09T249). The reporter stated that “The product hose was very stiff, making it difficult to use. It did not have the rubber segment but a rigid one and it did not have the regulating key” Later on, the reporter informed that there were two other events occurred at the International Clinic from the same batch for the same matter. The events occurred during the three surgeries with three patients. However, there was no patient injury, medical intervention, or adverse reaction associated with this event. There were no other deficient products used during the event. According to the conversation held with the sales specialist, the customer's perception is not related to a quality defect of the product but that they used to use a different code (ARC4005P)

Table 11-10: Customer Feedback Events for the MDD Legacy Devices for the Current DCP

Complaint PR#	Country of Origin	Narrative
		and found differences in it. It was confirmed by the Sales and Marketing team that the code change was made a year ago, it is most likely that the customer who reported the complaint was a customer of a distributor, which probably did not notify the customer of the change. A new notification was sent to the customer.
5038784	Great Britain	This event was reported to Baxter Great Britain on 10 June 2024 via email regarding one (1) unit of EASYFLOW BUBBLE TRAP MULTI SET (Product Code: EMC4055N, Serial Number: 23G15T284). The reporter stated that "It has been brought to my attention that the attached product does not have barcodes on. The barcode is on the box but not the individual products. I have attached an image of the products, is there any way of adding a GS1 standard barcode onto the packaging so when the products are used on patients, they can be scanned to the patient record?". Additional information received from the customer on 24 June 2024: “My original email isn’t a complaint exactly and there isn’t a reason for a return. I was just wondering if it is possible for Baxter to put barcodes on the EMC4055N packaging so it can be scanned to patients in theatres”. *Note: Barcodes were added within the MDR remediation of the Irrigation Sets.*

11.3.1.5.6 Post-Market Monitoring

Post-Market monitoring refers to the activities conducted to assess and track the performance, safety, and quality of a product or service after it has been released into the market. It involves gathering and analyzing data, monitoring feedback from users and stakeholders, and evaluating the product's ongoing compliance with regulatory requirements and customer expectations. The primary purpose of Post-Market Monitoring is to detect and address any issues, risks, or deficiencies that may arise during the product's real-world use.

Post-market monitoring plays a critical role in maintaining product quality, safety, and customer satisfaction. It enables companies to identify and address any issues that may arise during the product's lifecycle, ensuring that it continues to meet customer needs, comply with regulations, and evolve in response to changing market dynamics and user feedback.

11.3.1.5.6.1 Post-Market Risk Monitoring

Post-Market Risk Monitoring starts with evaluating the severity, frequency, and impact of identified risks to determine their significance and prioritize actions (GQP-10-04, Post-Market Risk Monitoring).

Each risk that is identified will be assigned a threshold value for detecting possible trends (according to GG-10-

06, Global Guidance for Post Market Threshold Determination and Implementation). These thresholds are specified in the Product Trending Table applicable (which for the DUE is BXU600027/A-Product Trending Table (PTT) for Irrigation Sets for Malta and BXU600026/A-Product Trending Table (PTT) for Irrigation Sets for Tunisia). The identification of potential trends relies on the data sources and operational rules outlined in GQI-01-05.

All incidents will undergo a thorough review using the PQDR process, as detailed in **GQP-01-03.** If a statistically significant trend emerges, appropriate actions or escalations are implemented. If new safety-related information arises, it will be escalated to the Risk Management Review (**GQP-10-05**).

Table 11-11 lists all triggers that were generated during the current DCP. The information concerning NCRs related to triggers can be found in **Section 11.3.1.5.8**.

During the DCP, three trend triggers with in total two NCR investigations occurred: Both NRCs resulted in a CAPA. **Section 11.3.1.5.8** provides further details on the NRCs. The details of these triggers are provided in this section.

Table 11-11: Trend Trigger Analysis[19] for the MDD Legacy Devices

Trigger Type	Trigger ID	Trigger Evaluation ID	Hazardous Situation	(S)NCR Initiated	(S)NCR ID	Description
Trend - Monthly	M20200115_74	1800919	LEAK	No	N/A	N/A
Trend - Monthly	M20200310_99	1835713	LEAK	No	N/A	N/A
Trend - CDA	D20210405_2	2103937	HS.IRR.15.8	No	N/A	N/A
Trend - Monthly	M20210609_11 M20210609_34 M20210609_35 M20210609_36 M20210609_85	2154662	HS.IRR.15.11 HS.IRR.12.2 HS.IRR.15.8 HS.IRR.20.8 LEAK	No	N/A	N/A
Trend - CDA	D20220825_5	2458381	HS.IRR.12.1	No	N/A	N/A
Trend - Monthly	M20221011_7	2491159	Damaged	Yes	2472960	N/A
Trend - Monthly	M20221213_21	2540464	Damaged	Yes	2472960	N/A
Trend - CDA	D20230317_2 D20230317_3 D20230317_4 D20230317_5	2606883	HS.IRR.4.1 HS.IRR.4.2 HS.IRR.4.3 HS.IRR.4.4	No	N/A	N/A
Trend - CDA	D20230317_2 D20230317_3	2610664	HS.IRR.4.1 HS.IRR.4.2	No	N/A	N/A

[19] The information concerning NCRs related to triggers can be found in **Section 11.3.1.5.8** - **Error! Reference source not found..**

Table 11-11: Trend Trigger Analysis[19] for the MDD Legacy Devices

Trigger Type	Trigger ID	Trigger Evaluation ID	Hazardous Situation	(S)NCR Initiated	(S)NCR ID	Description
	D20230317_4 D20230317_5		HS.IRR.4.3 HS.IRR.4.4			
Trend - CDA	D20230411_2 D20230411_3 D20230411_4 D20230411_5	2624563	HS.IRR.4.1 HS.IRR.4.2 HS.IRR.4.3 HS.IRR.4.4	No	N/A	N/A
Trend - Monthly	M20230711_34	2694415	Damaged	No	N/A	N/A
Trend - Monthly	M20230808_25	2714530	Damaged	No	N/A	N/A
Trend - Monthly	M20230912_18	2740294	Damaged	No	N/A	N/A
Trend - Monthly	M20240213_30	2851388	Damaged	Yes	2800569	N/A
Trend - CDA	D20240405_1 D20240405_2	2886848	HS.IRR.4.2 HS.IRR.4.3	No	N/A	N/A
Trend - Monthly	M20240409_41	2888866	Damaged	No	N/A	N/A
Trend - Monthly	M20240611_37	2935100	Damaged	No	N/A	N/A
Trend - Monthly	M20240813_37	2986357	Damaged	N/A	N/A	N/A

11.3.1.5.6.2 Periodic Risk Review

A Periodic Risk Review (PRR) is a type of risk management file review, which is performed after a specific time period, which is established in the Risk Management Plan. For the DUE this PRR will be performed every 24 months [1277312].

Based upon the review, the risks remain acceptable and the benefits of the product outweigh the risk. Actions on the risk documents are required following the periodic risk review, as listed in the document. [BXU601656]

11.3.1.5.6.3 Event Based Risk Review

An Event Based Risk Review (EBRR) is a type of risk review that is triggered by an event that, considering new information, may potentially change the product's risk profile and the results of which are documented in the risk management file of the DUE.

Based upon the event-based risk review, there are no new risks, the risks remain acceptable, and the benefits of the product outweigh the risk. Event based risk review is carried out in accordance with GQP-10-05.

11.3.1.5.6.4 Reliability Monitoring Field Report

The DUE and MDD legacy devices do not require a Reliability Monitoring Field Report, as they are not Electromechanical Devices (Medical devices containing software, firmware, or programmable logic), or Software (classified as, part of, component of, or accessory to a Medical Device).

11.3.1.5.6.5 Device Safety Signal Management

Device Safety Signal Management (1280466) is part of the Global Quality Management System (QMS) process for Global Patient Safety (GPS). The purpose is to review medical device adverse event data for Baxter devices to identify and analyze device safety signals, as well as to provide recommendations of further actions for the management of these signals.

A safety signal can be a new device adverse event, including an unanticipated event, an apparent clinically significant increase in the frequency of a known device adverse event, an apparent clinically significant increase in the severity of a known device adverse event, occurrence of a device adverse event thought to be extremely rare in the general or treated population. The safety signals can originate from various sources (e.g., PMS, literature, and press).

During the current DCP, no signals were initiated for the MDD legacy devices via the Device Safety Signal Management process.

11.3.1.5.6.6 Manufacturer Trend Reports

Baxter shall report any statistically significant increase in the frequency or severity of incidents that are not serious incidents, including use error or that are expected undesirable side-effects that could have a significant impact on the benefit-risk analysis and which have led or may lead to risks to the health or safety of patients, users or other persons that are unacceptable when weighed against the intended benefits (Article 88 and Annex III, Regulation (EU) 2017/745 (MDR)).

The significant increase shall be established in comparison to the foreseeable frequency or severity of such incidents in respect of the device, or category or group of devices, in question during a specific period as specified in the technical documentation and product information.

The threshold values to identify any potential trend are defined in the PTT [BXU600027, BXU600026]. The identification of potential trends relies on the data sources and operational rules outlined in GQI-01-05.

If there is new information for safety, the escalation will follow the Risk Management Review (GQP-10-05) which will assess whether there are changes needed to the risk documentation.

The management of events which are subject to trend reporting is performed according to:

- GQP-10-04, Post-Market Risk Monitoring;
- GQP-01-03, Product Quality Data Review; and,
- EMEAFSV002, EMEA Medical Device Reporting.

There were no Manufacturer Trend Reports submitted for the MDD legacy devices during the current DCP, as

there were no Non-Serious Incidents triggering a shift in the risk-benefit analysis for the MDD legacy devices.

11.3.1.5.7 Field Safety Corrective Actions (FSCAs)

The aim of this section is to present any Field Safety Corrective Action (FSCA) with respect of devices made available on the Union market, including any field safety corrective action undertaken in a third country in relation to a device which is also legally made available on the Union market, if the reason for the field safety corrective action is not limited to the device made available in the third country (Article 87 and Annex III, Regulation (EU) 2017/745 (MDR)).

Field Safety Corrective Actions (FSCAs) are corrective actions taken by a manufacturer, for technical or medical reasons, to prevent or reduce the risk of a serious incident in relation to a device made available on the market.

FSCAs are escalated, evaluated, and executed per the Global Field Action (FA) Procedure (GQP-05-05), and the Field Action Procedure - Region EMEA (EMEAFCA001).

Table 11-12 summarizes all FSCAs that were initiated during the current DCP for the MDD legacy devices, and those that were initiated during previous DCPs but are still in progress at the moment of writing this document. The information can possibly be repeated over multiple CERs, until the FSCA is closed, at which point the final outcomes will be presented, after which the item will be removed from the document in the next revision.

