Clinical Registry Study on Codman HAKIM Programmable Valve System

A Multi-center, Retrospective Registry Study on the Safety of Codman HAKIM Programmable Valve System

Product Name: Codman HAKIM Programmable Valve System

Model and Specifications: See Appendix 1

Proposal No.: C-HAKIM-001

Version No.: V1.1

Date of Version: November 18, 2019

Category of Test: Registry study

Lead Institution: Xuanwu Hospital, Capital Medical University

Sponsor: Integra LifeSciences (Shanghai) Co., Ltd.

NCT number: NCT04285489

Signature Page for the Review of the Study Protocol

Research Topic: A Multi-center, Retrospective Registry Study on the Safety of Codman HAKIM Programmable Valve System

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The signatures of the following team members indicate that, prior to submission to the Ethics Committee (EC), this clinical study, including understanding of techniques involved, statistical methods, research procedures, regulatory compliance, and quality control, has obtained the internal approval of Integra LifeSciences (Shanghai) Co., Ltd.

Role	Name	Signature	Date
Author of the proposal	Henry TANG	Henry Tang	Nov18, 2019
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Quality Assurance & Regulatory Affairs, Integra LifeSciences (Shanghai) Co., Ltd.	Jing CHEN	Jing Chen	18Nov. 2019
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Signature Page for Investigator:

Research Topic: A Multi-center, Retrospective Registry Study on the Safety of Codman HAKIM Programmable Valve System

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I, the signer, have reviewed the study proposal and its attachments. I will conduct this clinical study in accordance with the requirements of this proposal, Good Clinical Practice (GCP), the ethical principles of the Declaration of Helsinki, and all applicable laws and regulations. I will provide a copy of this proposal and all relevant and permanent information to the participating research staff and supervise them.

<Name> Investigator <Date>

<Institution> Hospital

Contents

Summary of the Proposal

Research Topic:	A Multi-center, Retrospective Registry Study on the Safety of Hakim Programmable Shunt System
Research Purpose:	This study aimed to collect safety information from subjects implanted with a shunt system (trade name: Hakim Shunt Programmable System) produced by Codman & Shurtleff, Inc. of the United States. Device safety would be assessed based on all the adverse events that occurred within one year after the subjects implanted the catheter.
No. of Subjects:	130
No. of Research Centers:	About six research centers
Research Design:	This study was designed to be single arm, multi-center, observational and retrospective trial. It is designed to gather information from actual clinical practice from the clinical records of patients in relation to the one-year clinical safety to the use of implant of Hakim programmable shunt system. A total of 130 patients would be retrospectively enrolled. Information would be collected on adverse events of subjects enrolled within one year after the implantation of the Hakim Shunt Programmable System from April 01, 2017 to August 31, 2019. The following information would be collected from subjects' medical records or hospitals' databases (if any): 1. General condition of the subjects 2. Intraoperative condition and shunt system implantation 3. Information on the shunt system product 4. Adverse events of subjects within one year after the operation and classification of the adverse events 5. Relevant examinations in case of postoperative infection 6. Other adverse event-related information (except anticipated adverse events)
Research Duration:	2019-2020
Inclusion Criteria:	Subjects who met all of the following inclusion criteria would be enrolled: 1. The informed consent was exempted by the Ethics Committee of a research center. Either a subject or his/her legal representative signed the informed consent form (ICF) prior to enrollment. 2. A subject had an indication suitable to use Hakim Shunt Programmable

	System. 3. A subject received a Hakim Shunt Programmable System at least one year ago.
Exclusion Criteria:	Subjects who met any of the following exclusion criterion were excluded: 1. A subject didn't have an indication suitable to use the product. 2. A subject was known to be allergic to a component or ingredient of the product to be implanted, including silicone tubing and other components. 3. According to the comprehensive judgment of an investigator, a subject had an infection of the implant site when the shunt system was implanted, such as ventriculitis, meningitis, peritonitis, and local implant skin infection. 4. A subject was simultaneously implanted with another shunt system different from Hakim Shunt Programmable System. 5. A subject had a contraindication of the shunt operation. 6. A subject had uncorrected coagulopathy or any bleeding disorder.
Endpoint	1. Non-infection rate of a subject within one year 2. Type and incidence of adverse events of a subject within one year

Schedule of Data Collection Form

	Screening	Preoperative	Operation	Postoperative follow-up
Time of data collection	NA	-30 to -1 days	0	Days 1-365
Signed the ICF (if applicable)[1]	X			
Review of inclusion and exclusion criteria	X			
Medical History		X		
Laboratory examination		X		X+
Operative process			X	
Device application record			X	
Adverse events[2]			X*	X*
Serious Adverse Events			X*	X*
End of study/exit			X	X
Record of concomitant medication[3]		X*	X*	X*
Record of concomitant treatment[4]			X*	X*

+	Suspicious or proven infection
*	If any

Notes: 1. The ICF (if applicable) needed to be completed before screening.