Table 11-12: Summary of FSCAs for MDD Legacy Devices

FSCA ID	Product Code(s)	Product Name(s)	Decision	Decision Date	Status	Action Type	Countries impacted	(S)NCR / CAPA / SCAR ID
FA-2021-027	E5MC4002, 955596, EMC3202A, EMC4015N, E5MC4002, RMC9624, XMC4284, E5MC4007N, RMC9615, 955595, EMC3294A, 106697, E3MC3805, JMC3437, VMC9627, 955467, NGB8064M, 955468, EMC7109, E3MC3802, E3MC3801A, R7MC3476, E3MC3800A, 107140, 115309, UMC3318, 115307, EMC0349, 106696, 107144, EMC7202, ZMC9625, R3MC8119, IVGP010XS, RMC3187, EMC5951	Access (Irrigation Sets, Basic Solution Sets, Stand-Alone Devices), Reconstitution Devices and Nutrition Devices	• HP-2021-036: The potentially impacted product for this issue is broader than the scope of this escalation and were distributed to multiple countries. This escalation is exclusively for the FA execution only to the customers in Switzerland as this is mandated by the Swiss MoH. The rationale for not escalating into the field action process is documented in the associated plant NCR TrackWise 8 PR# 2072124 (owned by Malta). • RN-2021-040: The potentially impacted product for this issue is broader than the scope of this escalation and were distributed to multiple countries. This escalation is exclusively for the FA execution only to the customers in the Germany as this is mandated by the German MoH. The rationale for not escalating into	29-APR-2021	Closed	Product Recall/ Removal	Australia, China, Korea, Malaysia, Singapore, Taiwan, United States, Brazil, Chile, Columbia, Bahrain, Belgium, Croatia, France, Germany, Greece, Italy, Kuwait, Morocco, Netherlands, Saudi Arabia, South Africa, Spain Switzerland, United	NCRs TrackWise 8 PR# 2077463[20] (owned by Meyzieu) and TrackWise 8 PR# 2072124

[20] PR#2077463 does not have any of the irrigation sets in scope.

			the field action process is documented in the associated plant NCRs TrackWise 8 PR# 2077463 (owned by Meyzieu) and TrackWise 8 PR# 2072124 (owned by Malta). • HP-2021-042: The potentially impacted product for this issue is broader than the scope of this escalation and were distributed to multiple countries. This escalation is exclusively for the FA execution only to the customers in the Germany as this is mandated by the German MoH. The rationale for not escalating into the field action process is documented in the associated plant NCRs TrackWise 8 PR# 2077463 (owned by Meyzieu) and TrackWise 8 PR# 2072124 (owned by Malta). • RN-2021-037: The potentially impacted product for this issue is broader than the scope of this escalation and were distributed to multiple countries. This escalation is exclusively for the FA execution only to the customers in Switzerland as this is mandated by the Swiss MoH. The rationale for not escalating into the field action process is documented in the associated plant				Kingdom	

			NCR TrackWise 8 PR# 2072124 (owned by Malta). • RN-2021-058: Although Baxter has objective evidence that supports the sterility of the products and the absence of negative impact on product performance or safety, the FDA has requested Baxter to inform US customers of the issue and recall the product. RN-2021-060: To meet BSI's expectation, out of an abundance of caution, Baxter will recall the impacted batches of Prismaflex sets.					
FA-2021-030	004640000, 004765000, 7400009A, 7401010A, AMC9606, AMC9607C, AMC9609, AMC9626, AMC9627, AMC9673, AMC9694, E2MC1119, E3MC3803, E4MC3464, E5MC4002, E5MC4007N, EMC0062M, EMC0349, EMC1402, EMC2421P, EMC3202A, EMC3269V, EMC3274, EMC3275V, EMC3293, EMC3294A, EMC3371, EMC3459A, EMC3475, EMC3478,	Access Irrigation Sets, Solution Sets, Stand-Alone Devices, Reconstitution Devices and Nutrition Devices	• HP-2021-075: The potentially impacted product for this issue is broader than the scope of this escalation and were distributed to multiple countries (EU and non-EU). This escalation is exclusively for the FA execution only to the customers in the EU as is mandated by BfArM. • HP-2021-043: The deviations to which the impacted devices were exposed, have the potential to compromise the effectiveness of the sterilization process and subsequent device functionality. • RN-2021-044: The Baxter product	12-MAY-2021	Closed	Product Recall/ Removal	Australia, Bangladesh, China, Hong Kong, India, Malaysia, New Zealand, Singapore, Thailand, Bahamas, Brazil, Canada, Chile, Colombia, Mexico, Algeria, Austria,	NCR TrackWise 8 PR# 2072124

	EMC3482, EMC4002A, EMC4015N, EMC4042, EMC4047, EMC4055N, EMC5846, EMC5905P, EMC5908P, EMC5930, EMC5948, EMC5951, EMC5967, EMC7105, EMC7109, EMC7110, EMC7131, EMC7332, EMC9190, EMC9191, EMC9584P, EMC9601N, EMC9603, EMC9608, EMC9611G, EMC9612, EMC9630, EMC9656C, EMC9657C, EMC9663C, EMC9664C, EMC9675, EMC9680, FMC5894P, FMC5905, FMC9650, FMC9651P, FMC9673, FNC1168N, FNC1173N, FNC2110N, FNC2220N, FNC3110N, FNC3120N, FNC3121N, FNC3220N, FNC8537N, IVGP010XS, LCC3818, M6MC9644, MMC2071B, MMC2081B, MMC2433, MMC3293, MMC3371K, MMC5913D, MMC5991, MMC9609L, MMC9611L, MMC9627S,		sterilized within the 169 sterilization batches for which data was not received or raw data is missing will be recalled. • HP-2021-078: The potentially impacted product for this issue is broader than the scope of this escalation and were distributed to multiple countries (EU and non-EU). This escalation is exclusively for the FA execution only for Israel as mandated by Israeli MOH. • RN-2021-076: The potentially impacted product for this issue is broader than the scope of this escalation and were distributed to multiple countries (EU and non-EU). This escalation is exclusively for the FA execution only to the customers in the EU as is mandated by BfArM. RN-2021-079: The potentially impacted product for this issue is broader than the scope of this escalation and were distributed to multiple countries (EU and non-EU). This escalation is exclusively for the FA execution only to the customers in the EU as is mandated by BfArM. The rationale for not escalating into the field action process is documented in the associated plant				Bahrain, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Israel, Italy, Jordan, Kuwait, Latvia, Lebanon, Luxemburg, Macedonia, Malta, Netherlands, Norway, Oman, Poland, Portugal, Qatar, Russia, Saudi Arabia, Slovakia, Slovenia, South Africa, Spain, Sudan, Sweden,	

	MMC9628, MMC9638, MMC9648, MMC9661, MMC9662, MMC9668L, MMC9675P, MMC9677, MMC96900L, MMC96901L, MMC9695A, NGB8064M, NMC3320V, NMC3325V, R7MC3476, RMC3347, RMC3477, RMC4916, RMC5849, RMC9597, RMC9604, RMC9615, RMC9622P, RMC9624, RMC9676, RMC9689, TMC2159, UMC3318, UMC3320, VMC0172P, VMC4005, VMC9606, VMC9607C, VMC9609, VMC9626, VMC9627, VMC9694, YMC7302, ZMC9625		NCR TrackWise 8 PR# 2072124 (owned by Malta).				Turkey, United Arab Emirates, United Kingdom	

For more information about the (S)NCRs, CAPAs, and/or SCARs, and their outcome, please refer to **Section 11.3.1.5.8**.
*Irrigation Sets product codes are underlined

11.3.1.5.8 (Significant) Non-Conformance Reports (NCRs), associated Corrective Actions and Preventive Actions (CAPAs), and Supplier Corrective Action Requests (SCARs)

If, in the course of the Post-Market Surveillance, a need for preventive or corrective action, or both, is identified, the manufacturer shall implement the appropriate measures and inform the competent authorities concerned and, where applicable, the notified body. Where a serious incident is identified or a field safety corrective action is implemented, it shall be reported in accordance with Article 87, Regulation (EU) 2017/745 (MDR) (Article 83(4) and Article 86, Regulation (EU) 2017/745 (MDR)).

The PSUR will be used as the tool to provide information about Corrective Action(s) or Preventive Action(s) (CAPA), including those that were already reported via other processes to the Competent Authorities, and/or Notified Bodies. The information provided will focus on:

- Significant NCRs (SNCRs);
- NCRs related to any complaint Incidents;
- NCRs related to FSCAs;
- NCRs related to Post-Market Risk Monitoring triggers; and,
- Relevant SCARs.

For the above-mentioned NCRs and/or SCARs, the related CAPAs will also be described.

Baxter's Global Quality Management System enables the identification and initiation of appropriate measures, including corrective actions:

- GQP-01-03 - Product Quality Data Review
- GQP-05-02 - Post-Market Surveillance Complaint Handling and Investigation
- GQP-06-01 - Nonconformance Management
- GQP-06-02 - Corrective Action/Preventive Action Management
- GQP-10-04 - Post-Market Risk Monitoring

Table 11-13 provides the summary of the above mentioned (S)NCRs, CAPAs and SCARs, that were initiated for the DUE during the current DCP, and those that were initiated during previous DCPs but are still in progress at the time of the writing of this CER. For the MDD legacy devices of the Irrigation Sets there were three NRCs (2072124, 2472960, 2800569) closed in the current DCP, all resulted in a CAPA (2135004, 2528601, 2854060).

Table 11-13: (S)NCR/SCAR/CAPA Status Summary

(S)NCR / SCAR Number	CAPA Number (if applicable)	(S)NCR / SCAR Initiation Date	Reason for Initiating NCR	NCR Root Cause or Contributing Cause	Resulting Correction, Containment, or Corrective Action
(S)NCRs/SCARs/CAPAs closed during the current DCP					
2072124	2135004	19-FEB-2021	On Tuesday 16th February 2021, our logistics supplier "Attrans" contacted Baxter Malta Shipping Coordinator to inform him that they tried to deliver a trailer load of product as per normal routine to Steril Milano and found the company closed. Following this, Baxter Malta Management tried to get in touch with Steril Milano through various contacts to try and get information, however no contact was made. On Wednesday Morning, Baxter Malta Sterility Assurance Responsible (was out of office on Tuesday), received an email (refer to attachment PR2072124 – Annex F) from Steril Milano stating they are stopping all onsite activities due to a quality issue that they are investigating. The communication also stated that we should keep any product in our warehouses on hold and refrain from sending any further product to their site until further notice. Meanwhile on Wednesday 17 Feb 2021, Baxter Malta Quality Manager also received information from within Baxter that TUV contacted Baxter to understand if we were aware that Steril Milano has stopped all activities. Following these communications, Baxter Malta and Tunisia stopped release of any batches that were sterilized in Steril Milano and still not released, as well as	1. That organized fraud was in place for many years and set up and maintained by former CEO of Steril Milano. 2. The falsifications mainly consisted of modifying the processing parameters of the batch records (either individual data and/or graphs) to make them match the target / validated	1) As an immediate correction, the sterilization activities at Steril Milano were stopped effective immediately 2) Following the review and complete analysis of the 581 cycles received (MT609_EA Rev C), Baxter decided to recall batches impacted by the following conditions only; Missing Cycles, Low/Unknown EO Concentration, Low Dwell Time, Incorrect Vessel Used. This decision was taken on 10 May 2021. FA-2021-030 HP-2021-043 Corrective Actions: Complete Validation of new Alternate Supplier Steris to replace Steril Milano capacity. This validation is being managed through Change Control PR# 2097942. Corrective Action Work with Supplier Quality team to identify potential improvements in they Supplier Audit

Table 11-13: (S)NCR/SCAR/CAPA Status Summary

(S)NCR / SCAR Number	CAPA Number (if applicable)	(S)NCR / SCAR Initiation Date	Reason for Initiating NCR	NCR Root Cause or Contributing Cause	Resulting Correction, Containment, or Corrective Action
			reversed release of any batches that were still in full ownership at Baxter and not yet distributed. However, at this stage information from Steril Milano with regards to impacted product was still vague and Baxter continued to try and make contact with supplier to get more information about which batches are impacted and what is the extent of the issue. On Thursday 18th February, Baxter Malta managed to organize a call with Ionisos (Company that Acquired Steril Milano in 2020) whereby it was confirmed that Steril Milano had observed non-conformances in the past and these were not reported to Baxter but instead data was manipulated to appear to be conforming. At initiation of NCR – Baxter was still waiting for further information to understand what these non-conformances were as the information received at first was that there were some minor discrepancies in temperature, pressure, humidity and EO concentration but extent of discrepancies and hence impact to product was unknown. Steril Milano also confirmed that such issues had been going back to at least End of 2019 but they had to review data prior to this.	process parameters / graphs.	process, to increase the chance of capturing any incidences related to falsification of data during supplier audits. This action will be followed through CA PR# 2135004, available in Trackwise).
2472960	2528601	16-SEP-2022	The defects reported by the customer was confirmed: DAMAGED SET - COLLAPSED OR KINKED in code E5MC4002 batches 21I21T742, 21L21T775,	Method: Repaired units (Detected with kink issue	Containment: An extra in process check for the problem kinked tube will be

Table 11-13: (S)NCR/SCAR/CAPA Status Summary

(S)NCR / SCAR Number	CAPA Number (if applicable)	(S)NCR / SCAR Initiation Date	Reason for Initiating NCR	NCR Root Cause or Contributing Cause	Resulting Correction, Containment, or Corrective Action
			22B18T046 and 22D03T273.	during the inspection) can become kinked after manipulation.	performed on the batches produced till the implementation of the corrective action Corrective Action: The TNPPE5MC4002 was reviewed and issued and effective on TCU on 20 December 2022 and the special precaution "the bad coiling and kinked tubing should be discarded" was added (See TNPPE5MC4002).
2800569	2854060	04-DEC-2023	Kinked tubing in code E5MC4002	Method: Irregular coiling Method: Putting the set in the sleeve by squeezing the set	Containment: A second 100% visual check was performed after 24 hours from packaging. Corrective Action: Set up a JIG for coiling and tool to facilitate loading the set in the sleeve. The two tools were combined in one jig and drawing was created in TcU - TNOP126, issued and effective in 26-MAR-24.
(S)NCRs/SCARs/CAPAs remaining open during the current DCP					
None					

11.3.1.6 Active PMS Surveys

Active PMS surveys are a systematic and proactive collection of clinical, quality, safety, performance, satisfaction, and usability experience gained from medical devices placed on the market; with the objective to:

- Confirm the safety and performance of the device
- Ensure the continued acceptability of identified risks
- Detect emerging risks
- Draw necessary conclusions and implementing necessary preventive and corrective actions

The selected active Post-Market Surveillance approach is documented within the PMS plan [1248528PMSP].

This section summarizes the Active PMS Surveys that were conducted for the DUE during the current DCP.

A customer general satisfaction score is gathered for all Baxter products via the Net Promoter Score (NPS), which is a widely used market research metric that is based on a single survey question asking respondents to rate the likelihood that they would recommend a company, product, or a service to a friend or colleague.

NPS assumes a subdivision of respondents into "promoters" who provide ratings of 9 or 10, "passives" who provide ratings of 7 or 8, and "detractors" who provide ratings of 6 or lower. The Net Promoter Score results from a calculation that involves subtracting the percentage of detractors from the percentage of promoters collected by the survey item. The core "On a scale from 0-10, how likely are you to recommend Baxter to a friend or colleague?" question is accompanied by several open-ended questions.

During the evaluation period [01-SEP-2019 to 31-AUG-2024], Baxter conducted NPS surveys for many products, including Irrigation Sets, as part of an active market-related experience.

Baxter issued 73,166 NPS surveys to healthcare professionals in 28 different countries for the evaluation period. A 4.8% response rate (3,541 responses) was received. No responses were found linked to the product quality of the Irrigation Sets with no detractor score.

11.3.2 Analysis of External Vigilance and Recall Databases for Non-Baxter Similar Devices

A search was conducted for non-Baxter similar devices for the current DCP. These searches were conducted in the following external vigilance & recall databases: MHRA, Swissmedic, BfArM, FDA MAUDE, and the FDA recall database, in accordance with GQP-05-16. The results of these searches are summarized in the subsections below. Following the search of the external vigilance & recall databases, the search results were analyzed to determine if the reported issues for the non-Baxter equivalent/similar devices are relevant to the DUE. The resulting relevant reports are captured in **Section 11.3.2.2** through **Section 11.3.2.6** below.

The DUE legacy devices are not included in the search of external vigilance & recall databases as the agencies responsible for these databases are required to submit all reports they receive to the manufacturer. As such, these complaints would already be in the Baxter complaint database and are analyzed in **Section 11.3.1**.

11.3.2.1 Details of the External Vigilance and Recall Databases Search Conduct

The search strategy is developed based on the similar device name(s)/term(s). Details of the search strategy is

provided below.

Alternate spellings of similar device names or search terms, common variations in punctuation and spacing as well as common abbreviations, acronyms, and initialisms are also searched.

Date of the search: 17-SEP-2024

DCP covered by the search: 01-SEP-2019 to 31-AUG-2024

Device names to be searched:

- Urology Set, B. Braun
- Irrigation Sets, Vital Concepts, Inc.
- Irrigation Sets, International Medsurg Connections, Inc.
- Urological Connector, ICU Medical
- Urological Connector, Hospira
- Eziflow, Fairmont Medical
- Quickflow, Fairmont Medical
- TUR/Cystoscopy Sets, Fairmont Medical
- Irrigation Set Disposable Urology Set, Single bag, Fairmont Medical
- Irrigation Set Disposable Urology Set, Double bag, Fairmont Medical
- Irrigation Set Single bottle set wide bore urological flowfusor cystoscopy, Fresenius Kabi
- Irrigation Set Two bottle universal set for TUR post-operative wide bore, Fresenius Kabi

Name of person who created the search strategy: Paul N. Danese (FDAble LLC)

Name of person who conducted the search: Paul N. Danese (FDAble LLC)

External Vigilance and Recall Databases Searched:

- MHRA
- Swissmedic
- BfArM
- US FDA MAUDE
- US FDA Recalls

Conducting the search: case-insensitivity and wild-cards

Using the relevant device names and/or search terms and date filters, a search is conducted using the most recent monthly release of the relevant database. Searches are conducted in a case-insensitive fashion and wild cards were used if needed. The results of the external vigilance and recall database searches are summarized in the subsection below.

11.3.2.2 MHRA Database

The Medicines and Healthcare products Regulatory Agency (MHRA) is an executive agency of the Department

of Health in the United Kingdom. Its responsibility is to ensure that medicines and medical devices work and are acceptably safe. The MHRA was formed in April 2003.

This search led to no reports.

11.3.2.3 Swissmedic Database

Swissmedic is the Swiss agency for the authorization and supervision of therapeutic products. It provides, within the scope of market surveillance, a recall list of medical devices. Swissmedic started operations in January 2002.

This search led to no reports.

11.3.2.4 BfArM Database

The Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) is the federal institute for drugs and medical devices in Germany, operating under the Federal Ministry of Health. It ensures the central collection of a manufacturer's field corrective actions and recommendations by the BfArM, mainly derived from the evaluation of incident reports received under the medical devices vigilance system. The BfArM was founded in June 1994.

This search led to no reports.

11.3.2.5 FDA MAUDE Database

The Manufacturer and User Facility Device Experience (MAUDE) database compiles adverse event reports involving medical devices, which have been reported to the U.S. Food and Drug Administration (FDA). The data consists of voluntary reports since June 1993, user facility reports since 1991, distributor reports since 1993, and manufacturer reports since August 1996. The MAUDE data may not include reports made according to exemptions, variances, or alternative reporting requirements granted under 21 CFR 803.19. The MAUDE data is scheduled to be updated quarterly.

MAUDE will not identify reports received prior to the year 1991 and will not identify reports received after the most recent monthly data release.

This search led to a total of 15 reports. Of these reports, 11 were considered relevant to the DUE. These relevant reports are summarized in **Table 11-14** below along with the identification of any hazards/harms related to the reported event. In order to determine if a harm or hazard is new or existing, a comparison was done between the harms and/or hazards identified from the MAUDE database and those listed in the IFU and Risk Management Documents. The result of this analysis is presented in **Table 15-1**.

Table 11-14: FDA MAUDE Database Search Results Relevant to the DUE

Series No.	Device Name	Device Problem Description	Number of Events	Identified Hazards/Harms in the Reported Event	Patient Problem Description	Number of Events	Identified Hazards/Harms in the Reported Event
Non-Baxter Similar Device#1							
1.	Irrigation Set, B. Braun	Improper flow or infusion	1	Bubbles	No known impact or consequence to patient	0	N/A
2.		Improper flow or infusion	1	Leakage from the urology housing assembly	No known impact or consequence to patient	0	N/A
3.		Free or unrestricted flow	1	Defective roller clamp	No known impact or consequence to patient	0	N/A
4.		Detachment of device or device component; free or unrestricted flow	1	Defective roller clamp	No known impact or consequence to patient	0	N/A
5.		Detachment of device or device component; free or unrestricted flow	1	Defective clamp	No known impact or consequence to patient	0	N/A
6.		Detachment of device or device component; free or unrestricted flow	1	Defective roller clamp	No known impact or consequence to patient	0	N/A
7.		Free or unrestricted flow	1	Defective roller clamp	No known impact or consequence to patient	0	N/A
8.		Break; contamination	1	Contamination	No clinical signs,	1	N/A

Table 11-14: FDA MAUDE Database Search Results Relevant to the DUE

Series No.	Device Name	Device Problem Description	Number of Events	Identified Hazards/Harms in the Reported Event	Patient Problem Description	Number of Events	Identified Hazards/Harms in the Reported Event
		/decontamination problem			symptoms or conditions		
Non-Baxter Similar Device#2							
9.	Four-Bag-Irrigation Set, B. Braun	Fluid/blood leak; material puncture/hole	1	Defective chamber tubing; adapter not fitting	No clinical signs, symptoms or conditions	1	N/A
Non-Baxter Similar Device#3							
10.	LTXFR CystoscopY Irr, ICU Medica	Particulates	1	Contamination	No patient involvement	0	N/A
Non-Baxter Similar Device#4							
11.	T-U-R Y-SET, Nonvented, 96 Inch, ICU Medica	Device contamination with chemical or other material	1	Contamination	No clinical signs, symptoms or conditions	0	N/A

11.3.2.6 FDA Recall Database

The FDA posts consumer information about the most serious medical device recalls in the medical and radiation emitting device recalls database. Products are on the list because there is a reasonable chance that they could cause serious health problems or death. The database contains a list of classified medical device recalls since 01-November-2002.

This search led to no reports.

11.3.3 Conclusion from Analysis of Internal and External Market Experience Data included in the CER

This subsection provides an overall conclusion of the analysis of all market experience data in each device category.

11.3.3.1 Summary and Conclusion of Market Experience Data Related to the DUE and MDD Legacy Devices

During the current DCP [01-SEP-2019 to 31-AUG-2024]:

- There have been 5,001,478 units of Irrigation Sets sold globally (**Section 11.3.1.1**)
- The CIPM was 677.8 (**Section 11.3.1.5.1**)
- The top three Medical Device Problems reported for the Irrigation Sets are (**Section 11.3.1.5.2**):
  (1) Damaged set - collapsed or kinked (226)
  (2) Leaks – separated (30)
  (3) No flow (10)
- In total, 38 malfunctions, no serious injuries or deaths were reported for the Irrigation Sets (**Section 11.3.1.5.3**)
- No use errors were reported for the Irrigation Sets (**Section 11.3.1.5.4**)
- Two customer feedback were received for the Irrigation Sets (**Section 11.3.1.5.5**)
- Three trend triggers with an NCR/SNCR investigation occurred for the Irrigation Sets, of those three trend triggers, none required action (**Section 11.3.1.5.6.1**)
- A Periodic Risk Review was performed for the Irrigation Sets; actions on the risk documents are required following the periodic risk review, as listed in the document. [BXU601656] (**Section 11.3.1.5.6.2**)
- An Event Based Risk Review was performed for the Irrigation Sets; there are no new risks, the risks remain acceptable, and the benefits of the product outweigh the risk (**Section 11.3.1.5.6.3**)
- The Irrigation Sets do not require a Reliability Monitoring Field Report (**Section 11.3.1.5.6.4**)
- No signals for the Irrigation Sets were initiated via the Device Safety Signal Management (**Section 11.3.1.5.6.5**)
- There were no Manufacturer Trend Reports submitted for the Irrigation Sets (**Section 11.3.1.5.6.6**)
- Two FSCA (FA-2021-027, FA-2021-030) were closed for the Irrigation Sets (**Section 11.3.1.5.7**)
- Three NCRs with resulting CAPAs were closed and no SCARs were initiated or are still open for the Irrigation Sets (**Section 11.3.1.5.8**)
- A NPS Survey was conducted for the Irrigation Sets; however, no responses were found linked to the product quality of the Irrigation Sets (**Section 11.3.1.6**)

In summary, no new risks related to the Irrigation Sets were identified. It is confirmed that there are no unacceptable risks and all risks are reduced as far as possible when considering state-of-the-art technology.

Based on the evaluation of data collected, it was concluded that there is no need to update the product risk analysis process or PMS plan. Adequate PMS systems and product risk management activities have been implemented by the manufacturer to monitor the safety and performance of the Irrigation sets on an ongoing basis.

11.3.3.2 Summary and Conclusions of Market Experience Data Related to Non-Baxter Similar Devices

For the current DCP, the analysis of the external vigilance & recall databases for the identified similar devices identified 11 reports or recalls relevant to the DUE. The search results for each of the external databases are summarized in the relevant subsections above.

From 01-SEP-2019 to 31-AUG-2024 the analysis of the external vigilance/recall databases MHRA, Swissmedic, BfArM, and FDA Recall for the identified devices led to no reports. However, the analysis of FDA MAUDE considered 15 reports for the non-Baxter similar devices. Of these reports, 11 were considered relevant to the DUE. Those reports were found to be relevant as input for the usability and risk management. The results are summarized in **Section 11.3.2.5**.

For the current DCPs identified device problem descriptions within the MAUDE database were the following:

- Detachment of device or device component; free or unrestricted flow (3)
- Free or unrestricted flow (2)
- Improper flow or infusion (2)
- Break; contamination /decontamination problem (1)
- Device contamination with chemical or other material (1)
- Fluid/blood leak; material puncture/hole (1)
- Particulates (1)

For the current DCPs identified relevant hazards/harm within the MAUDE database were the following:

- Defective roller clamp (4)
- Contamination (3)
- Defective chamber tubing; adapter not fitting (1)
- Bubbles (1)
- Defective clamp (1)
- Leakage from the urology housing assembly (1)

The analysis of the market experience data did not identify any new risks that have not yet been discussed within the risk management process (see **Section 8**). The analysis of the market experience data supports the safety and clinical performance of the devices under evaluation.

12 SUMMARY AND CONCLUSION OF PERTINENT DATA FOR ALL DCPS

This section includes a summary of the scientific literature, supplemental internet literature and other pertinent data (e.g., non-clinical data, clinical data, and market experience data) for the current DCP.

The **Table 23-2** and the LSR in **APPENDIX B** provide a summary of the included and excluded scientific literature for all search categories (SotA-Clinical Landscape, SotA-Similar (Benchmark) Devices, and DUE) and supplemental internet literature searches (manual and grey literature) from the current DCPs.

The summary of the pertinent data in this section includes an objective analysis of potential flaws, limitations,

risks of bias, transferability of the results, and remaining uncertainties etc. for the data sets. This section includes both favorable and unfavorable data in order to objectively analyze and demonstrate the safety and clinical performance of the device.

12.1 Key Safety Findings from the Pertinent Data

The Access Validation Study [63129FR] (**Section 11.1.3.2**) was executed to perform the simulated use test to validate Irrigation Sets along with other access product families to ensure that the devices have mitigated potential use errors and abnormal use, identified in the risk document. All the 15 participants completed 100% of all the tasks in the scenario and met the acceptance criteria of the study. The study demonstrated Irrigation Sets could safely be used for their intended uses in the intended use environments. All use errors observed during this validation study were analyzed against risks. A sound rationale was documented for each task failure as to why safety was or was not impacted. New issues discovered during the study that impacted safety were reviewed by the core team and the respective risk files were updated.

Biocompatibility testing has been performed on code EMC4015N as the worse-case representative code based on containing the most diversity of materials of construction covering all materials within the impacted codes, same manufacturing process, and sterilization in accordance with ISO 10993 Part 1: Biological Evaluation of Medical Device. Testing was performed on the finished device post ethylene oxide sterilization to meet a dual ISO 10993-1 category of surface device, mucosal membrane prolonged contact duration and external communicating device, tissue/bone/dentin for a limited contact duration. The devices were found to be biocompatible for their intended use (**Section 11.1.1**).

Furthermore, a non-clinical study [12] detailed that gravity irrigation is known to be the safest method of irrigation in open fracture management.

Clinical publications on intermittent/continuous irrigation usually do not focus on details of the irrigation sets used. Therefore, the clinical data included are more related to the irrigation procedure itself than to any type of irrigation device. As a result, the data obtained on the procedure cannot be used directly as any kind of clinical evidence for the Irrigation Sets. However, the information is included below as it is considered to provide supportive and indirect input to the clinical evaluation of the DUE. One study [3] reported that CBI has been shown to be safe in patients with low to intermediate risk NMIBC.

12.2 Key Clinical Performance Findings from the Pertinent Data

The Access Validation Study [63129FR] (**Section 11.1.3.2**) was executed to perform the simulated use test to validate Irrigation Sets along with other access product families to ensure that the final products conform to the user needs and the intended uses. All the 15 participants completed 100% of all the tasks in the scenario and met the acceptance criteria of the study. The study demonstrated Irrigation Sets could effectively be used for their intended uses in the intended use environments. Overall, all user needs and intended uses were successfully validated and no additional tests were required.

Since Irrigation Sets are subjected to pressures for a period of time, they are designed to meet certain requirements ensuring that no leaks are present during the stipulated period. Irrigation Sets are designed to

meet certain requirements whereby they can withstand a tensile force for a period of time ensuring that junctions can withstand certain loads and will not separate under the conditions stipulated. The design of Irrigation sets is optimized to reduce the likelihood of the presence of particulate matter. Functionality of the Irrigation Sets is verified to ensure that the set and its constituents serve their purpose well. The components of the Irrigation Sets are verified to requirements (**Section 11.1.3.1**).

Furthermore, a non-clinical study [12] compared three different apparatuses with varying quantities of irrigation fluid to assess efficiency of administration and evaluate overall time for fluid administration. The authors concluded that gravity irrigation is known to be the most efficient method of irrigation in open fracture management. However, the study demonstrates the use of nonconducting suction tubing as an alternative to cystoscopy tubing for irrigation and debridement procedures can be beneficial.

Clinical publications on intermittent/continuous irrigation usually do not focus on details of the irrigation sets used. Therefore, the clinical data included are more related to the irrigation procedure itself than to any type of irrigation device. As a result, the data obtained on the procedure cannot be used directly as any kind of clinical evidence for the Irrigation Sets. However, the information is included below as it is considered to provide supportive and indirect input to the clinical evaluation of the DUE.

12.3 Key Finding Regarding Indirect Benefits from the Pertinent Data

The indirect benefits and technical outcome parameters based on SotA for the Irrigation Sets are listed in **Section 5.12**. The Irrigation Sets have demonstrated to meet technical outcome parameters, see **Table 5-2** for details.

12.4 Key Findings Regarding Usability from the Pertinent Data

The analysis of the literature did not result in any usability aspects regarding the use of the Irrigation Sets. However, two publications reported on the general usability of CBI:

- CBI has a relative ease of administration (compared to intravesical chemotherapy).[1]
- CBI has the advantages of easy management, low toxicity and cost saving.[4]

Furthermore, the literature did not reveal a product issue or design failure impacting usability.

All use errors observed during the Access Validation Study [63129FR] (**Section 11.1.3.2**) were analyzed against risks. A sound rationale was documented for each task failure as to why safety was or was not impacted. New issues discovered during the study that impacted safety were reviewed by the core team and the respective risk files were updated.

13 SUMMARY OF DATA SUPPORTING SAFETY AND CLINICAL PERFORMANCE OBJECTIVES AND ACCEPTANCE CRITERIA

The safety and clinical performance objectives and acceptance criteria specific to the DUE are provided in **Table 13-1**. In addition, data from the review of literature, pre- and post-market non-clinical and clinical studies, and

post-market surveillance for the MDD legacy devices, are provided as evidence to demonstrate that the DUE meets or exceeds the acceptance criteria.

Table 13-1: Data Supporting Safety and Clinical Performance Objectives and Acceptance Criteria for Irrigation Sets

Device or Component	Safety or Clinical Performance Objectives (Indicative List)	Acceptance Criteria (Specification of Parameters)	Reference Citations Used to Demonstrate Whether the DUE Meets or Exceeds the AC	Conclusion
Safety Objectives				
All except RMC4916	The Irrigation Sets shall be designed to allow the detection of air bubbles in the set.	The fluid path components and tubing on the Irrigation Sets shall be sufficiently translucent to allow the visualization of air bubbles in the set. The drip chamber shall facilitate the priming procedure.	Reference #1: Simulation of Use Test (**Section 11.1.3.1**) Summary: The purpose of this test was to verify that the set and set components exhibit the expected functionality and maintain physical integrity during use while inspecting the set for any leaks, junction disconnections and damaged components. A minimum of 298 samples per code to be tested. Requirement: The drip chamber shall facilitate the priming procedure Result: passed ☒ Existing Reference ☐ New Reference from current DCP	The data on the Irrigation Sets complies with the requirements of the acceptance criterion and thereby the Irrigation Sets fulfill the clinical safety objective.
Clinical Performance Objectives				
All except RMC4916	The Irrigation Sets shall be designed to meet the intended irrigation flow rate requirements.	The Irrigation Sets shall be compliant to a flow rate of ≥200 ml/min.	Reference #1: Flow Rate Test (**Section 11.1.3.1**) Summary: This test was performed to determine the volume of water that flows through the irrigation set at a determined height for a specific period of time. Such a test shows conformance to ISO 16391 (2002)5. A minimum of 30 samples per code are to be tested. Requirement: The set shall allow a flow rate of at least 200 mL water in 1 min	The data on the Irrigation Sets complies with the requirements of the acceptance criterion and

			under a static head of 0.6m. Result: passed ☒ Existing Reference ☐ New Reference from current DCP	thereby the Irrigation Sets fulfill the performance objective.
			Reference #2: Hyland et al. (2023)[12] (**Section 11.1.4**) Summary: Hyland et al. (2023) to compare three different apparatuses with varying quantities of irrigation fluid to assess efficiency of administration and evaluate overall time for fluid administration. Cystoscopy tubing with standard 4.95mm internal diameter and 2.1m length in both single lumen and Y-type TUR/bladder irrigation double lumen (Baxter International) was used. The third delivery method consisted of 6.0mm internal diameter and standard 3.7m length, nonconductive suction tubing (Cardinal Health). Irrigation times were assessed for varying volumes of 3, 6, and 9L to investigate the relationship between bag changes and irrigation time. The flow rates of the single-lumen cystoscopy tubing were 1284.43ml/min (3L), 1259.49ml/min (6L) and 1267.19ml/min (9L). The flow rates of the double-lumen cystoscopy were 1368.09ml/min (3L), 1380.05ml/min (6L) and 1337.56ml/min (9L). ☐ Existing Reference ☒ New Reference from current DCP	

14 OFF-LABEL USE IDENTIFIED DURING THE CLINICAL EVALUATION

The reviews of scientific literature, grey literature and PMS data did not identify any systematic misuse or off-label use of the DUE.

15 CONSISTENCY ACROSS THE CLINICAL EVALUATION DATA, RISK MANAGEMENT DOCUMENTS, AND IFU

Table 15-1 provides an assessment of the consistency between the clinical data (e.g., clinical investigations, scientific literature) and external vigilance & recall database data obtained during the clinical evaluation with the IFU and risk management documentation for the DUE. Relevant hazards and harms have been identified and analyzed appropriately. Any hazards or harms identified from internal market experience data (internal complaints) are not included in **Table 15-1** as they have been considered and processed by Baxter's PMS system.

Table 15-1: Comparison of Hazards/Harms Identified During the Clinical Evaluation vs. Hazards/Harms Listed in the IFU and Risk Management Documents

Hazard/Harm Relevant to the DUE Identified During the Clinical Evaluation	DUE Name	Hazard or Harm?	Hazard/Harm Is Already Addressed in the Risk Management Documents? (Yes/No)	Hazard/Harm Is Already Addressed in the IFU? (Yes/No)	Outcome/Conclusion
Hazards or Harms Identified from Literature					
Not applicable since the analysis of literature in this DCP considered no publications relevant to the DUE. Any hazard/harm detailed in the included publications was found to be related more to the procedure than to the devices (irrigation sets) used.					
Hazards or Harms Identified from External Vigilance & Recall Database Reports					
Bubbles	Irrigation Set, B. Braun	Hazard	Yes (Air in system)	Yes Do not allow air to be trapped in set.	No action required as this hazard has already been addressed in the risk file and IFU.
Leakage from the urology housing assembly	Irrigation Set, B. Braun	Hazard	Yes (Delay in therapy)	No	No action required as this hazard has already been addressed in the risk file.
Defective (roller) clamp	Irrigation Set, B. Braun	Hazard	Yes (Delay in therapy)	Yes Do not use if package has been opened or damaged or if tip protectors are loose or missing.	No action required as this hazard has already been addressed in the risk file and IFU.

Contamination	Irrigation Set, B. Braun LTXFR CystoscopY Irr, ICU Medica T-U-R Y-SET, Nonvented, 96 Inch, ICU Medica	Hazard	Yes (Particulate matter)	No	No action required as this hazard has already been addressed in the risk file.
Defective chamber tubing	Four-Bag-Irrigation Set, B. Braun	Hazard	Yes (Delay in therapy)	Yes Do not use if package has been opened or damaged or if tip protectors are loose or missing.	No action required as this hazard has already been addressed in the risk file and IFU.
Adapter not fitting	Four-Bag-Irrigation Set, B. Braun	Hazard	Yes (Incorrect product)	No	No action required as this hazard has already been addressed in the risk file and IFU.

16 COMPLIANCE WITH GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

Table 16-1 provides all General Safety and Performance Requirements (GSPRs) that were used in the development of Irrigation Sets which require support from the Clinical Evaluation. In addition, **Table 16-1** provides a summary of the evidence supporting compliance with these requirements.

Table 16-1: Compliance with General Safety and Performance Requirements

GSPR	General Safety and Performance Requirement	Evidence
GSPR 1	Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.	Clinical data are needed to support the intended use, safety, and performance and to state how the analysis is conducted to weigh the risk-benefit profile. However, since the demonstration of conformity with GSPRs based on clinical data is not deemed appropriate for the DUE, any additional available non-clinical data (e.g., from non-clinical publications, bench tests or testing with regard to common specifications and harmonized standards) are presented and discussed in detail to justify the performance and safety of the device. A detailed justification for this approach is provided in the CEP [BXU601670_MDR_CEP]. To verify the requirement, the indirect benefits and risks were assessed from the currently available clinical experience data, and the acceptability of the risk-benefit ratio was verified with respect to the SOTA (see **Sections 9.5** and **9.6**). The assessment of the risk control measures, and their applicability was conducted to ensure that the risks are reduced as far as possible. To verify this requirement, the identified risks during the clinical evaluation were properly analyzed in the risk management documents and, if any new risks were identified, appropriate risk management measures were considered. This also ensured that any residual risks according to risk management documents are listed in the labeling documents. No new risks/increased incidence of risks relevant to the Irrigation Sets were identified in the literature data of similar devices (see **Section 9.5**), literature data for the DUE (see **Sections 11.2.6.3** and **15**), and in the PMS data (see **Section 11.3**). All the risks listed have been appropriately addressed either in the IFU or in the risk files.

Table 16-1: Compliance with General Safety and Performance Requirements

GSPR	General Safety and Performance Requirement	Evidence
		The device description and labeling information in **Sections 4.2** and **5** provide a thorough synopsis of the device's intended performance, mechanism of action/principles of operation, and guidance for use of the Irrigation Sets. Biocompatibility studies concluded that the Irrigation Sets were biocompatible in accordance with ISO 10993 (see **Section 11.1.1**). Design verification and validation tests were performed in accordance with defined protocols and procedures (see **Section 11.1.3.1**). All bench tests, including biocompatibility studies, shelf-life studies, and verification and validation tests, met their design and manufacturing requirements (see **Section 11.1**). The risk mitigation measures are effective, and all risks are reduced as far as possible when considering the state-of-the-art technology and current practices.
GSPR 2	The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.	The IFU contains correct information to reduce the risk of use error, information on residual risks and their management, as supported by sufficient pertinent evidence (see **Section 5**). This includes handling instructions, description of risks, warnings, precautions, contraindications, and instructions for managing foreseeable unwanted situations.
GSPR 3e	Evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability.	The PMS system is in place to continuously monitor the safety and performance of the product during the post commercialization phase of the product's life cycle. The evaluation of PMS activities after product MDD CE marking and market introduction (MDD legacy devices) conclude that there were no new risks or trends observed, and this supports the safety and performance of Irrigation Sets devices (see **Sections 11.3.3.1** and **15**).

Table 16-1: Compliance with General Safety and Performance Requirements

GSPR	General Safety and Performance Requirement	Evidence
GSPR 8	All known and foreseeable risks, and any undesirable side-effects, shall be minimized and be acceptable when weighed against the evaluated benefits to the patient and/or user arising from the achieved performance of the device during normal conditions of use.	Clinical data are needed to support the intended use, safety, and performance and to state how the analysis is conducted to weigh the risk-benefit profile. However, since the demonstration of conformity with GSPRs based on clinical data is not deemed appropriate for the DUE, any additional available non-clinical data (e.g., from non-clinical publications, bench tests or testing with regard to common specifications and harmonized standards) are presented and discussed in detail to justify the performance and safety of the device. A detailed justification for this approach is provided in the CEP [BXU601670_MDR_CEP]. The data was analyzed and evaluated in relation to the device's safety and performance objectives as well as acceptance criteria (see **Section 13**) under consideration of the current state of the art of the device category (see **Sections 9.5** and **9.6**). By this, the performance of the device was evaluated and confirmed throughout the expected lifetime of the DUE. No new risks were identified. The safety was confirmed throughout the expected lifetime of the DUE. All risks identified within the literature research (see **Section 12.1**) are included within the risk management system of the device (see **Sections 8** and **15**). In addition, the pre-clinical data demonstrates the biological safety and biocompatibility of the DUE (see **Section 11.1.1**). In short, the DUE is a safe and reliable system. The evaluation of internal and external experience databases did not reveal any additional risks which are not covered within the risk management (see **Section 15**). The analysis of the market experience data of the MDD legacy devices supports the safety and clinical performance of the devices under evaluation (see **Section 11.3.3.1**).

17 PMCF PLAN AND JUSTIFICATION

Post-Market Clinical Follow-Up (PMCF) will be conducted with the aim of confirming the safety and clinical performance of the DUE. The following general PMCF activities will be conducted: review of scientific & supplemental internet literature, and review of clinical trial registries, a summary of complaint data including CAPAs, FSCAs, etc. Additional general PMCF activities may need to be included in the PMCFP based on the device type or general information needed (clinical use data, etc.), such as: Clinical experience gained, feedback from users (e.g., focus groups, HCP questionnaires, simple field surveys). No specific PMCF studies are planned as the device under evaluation is well-established with sufficient non-clinical and technical data to support safety and performance when the device is used as intended. Furthermore, there are no unanswered questions about the device´s safety and performance. Additionally, no new risks were identified during the clinical evaluation.

The detailed methodologies that will be used to collect this additional clinical data will be outlined in the PMCFP which will be developed at the conclusion of this clinical evaluation. The PMCF Plan (PMCFP) will outline the methods and procedures for conducting the planned PMCF activities along with their scheduled frequency. The findings of the PMCF shall be analyzed by the product team and documented in a PMCF evaluation report (PMCFER).

18 CONCLUSIONS

In summary, the clinical evaluation confirms that:

- The Irrigation Sets demonstrate non-clinical evidence for the conformity with relevant aspects of the GSPRs 1, 2, 3e, and 8 (**Section 16**),
- The intended safety & clinical performance objectives and acceptance criteria have been achieved during intended use (**Section 13**),
- Product information and product labeling reflect available evidence and has been verified and validated accordingly (**Section 5**),
- The Irrigation Sets are adequate for the intended purpose,
- The Irrigation Sets comply with the current knowledge/ state-of-the-art technology (**Section 9**),
- The Irrigation Sets are suitable for the intended users and the usability aspects, and indirect clinical benefits for the patient are achieved and the benefit from the use of the device outweighs possible adverse effects and risks.
- Verification testing and Human Factors summative testing demonstrate that the intended performance is achieved under normal conditions of use (**Section 11.1.3**)

Identified, reviewed, assessed and analyzed clinical data (**Section 11.2**) were evaluated and are considered sufficient to provide evidence of conformity of the Irrigation Sets with the MDR.

The long-term safety of the Irrigation Sets is considered fully established, because the market experience with the product spans over 40 years and more than 5,001,478 units of the DUE have been sold worldwide in the current DCP (**Section 11.3.1.1**). The date of the first MDD CE mark for Irrigation Sets can be found detailed per

code in **Table 4-2**, the current MDD CE mark was acquired on 18-NOV-2019. During the current data collection period [01-SEP-2019 to 31-AUG-2024], the total global complaint incidents per million (CIPM) were 677.8 for the DUE. Regarding serious complaint incidents, there were no reported deaths or serious injuries. In total, 38 malfunctions have been reported in the current DCP (**Section 11.3.1.5.3**). No unknown side effects, emergent risks or possible systematic mis-use or off-label use of the device was identified. No case of use error was reported in post-market surveillance data (**Section 11.3.1.5.4**).

Moreover, results from current state of the art, benchmark devices and medical alternatives, revealed that the performance of the device under evaluation poses no unacceptable or undesirable side effects. Furthermore, the overall residual design risks, manufacturing risks and the benefit/risk ratio of the devices when used according to the manufacturer's instructions for use are fully acceptable (**Section 9**).

No new risk was identified from the literature and market experience data for the current assessment period (**Section 15**). Review of the risk documents, applicable for the products in scope for this CER indicate that the known and foreseeable risks associated with the use of the devices are minimized and acceptable when weighed against the benefits to the patient. Therefore, the overall risk-benefit analysis for the products in scope for this CER is considered acceptable. It is confirmed that there are no unacceptable risks, and all risks are reduced as far as possible when considering state of the art technology and practice existing at the time of the design. Moreover, the risk management plan and risk management processes are in place to identify any new risks.

The safety, clinical performance, and indirect benefit of the Irrigation Sets were demonstrated with this clinical evaluation. This clinical evaluation report demonstrates that the Irrigation Sets comply with the relevant GSPRs 1, 2, 3e, and 8 (ANNEX I, Regulation (EU) 2017/745) under normal conditions of the intended use of the device (**Section 16**).

The clinical and non-clinical data support that benefits and risks are acceptable for all medical conditions and target populations covered by the intended use of the Irrigation Sets when compared with the current state of the art in the corresponding medical field.

The result of this clinical evaluation clearly indicates that the benefits of Irrigation Sets outweigh any identified risks.

19 TIMEFRAME FREQUENCY FOR NEXT CLINICAL EVALUATION

Based on the positive results of this critical CER and the risk classification as class Is, a timeline of 5 years is deemed adequate for the next scheduled update of the CER.

This frequency of updates is justified considering the facts that:

- The device is well-established with sufficient non-clinical data to support safety & clinical performance when the device is used as intended.
- There are no unanswered questions about the device's safety & performance.
- No new risks have been identified.

- The design and technology of the device, the materials used, the principle of operation, and the medical indications treated with the devices are not novel.
- No significant changes to the devices or their intended use have occurred since the product launch.
- No unanticipated failure modes were reported from literature or PMS activities.
- No new risks or increased incidence of risks, or any unacceptable residual risk for the patient have been identified from the results of PMS activities and the published literature.
- The devices do not incorporate any novel technology.
- The complexity of the device is low.

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21 RELATED DOCUMENTS

21.1 External References

Table 21-1 lists the applicable guidance and regulations that were followed for this clinical evaluation.

Table 21-1: External References

Series No.	Document ID and Revision/Date	Document Name
1.	MEDDEV 2.12/1	European Commission (EC) Guidelines on a Medical Device Vigilance System
2.	MEDDEV 2.7/1	Guidelines on Medical Device: Clinical Evaluation
3.	Regulation (EU) 2017/745	European Medical Device Regulations (MDR)
4.	MDCG 2020-13	Clinical evaluation assessment report template
5.	MDCG 2020-6	Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC. A guide for manufacturers and notified bodies
6.	MDCG 2020-7	Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies
7.	MDCG 2021-24	Guidance on classification of medical devices
8.	MDCG 2020-3	Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD
9.	MDCG 2022-4	Guidance on appropriate surveillance regarding the transitional provisions under Article 120 of the MDR with regard to devices covered by certificates according to the MDD or the AIMDD

21.2 Internal QMS References

Table 21-2: Internal QMS References

Series No.	Document ID	Document Name
1.	Glossary	Baxter's Glossary
2.	GQR-10	Product Risk Management
3.	GQP-04-01	Archiving Records
4.	GQP-09-13	Baxter Corporate Ad Prom Process
5.	GQP-09-22	Process for Managing Product Files and Records
6.	GQP-09-31	Medical Device Clinical Evaluations for the EU
7.	GQP-09-35	Post-Market Surveillance System and Lifecycle Management
8.	GQP-05-16	Post-Market Surveillance System – Reviews of Literature, External Vigilance and Recall Databases, and Clinical Trial Registries
9.	GQP-10-05	Risk Management Review
10.	GQT-05-16-01	Literature and Clinical Trial Registry Search Strategy and Results for <Device/Family Name> <CER or PMCFER>
11.	GQT-05-16-02	External Vigilance and Recalls Database Searches_US for <Device/Family Name> <CER>
12.	GQT-05-16-03	External Vigilance and Recalls Database Searches_OUS for <Device/Family Name> <CER>
13.	GQT-05-16-04	SEARCH REQUEST (SRT) FOR <DEVICE/FAMILY NAME> <CER or PMCFER>
14.	GQT-05-16-07	Literature Search Protocol (LSP)
15.	GQT-05-16-08	Literature Search Report (LSR)
16.	GQT-05-16-09	Complaint Identification Form (CIF)
17.	GQT-09-31-02	Clinical Evaluation Plan (CEP) for <Device/Family Name>
18.	GQT-09-31-01	Clinical Evaluation Report (CER) for <Device/Family Name>
19.	GG-09-46	Global Guidance for EU Medical Device Clinical Evaluation Plans (CEP)

21.3 Irrigation Sets References

Table 21-3: Irrigation Sets References

Series No.	Document ID	Document Name
1.	81548-DHF-ERD	DHF number
2.	07-19-00-4283	Label 7400009A
3.	07-19-00-4284	Label 7401010A
4.	07-19-00-4768	Label E5MC4002
5.	07-19-00-4769, 07-19-00-4304	Label E5MC4007N
6.	07-19-00-4773, 07-19-00-3744	Label EMC4015N
7.	07-19-00-7245, 07-19-00-3743	Label EMC4042
8.	07-19-00-4775, 07-19-00-3746	Label EMC4047
9.	07-19-00-5643, 07-19-00-3745	Label EMC4055N
10.	07-36-00-4780, 07-36-00-4306	Label RMC4916 (see Appendix H)
11.	07-19-00-5644, 07-19-00-4307	Label VMC4005 (see Appendix I)
12.	1248528_CER	Medical Device Clinical Evaluation Report (CER) for Irrigation Sets [MDD]
13.	BXU601670_MDR_CEP	Clinical Evaluation Plan (CEP) for Irrigation Sets [MDR]
14.	BXU574574	Design Input - Requirements for Access Products in scope of Medication Delivery EU MDR Compliance Change Controls
15.	BXU600002	Irrigation Sets Risk Assessment Control Table (RACT)
16.	1277312	Risk Management Report (RMR) for Irrigation Sets
17.	1277308	Clinical Risk Benefit Analysis (RBA) Irrigation Sets
18.	BXU586239	Biological Evaluation Report for Irrigation Sets
19.	Toxikon-19-03002-G1	Cytotoxicity – L929 Elution

Table 21-3: Irrigation Sets References

Series No.	Document ID	Document Name
20.	Toxikon-19-03002-G2	Sensitization – Maximization
21.	Toxikon-19-03002-G3	Irritation / Intracutaneous – Reactivity
22.	Toxikon-19-03002-G4	Acute / Systemic Toxicity
23.	Toxikon-19-03002-G5	Material Mediated Pyrogen Test
24.	BXU542284	Irrigation Sets Traceability Matrix Design Inputs Requirements to Verification
25.	1269720	Stability Testing Tracker
26.	63129FR	Access Validation Study
27.	BXU578606	Irrigation Sets (Malta Access Codes) Human Factors/Usability Engineering Evaluation Report
28.	BXU542980	Design Validation of the Malta Design Owned Access Codes: Irrigation Sets
29.	1248528PMSP	Post Market Surveillance Plan for Irrigation Sets
30.	BXU600027	Product Trending Table (PTT) for Irrigation Sets for Malta
31.	BXU600026	Product Trending Table (PTT) for Irrigation Sets for Tunisia
32.	BXU601656	Periodic Risk Review Irrigation Sets 2024

22 ABBREVIATIONS AND DEFINITIONS

The terms and definitions below have been primarily obtained from the Baxter Glossary; additional terms/definitions have been added, as needed.

Abbreviation/Acronym	Definition or Description
Accessory	An article which, whilst not being itself a medical device, is intended by its manufacturer to be used together with one or several particular medical device(s) to specifically enable the medical device(s) to be used in accordance with its/their intended purpose(s) or to specifically and directly assist the medical functionality of the medical device(s) in terms of its/their intended purpose(s). [Regulation (EU) 2017/745, Article 2(2)]
Active Device	Any device, the operation of which depends on a source of energy other than that generated by the human body for that purpose, or by gravity, and which acts by changing the density of or converting that energy. Devices intended to transmit energy, substances or other elements between an active device and the patient, without any significant change, shall not be deemed to be active devices. Software shall also be deemed to be an active device. [Regulation (EU) 2017/745, Article 2(4)]
AE	**Adverse Event (for Medical Devices)** Any untoward medical occurrence, unintended disease, injury, or clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the medical device.
Basic UDI-DI	**The Basic Unique Device Identification-Device Identifier** The Basic UDI-DI is the main access key for device-related information in the EUDAMED database and it is referenced in relevant documentation [e.g., certificates (including certificate of free sale), EU declaration of conformity, technical documentation, and summary of safety and (clinical) performance)]. It is intended to identify and connect devices with the same intended purpose, risk class and essential design and manufacturing characteristics.
Benefit-Risk Determination	The analysis of all assessments of benefit and risk of possible relevance for the use of the device for the intended purpose, when used in accordance with the intended purpose given by the manufacturer.
BER	**Biocompatibility Evaluation Report**
BfArM	**Bundesinstitut für Arzneimittel und Medizinprodukte** (Federal Institute for Drugs and Medical Devices)
BPH	**Benign Prostatic Hyperplasia**

Abbreviation/Acronym	Definition or Description
CAPA	**Corrective Action and Preventive Action** Corrective action: action taken to eliminate the causes of a detected non-conformity, defect, or other undesirable situation in order to prevent recurrence. Preventive action: action taken to eliminate the cause(s) of a potential nonconformity, defect, or other undesirable situation in order to prevent occurrence
CBI	**Continuous Bladder Irrigation**
CDP	**Clinical Strategy and Development Plan** A document that indicates progression from exploratory investigations, such as first-in-man studies, feasibility, and pilot studies, to confirmatory investigations, such as pivotal clinical investigations, and a Post Market Clinical Follow-up with an indication of milestones and a description of potential acceptance criteria.
CE	**Conformité Européenne** (European Conformity)
CE Marking or CE Marking of Conformity	A marking by which a manufacturer indicates that a device is in conformity with the applicable requirements set out in the Medical Devices Directive 93/42/EEC or Medical Device Regulation EU 2017/745 and other applicable Union harmonization legislation providing for its affixing.
CEP	**Clinical Evaluation Plan** A document that provides a systematic plan to continuously generate, collect, analyze, and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer.
CER	**Clinical Evaluation Report** A report summarizing the results and the clinical evidence derived from the Clinical Evaluation outlined in the Clinical Evaluation Plan (CEP).
CI	**Complaint Incidents / Confidence Interval**
CIP or CSP	**Clinical Investigation Plan/ Clinical Study Protocol** A document that describes the rationale, objectives, design, methodology, monitoring, statistical considerations, organization, and conduct of a clinical investigation.
CIR or CSR	**Clinical Investigation Report** or **Clinical Study Report** Document describing the design, execution, statistical analysis, and results of a clinical investigation.
Clinical Benefit	The positive impact of a device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, or a positive impact on patient management or public health. [Regulation (EU) 2017/745, Article 2(53)]

Abbreviation/Acronym	Definition or Description
Clinical Claim	A statement made by a manufacturer related to the clinical safety and clinical performance of a medical device which leads to a claimed clinical benefit.
Clinical Data	Information concerning safety or performance that is generated from the use of a device [DUE] and is sourced from the following: • clinical investigation(s) of the device concerned [DUE], • clinical investigation(s) or other studies reported in scientific literature, of a device for which equivalence to the device in question [DUE] can be demonstrated, • reports published in peer reviewed scientific literature on other clinical experience of either the device in question [DUE] or a device for which equivalence to the device in question [DUE] can be demonstrated, • clinically relevant information coming from post-market surveillance, in particular the post-market clinical follow-up. [Regulation (EU) 2017/745, Article 2(48)]
Clinical Evaluation	A systematic and planned process to continuously generate, collect, analyze and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer. [Regulation (EU) 2017/745, Article 2(44)]
Clinical Evidence	Clinical data and clinical evaluation results pertaining to a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer. [Regulation (EU) 2017/745, Article 2(51)]
Clinical Investigation	Any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device. [Regulation (EU) 2017/745, Article 2(52)]
Clinical Performance	The ability of a device, resulting from any direct or indirect medical effects which stem from its technical or functional characteristics, including diagnostic characteristics, to achieve its intended purpose as claimed by the manufacturer, thereby leading to a clinical benefit for patients, when used as intended by the manufacturer. [Regulation (EU) 2017/745, Article 2(52)]
CMR	**Carcinogenic, Mutagenic, or Toxic to Reproduction**
Cochrane Library	Database for systematic reviews in health care
Cochrane Library	Database for systematic reviews in health care
Conformity Assessment	The process demonstrating whether the requirements of applicable regulation(s) relating to a device have been fulfilled.

Abbreviation/Acronym	Definition or Description
cRBA	**Clinical Risk-Benefit Analysis** A document written by Baxter Medical Affairs that considers the product-specific hazards, hazardous situations, and harms identified in the product's Risk Assessment and Control Table (RACT) or equivalent document and weighs the risks against the identified benefits.
CS	**Common Specifications** Common Specifications means a set of technical and/or clinical requirements, other than a standard, that provides a means of complying with the legal obligations applicable to a device, process or system. [Regulation (EU) 2017/745, Article 2(71)]
CV	**Curriculum Vitae**
DCP	**Data Collection Period** The start date and end date of the periodic data included in the scope of the clinical evaluation.
Death (relevant to complaints)	A Serious Incident that led to a Death, which is attributable to a Baxter Device.
DEHP	**Diethylhexyl Phthalate**
DHF	**Design History File** A compilation of records which describes the design history of a finished device
DMEM	**Dulbeccos Modified Eagle Medium**
DoC	**Declaration of Conformity** A document that declares the conformity to the essential requirements according to the Medical Device Directive or according to other Directives, (e.g., Low Voltage Directive, EMC Directive, R&TTE Directive)
DOE References	**Description of Evaluated References** Publications, etc. that are referenced in the clinical investigations (in the bibliography or reference section)
DOI	**Declaration of Interest** A statement or document that should be held by the manufacturer and signed/dated by the evaluator(s) covering relevant financial interests outside the current work as an evaluator.
DUE	**Device(s) Under Evaluation** This represents the subject device(s) that are being evaluated in the medical device reports.

Abbreviation/Acronym	Definition or Description
EDs	**Endocrine-Disrupting Substances**
EEA+TR+XI	**European Economic Area, Turkey, and Northern Ireland** The EEA links the EU member states and three European Free Trade Association (EFTA) states (Iceland, Liechtenstein, and Norway) into an internal market governed by the same basic rules. The Union Harmonisation Legislation applies to all Member states of the European Union (the Official Journal of the European Union (C247)), as well as the EFTA States (Iceland, Liechtenstein, and Norway). Pursuant to article 355(1), TFEU, the Union Harmonisation Legislation also applies to Guadeloupe, French Guiana, Martinique, Madeira, Mayotte, Réunion, and Saint Martin, the Azores, the Canary Islands Furthermore, the customs union agreements between countries and/or the European Union, make the Union Harmonisation Legislation also applicable in Andorra, Monaco, San Marino, and Turkey. The Protocol on Ireland / Northern Ireland provides that all Union Harmonisation Legislation also applies to and in the United Kingdom in respect of Northern Ireland.
EMDN	**European Medical Device Nomenclature** Codes which are used to reflect the design and intended purpose of EU UDI-DIs. All EU UDI-DIs (that are not a parent package) must have at least one EMDN code from the EU EMDN Codes page assigned. The EMDN system is hierarchical. It divides the medical devices into classes and assigns codes to these classes.
EMEA	**Europe, Middle East, and Africa**
EO	**Ethylene Oxide**
ERBT	***En Bloc* Resection of Bladder Tumor**
EU	**European Union**
EU MDR	**European Union Medical Device Regulation** Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

Abbreviation/Acronym	Definition or Description
Expected Lifetime (Medical Device)	The maximum time period specified by the manufacturer during which the medical device is expected to maintain safe and effective use. This is not synonymous with shelf life. It can be thought of as the time the device remains functional once in use, performing according to intended use. The lifetime of an active device may be determined by the period for which the manufacturer will support the devices by way of availability of spare parts, manuals, training, service/repairs, etc. The device lifetime may reflect a time-related deterioration in characteristics that are important to device safety and performance.
FDA	**U.S. Food and Drug Administration**
FSCA	**Field Safety Corrective Action** A corrective action taken by a manufacturer for technical or medical reasons to prevent or reduce the risk of a serious incident in relation to a device made available on the market.
FSN	**Field Safety Notice** A communication sent by a manufacturer to users or customers in relation to a field safety corrective action.
Generic Device Group	A set of devices having the same or similar intended purposes or a commonality of technology allowing them to be classified in a generic manner not reflecting specific characteristics. [Regulation (EU) 2017/745, Article 2(7)]
GITMO	**Italian Group for Bone Marrow Transplantation**
GMDN	**Global Medical Device Nomenclature** The GMDN is a comprehensive set of terms, within a structured category hierarchy, which name and group ALL medical device products including implantables, medical equipment, consumables, and diagnostic devices. The GMDN is used for: • Data exchange between manufacturers, regulators and healthcare authorities • Exchange of post-market vigilance information • Supporting inventory control in hospitals • Purchasing and supply chain management Information in the form of a 5-digit numeric GMDN Code is cross-referenced to a precisely defined Term Name and Definition
GreenLEP	**Greenlight Laser Enucleation of the Prostate**

Abbreviation/Acronym	Definition or Description
GSPR	**General Safety and Performance Requirements** A concept specific to European medical device legislation and one of the central concepts of European Medical Device (MDR) and In Vitro Medical Device (IVDR) Regulations. GSPRs provide broad, high-level criteria for safety and performance applicable to design, production, and postproduction aspects, throughout the lifecycle of all medical devices.
Hazard	Potential source of harm (e.g., physical injury or damage to the health of people, or damage to property or the environment.)
HC	**Hemorrhagic Cystitis**
HF	**Human Factors**
HoLEP	**Holmium Laser Enucleation of the Prostate**
HSCT	**Hematopoietic Stem Cell Transplantation**
IC	**Intravesical Chemotherapy**
IFU	**Instructions For Use** The information provided by the manufacturer to inform the user of a device's intended purpose and proper use and of any precautions to be taken.
IIR or IIS	**Investigator Initiated Research, or Investigator Initiated Study** A research study with the following characteristics: • Baxter is not acting as the sponsor for the purposes of the applications to Ethics Committees and Regulatory Authorities. The investigator is independent from Baxter control or undue influence. • The principal investigator or the hospital/institution is responsible for the development and execution of study protocol and procedures independent of Baxter influence. • Baxter is supporting an institution or investigator who is acting as study sponsor, by providing monetary support and/or a supply of the study materials provided free of charge to conduct the study. • An IIR study may be of interventional or non-interventional design.
IMC	**Information Management Center**
Indication, Indication for Use'	Refers to the clinical condition that is to be diagnosed, prevented, monitored, treated, alleviated, compensated for, replaced, modified or controlled by the medical device. It should be distinguished from 'intended purpose/intended use', which describes the effect of a device. All devices have an intended purpose/intended use, but not all devices have an indication (e.g., medical devices with an intended purpose of disinfection or sterilization of devices). [MDCG_2020-6]

Abbreviation/Acronym	Definition or Description
Intended Purpose	The use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use or in promotional or sales materials or statements and as specified by the manufacturer in the clinical evaluation.
Intended Use	Should be considered to have the same meaning as 'Intended Purpose'. [MDCG_2020-6]
IPSS	**International Prostate Symptom Score**
ISO	**International Organization for Standardization**
Legacy Devices (MDD/AIMDD)	This is considered to include all devices previously CE marked under the European Medical Devices Directive 93/42/EEC (MDD) or Active Implantable Medical Devices Directive 90/385/EEC (AIMDD). [MDCG_2020-6]
Level of Clinical Evidence	This terminology is used in the MDR with respect to requirements for demonstration of conformity with the relevant GSPR and overall benefit-risk14. It is understood to encompass the amount and quality of evidence (i.e., its characterization by quality, quantity, completeness and statistical validity, etc.) required to demonstrate safety, performance and the benefit-risk conclusion of a medical device. It should not be confused with the term 'levels of evidence'. [MDCG_2020-6]
Level of Evidence	As used in evidence-based medicine, it is used to rank study designs, and is only a part of the concept 'level of clinical evidence'. [MDCG_2020-6]
MA	Medical Affairs
Malfunction (relevant to complaints)	Serious Incident that did not lead to a Death or a Serious Injury, however, have the potential to lead to a Death or Serious Injury if to reoccur.
MAUDE	**Manufacturer and User facility Device Experience database**
MDCG	**Medical Device Coordination Group** Composed of representatives of all Member States and is chaired by a representative of the EU.
MDD	**Medical Device Directive** Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, OJ No L 169/1 of 1993-07-12 is intended to harmonize the laws relating to medical devices within the European Union
MDR	**Medical Device Regulation**: The new EU Medical Device regulation 2017/745 which becomes effective May 26, 2021. It replaces the Medical Device Directive (MDD) 2001/83/EC.

Abbreviation/Acronym	Definition or Description
MDSW	**Medical Device Software** Medical device software is software that is intended to be used, alone or in combination, for a purpose as specified in the definition of a "medical device" in the medical devices regulation or in vitro diagnostic medical devices regulation. [MDCG_2019-11]
MDV	**Medical Device Vigilance**
MEDDEV	**MEDical DEVices** The MEDDEV Guidance Documents are developed by various working groups on behalf of the European Commission to assist stakeholders in implementing directives related to medical devices. The MEDDEVs promote a common approach to be followed by manufacturers and notified bodies that are involved in conformity assessment procedures. Although the guidelines are not legally binding, it is expected that the guidelines be followed, ensuring the uniform application of relevant directive provisions.
Medical Device	Any instrument, apparatus, appliance, software, implant, reagent, material, or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes: • diagnosis, prevention, monitoring, prediction, prognosis, treatment, or alleviation of disease, • diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability, • investigation, replacement, or modification of the anatomy or of a physiological or pathological process or state, • providing information by means of in vitro examination of specimens derived from the human body, including organ, blood, and tissue donations, • and which does not achieve its principal intended action by pharmacological, immunological, or metabolic means, in or on the human body, but which may be assisted in its function by such means. The following products shall also be deemed to be medical devices: • devices for the control or support of conception; • products specifically intended for the cleaning, disinfection or sterilization of devices as referred to in Article 1(4) and of those referred to in the first paragraph of this point. [Regulation (EU) 2017/745, Article 2(1)]
MEDLINE	Medical Literature Analysis and Retrieval System Online; bibliographic database of life sciences and biomedical information compiled by the National Library of Medicine.
MHRA	**Medicines and Healthcare Products Regulatory Agency (Great Britain)**

Abbreviation/Acronym	Definition or Description
MMC	**Mitomycin**
N/A	**Not Applicable**
nDEHP	**non-Diethylhexyl Phthalate**
NMIBC	**Non-Muscle Invasive Bladder Cancer**
NPS	**Net Promoter Score**
OR	**Odds Ratio**
PDO	**Product Design Owner**
PFS	**Progression-Free Survival**
PMCF	**Post-Market Clinical Follow-Up** A continuous process that updates the clinical evaluation, if required. In this case the manufacturer proactively collects and evaluates clinical data from the use in or on humans of a device which bears the CE marking. [Regulation (EU) 2017/745, Annex XIV, Part B, Section 5]
PMCF Study	**Post-Market Clinical Follow-up Study** A study carried out following the CE marking of a device and intended to answer specific questions relating to clinical safety or performance (e.g., residual risks) of a device when used in accordance with its approved labelling.
PMCFER	**Post-Market Clinical Follow-up Evaluation Report** A document which summarizes the findings coming from the activities outlined in the manufacturer's PMCFP. The findings documented in the PMCFER shall become a part of the clinical evaluation report (CER) and the technical documentation. The conclusions of the PMCFER shall be taken into account to update eventually the clinical evaluation, the risk management documentation, the post market surveillance plan and the SSCP, if applicable.

Abbreviation/Acronym	Definition or Description
PMCFP	**Post-Market Clinical Follow-up Plan** A document that specifies the methods and procedures for proactively collecting and evaluating clinical data with the aim of: • confirming the safety and performance of the device throughout its expected lifetime; • identifying previously unknown side-effects and monitoring the identified side-effects and contraindications; • identifying and analyzing emergent risks on the basis of factual evidence; • ensuring the continued acceptability of the benefit-risk ratio; • identifying possible systematic misuse or off-label use of the device with a view to verifying that the intended purpose is correct
PMS	**Post-Market Surveillance** All activities carried out by manufacturers in cooperation with other economic operators to institute and keep up to date a systematic procedure to proactively collect and review experience gained from devices they place on the market, make available on the market, or put into service for the purpose of identifying any need to immediately apply any necessary corrective or preventive actions.
PP	**Pathfinder Plus**
PRMO	**Product Risk Management Owner**
PSM	**Propensity Score Matching**
PSUR	**Periodic Safety Update Report** A PSUR is intended to present the worldwide safety experience of a therapeutic product at defined times post-authorization in order to: • Report all new relevant safety information from appropriate sources; • Relate the data to patient exposure; • Summarize the market authorization status in different countries and any significant variations related to safety; • Periodically create the opportunity for an overall safety re-evaluation; • Indicate whether changes should be made to product information in order to optimize the use of the product A PSUR is required for class IIa, class IIb, and class III CE marked medical devices. The report provides a summary of the results and conclusions of the analysis of Post-Market Surveillance (PMS) data gathered as a result of the Post-Market Surveillance Plan (PMSP) together with a rationale and description of any preventive or corrective actions taken.

Abbreviation/Acronym	Definition or Description
PVP	**Photoselective Vaporization of the Prostate**
PVR	**Postvoid Residual** urine
QA	**Quality Assurance**
Qmax	Maximum urinary flow rate
QMS	**Quality Management System** A formalized business practices that define management responsibilities for organizational structure, processes, procedures, and resources needed to fulfill product/service requirements, customer satisfaction, and continual improvement.
QOL	**Quality Of Life**
RA	**Regulatory Affairs**
RACT	**Risk Assessment and Control Table**
RBA	**Risk Benefit Analysis**
RCT	**Randomized Controlled Trial**
RFS	**Recurrence-Free Survival**
Risk	The combination of the probability of occurrence of harm and the severity of that harm
Risk Management	Systematic application of management policies, procedures, and practices to the tasks of analyzing, evaluating, controlling, and monitoring risk
ROC	**Receiver Operating Characteristic**
S&P	**Safety and Performance**
SAE	**Serious Adverse Event**
SAP	**Single Action Pumping** System
SCAR	**Supplier Corrective Action Request**
Scientific Validity, Scientifically Valid	This terminology is used in the MDR in reference to clinical data planning, evaluation and conclusions. Clinical evaluations must follow a “defined and methodologically sound procedure”, for which expectations of scientific validity are implicit. Embedded in the term ‘scientific validity’ are concepts including adequacy of study design and controls for bias, appropriateness and relevance of research questions, adequacy of sample sizes and statistical analyses, completeness of data, adequacy of follow up period, and appropriateness of conclusions on the basis of objective evidence. Section 9.3.1 of MEDDEV 2.7/1 rev. 4 provides guidance for the evaluation of methodological quality and scientific validity under the MDD/AIMDD which are equally valid under the MDR which can be considered to apply when referencing ‘scientific validity’ in this guidance. [MDCG 2020_6]

Abbreviation/Acronym	Definition or Description
Serious Incident (relevant to complaints)	Any incident that directly or indirectly led, might have led or might lead to any of the following: 1) The death of a patient, user, or other person, 2) The temporary or permanent serious deterioration of a patient's, user's, or other person's state of health, 3) A serious public health threat.
Serious Injury (related to complaints)	A Serious Incident that led to a Serious Injury, which is attributable to a Baxter device.
Serious Public Health Threat (relevant to complaints)	An event which could result in imminent risk of death, serious deterioration in a person's state of health, or serious illness, that may require prompt remedial action, and that may cause significant morbidity or mortality in humans, or that is unusual or unexpected for the given place and time
Similar Device	Devices belonging to the same generic device group. The MDR defines this as a set of devices having the same or similar intended purposes or a commonality of technology allowing them to be classified in a generic manner not reflecting specific characteristics. [MDCG_2020-6]
Software	A set of instructions that processes input data and creates output data. [MDCG_2019-11]
Software driving or influencing the use of a device	Software which is intended to drive or influence the use of a (hardware) medical device and does not have or perform a medical purpose on its own, nor does it create information on its own for one or more of the medical purposes described in the definition of a medical device or an in vitro diagnostic medical device. This software can, but is not limited to: a) operate, modify the state of, or control the device either through an interface (e.g., software, hardware) or via the operator of this device b) or supply output related to the (hardware) functioning of that device Note: Software driving or influencing the use of a (hardware) medical device may be qualified as an accessory for a (hardware) medical device. [MDCG_2019-11]

Abbreviation/Acronym	Definition or Description
SotA	**State-of-the-Art** Developed stage of current technical capability and/or accepted clinical practice in regard to products, processes, and patient management, based on the relevant consolidated findings of science, technology, and experience. Note: The state-of-the-art embodies what is currently and generally accepted as good practice in technology and medicine. The state-of-the-art does not necessarily imply the most technologically advanced solution. The state-of-the-art described here is sometimes referred to as the "generally acknowledged state-of-the-art. [MDCG 2020-6 / IMDRF/GRRP WG/N47]
SRN	Single Registration Number for an economic operator
SSCP	**Summary of Safety and Clinical Performance** A document that summarizes the place of the device in the context of diagnostic or therapeutic options, taking into account the clinical evaluation of that device when compared to the diagnostic or therapeutic alternatives and the specific conditions under which that device and its alternatives can be considered. Required for implantable and Class III devices.
STED	**Summary of Technical Documentation**
Sufficient Clinical Evidence	Is understood as "the present result of the qualified assessment which has reached the conclusion that the device is safe and achieves the intended benefits". [MDCG_2020-6]
Swissmedic	The Swiss Agency for Therapeutic Products (Swissmedic) is the Swiss surveillance authority for medicines and medical devices, registered in Berne.
TFMS	**Thermedx Fluid Management System**
ThuLEP	**Thulium Laser Enucleation of the Prostate**
TmLRBT	**Thulium Laser *en bloc* Resection of Bladder Tumor**
TURBT	**Transurethral Resection of Bladder Tumor**
TURP	**Transurethral Resection of The Prostate**
UDI-DI	**Unique Device Identifier-Device Identifier**
Undesirable Effects	Can be understood as any undesirable side-effect related to the device and that is experienced by the patient and/or can be diagnosed and/or measured in the patient. [per MDCG_2019-9]
URS	**Ureteroscopy**
UTIs	**Urinary Tract Infections**

Abbreviation/Acronym	Definition or Description
WET	**Well Established Technology** Per MDCG_2020-6: The common features of devices which are well established technologies are that they all have: • relatively simple, common, and stable designs with little evolution; • their generic device group has well-known safety and has not been associated with safety issues in the past; • well-known clinical performance characteristics and their generic device group are standard of care devices where there is little evolution in indications and the state of the art; • a long history on the market. Therefore, any devices that meet all these criteria may be considered “well established technologies”.
YAG	**Yttrium Aluminum Garnet**

23 APPENDICES

APPENDIX A: LITERATURE SEARCH PROTOCOL

The Literature Search Protocol for Irrigation Sets [Appendix A_BXU601670_MDR_CER_LSP Rev A] is included as a separate appendix attachment.

APPENDIX B: LITERATURE SEARCH REPORT

The Literature Search Report for Irrigation Sets [Appendix A_BXU601670_MDR_CER_LSR Rev A] is included as a separate appendix attachment.

APPENDIX C: HIERARCHY OF EVIDENCE FOR CONFIRMATION OF CONFORMITY WITH RELEVANT GSPRS UNDER THE MDR

Table 23-1: Hierarchy of Evidence and Considerations for Application Ranked from Strongest to Weakest

Rank	Types of clinical data and evidence	Considerations / Comments
1	Results of high-quality Clinical investigations covering all device variants, indications, patient populations, duration of treatment effect, etc.	This may not feasible or necessary for certain well-established devices with broad indications (e.g., Class IIb legacy sutures, which could be used in every conceivable patient population)
2	Results of high-quality clinical investigations with some gaps	Gaps must be justified / addressed with other Evidence in line with an appropriate risk assessment, and clinical safety, performance, benefit and device claims. Assuming the gaps can be justified, there should be an appropriate PMCF plan to address residual risks. Otherwise, manufacturers shall narrow the intended purpose of the device until sufficient clinical data has also been generated.
3	Outcomes from high quality clinical data collection systems such as registries	Is there sufficient evidence of the quality of the data collected by the registry? Are the devices adequately represented? Are the data appropriately stratified? Are the endpoints appropriate to the safety, performances and endpoints identified in the clinical evaluation plan?
4	Outcomes from studies with potential methodological flaws but where data can still be quantified and acceptability justified	Many literature sources fall into this category, due to limitations such as missing information, publication bias, time lag bias, etc. This applies equally to publications in the peer-reviewed scientific literature. However, for legacy devices where no safety or performance concerns have been identified, these sources can be sufficient for confirmation of conformity to the relevant GSPRs if appropriately appraised and the gaps are identified and handled.

Table 23-1: Hierarchy of Evidence and Considerations for Application Ranked from Strongest to Weakest

Rank	Types of clinical data and evidence	Considerations / Comments
		High quality surveys may also fall into this category.
Class III legacy devices and implantable legacy devices which are not well-established technologies should have sufficient clinical data as a minimum at level 4. Those devices which are well-established technologies may be able to confirm conformity with the relevant GSPRs via an evaluation of cumulative evidence from additional sources as listed below. Reliance solely on complaints and vigilance is not sufficient.		
5	Equivalence data (reliable / quantifiable)	Equivalence must meet MDR criteria. It is normally expected that manufacturers should gather data on their own devices in the post-market phase, therefore reliance on equivalence should be duly justified, and linked to appropriate PMCF or proactive PMS.
6	Evaluation of state of the art, including evaluation of clinical data from similar devices as defined in Section 1.2 of MDCG 2020-6	This is not considered clinical data under the MDR, but for well-established technologies only can be considered supportive of confirmation of conformity to the relevant GSPRs. Data from similar devices may be also important to establish whether the device under evaluation and similar devices belong to the group of devices considered as “well established technologies” (WET). See section 1.2 in this document for the criteria for WET. Data from similar devices may be used, for example, to demonstrate ubiquity of design, lack of novelty, known safety and performance profile of a generic group of devices, etc.
7	Complaints and vigilance data; curated data	This falls within the definition of clinical data under MDR Article 2(48), but is not generally considered a high-quality source of data due to limitations in reporting. It may be useful for identifying safety trends or performance issues. High volume data collected within a robust quality system may provide supportive evidence of device safety.
8	Proactive PMS data, such as that derived from surveys	This falls within the definition of clinical data under MDR Article 2(48) but is not generally considered a high-quality source of data due to limitations associated with sources of bias and quality of data collection. It may be useful for identifying safetyconcerns or performance issues
9	Individual case reports on the subject device	This falls within the definition of clinical data under MDR Article 2(48), but is not considered a high-quality source of data due to limitations in generalizing findings to a wider patient population, reporting bias, etc. It may provide supportive or illustrative information with respect to specific claims.
10	Compliance to non-clinical elements of common specifications considered	Common specifications which address clinical investigation or data requirements directly would rank higher in this hierarchy. Common

Table 23-1: Hierarchy of Evidence and Considerations for Application Ranked from Strongest to Weakest

Rank	Types of clinical data and evidence	Considerations / Comments
	relevant to device safety and performance	specifications may address clinically relevant endpoints through non-clinical evidence such as mechanical testing for strength and endurance, biological safety, usability, etc.
11	Simulated use / animal / cadaveric testing involving healthcare professionals or other end users	This is not clinical data but may be considered evidence of confirmation of conformity to relevant GSPRs, particularly in terms of usability, such as for accessories or instruments.
12	Pre-clinical and bench testing / compliance to standards	Pre-clinical and bench testing may address clinically relevant endpoints through non-clinical evidence such asmechanical testing for strength and endurance, biological safety, usability, etc.

APPENDIX D: SUMMARY OF INCLUDED AND EXCLUDED PUBLICATIONS IN THE CER

Table 23-2: Summary of Included and Excluded Publications in the CER

Search Category	Systematic Scientific Literature (Current DCP)		Supplemental Manual Literature (Current DCP)	Grey Literature (Current DCP)	Systematic Scientific Literature (Previous DCPs)		Supplemental Manual Literature (Previous DCPs)	Grey Literature (Previous DCPs)	Totals	Totals
	Included	Excluded	Included	Included	Included	Excluded	Included	Included	Included	Excluded
DUE	1	5	0	0	N/A	N/A	N/A	N/A	1	5
SotA-Similar (Benchmark) Devices	0	5	0	0	N/A	N/A	N/A	N/A	0	5
SotA-Clinical Landscape	14	82	0	0	N/A	N/A	N/A	N/A	14	82
Totals	**15**	**92**	**0**	**0**	**N/A**	**N/A**	**N/A**	**N/A**	**15**	**92**

APPENDIX E: PREVIOUSLY INCLUDED PUBLICATIONS DEEMED NO LONGER APPLICABLE

This section is not applicable.

APPENDIX F: FULL TEXT PUBLICATIONS INCLUDED IN THE CER

Full Text Publications Included in the CER for Irrigation Sets [Appendix F_BXU601670_MDR_CER_Publications Rev A] is included as a separate appendix attachment.

APPENDIX G: CV OF AUTHOR(S) AND CLINICAL EVALUATOR(S)

CVs for the MW/author and MA-Clinical Evaluator(s) for this Irrigation Sets CER are included as a separate appendix attachment.

APPENDIX H: CONTENT-APPROVED REDLINED IFU FOR THE IRRIGATION JET [RMC4916]

A content-approved redlined version of the IFU [07-36-00-4780, 07-36-00-4306] for the Irrigation Jet [RMC4916] is included as a separate appendix attachment.

APPENDIX I: CONTENT-APPROVED REDLINED IFU FOR THE Y-TYPE IRRIGATION SET [VMC4005]

A content-approved redlined version of the IFU [07-19-00-5644, 07-19-00-4307] for the Y-Type Irrigation Set [VMC4005] is included as a separate appendix attachment.

Baxter

TcU ELECTRONIC SIGNATURE REPORT

REVISION INFORMATION

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Name	Role	Workflow Step	Date of Signature	Decision Taken
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