2. A postoperative anticipated adverse event was not counted as an adverse event.

3. Only antibiotics and medications related to postoperative adverse events were recorded. Only the administration of antibiotics within seven days prior to the operation was recorded.

4. Only the treatment and operation associated with postoperative adverse events were recorded.

Abbreviations:

AE	Adverse events
CRF	Case Record Form
CV	Curriculum Vitae
EC	Ethics Committee
ICF	Informed Consent Form
IFU	Instructions for Use
GCP	Good Clinical Practice
NMPA	National Medical Products Administration
SAE	Serious adverse event
SDV	Source data verification
UADE	Unanticipated adverse device effect

1 Introduction

1.1 Background and principle

Abnormal enlargement of part or all of subarachnoid space or ventricles, the abnormal accumulation of cerebrospinal fluid (CSF) in subarachnoid space or ventricles is called hydrocephalus. It is a circulation disorder of CSF caused by many pathological reasons[1]. A shunt system mainly drains CSF from the accumulation site to the abdominal cavity, the lumbar cistern, and the atria through a catheter so as to address dilated ventricles and alleviate the pressure on the brain.

The earliest permanent CSF shunt operation occurred in 1893. A glass catheter was placed in a lateral ventricle of a patient with hydrocephalus, the end of which was placed under the skin. The head circumference of the patient was significantly reduced after the operation[2]. The principle of modern shunt operation can be dated back to the 1870s. Ventriculo-peritoneal shunt operation had become a common treatment for hydrocephalus[3]. China released *Specialist Consensus on the Standardized Treatment of Hydrocephalus in China* in 2013, which regarded CSF shunt as an important operation for hydrocephalus and proposed suggestions on technical key points.

However, in terms of the treatment of neurosurgical diseases, the incidence of complications of shunt operations is the highest, mainly including shunt infection, obstruction or rupture of a shunt catheter, displacement of an intracranial or abdominal shunt catheter, excessive or insufficient drainage of CSF, intracranial hemorrhage, and epilepsy[1]. Infection is a common complication and important cause of revision. Its incidence rate is 3-29%. Approximately 90% of the cases occur within one year after the operation. If it is combined with ventriculitis, the mortality rate can be as high as 30-40%[3]. For children, even if the infection can be controlled, long-term complications, such as epilepsy, cognitive impairment, and physical and delayed psychological development, may occur[4].

According to the analysis of recent literature, among a total of 8,588 shunt operations (3,291 cases with an antibiotic-impregnated catheter, 5,297 cases with a non-antibiotic-impregnated catheter), the postoperative infection of normal shunt system was 7.2%[5].

In addition to infection, complications of CSF shunt operations include excessive and insufficient drainage of CSF associated with pressure regulation; obstruction of the shunt catheter, usually due to a poor position of an intracranial shunt catheter, the accumulation of red blood cells or brain tissues in the shunt pump, or wrapping of a shunt catheter by abdominal omentum majus; rupture of shunt catheter, mostly occurring at the junction of the catheter and the pump and a subcutaneous area; and rare complications, such as displacement of a shunt catheter, wound, intracranial hemorrhage, and symptoms of Parkinson's Disease[1].

Hakim Programmable Shunt System manufactured by Codman & Shurtleff, Inc. in the United States constitute of a systemic silicon catheters and programmable valves. Hakim Programmable Shunt System has been safely used around the world for more than a decade. However, there is a lack of data on the safety of the product in long-term follow-up and clinical application in the Chinese population.

1.2 Research-related devices

Devices verified in this study were programmable shunt system catheters (trade name: Hakim programmable shunt system) manufactured by Codman & Shurtleff, Inc., U.S.A. Its registration number is G.S.Y.J.X. (J) 2017 3661104. Please refer to the Appendix 1 for the product specifications and models in this study.

2. Benefits/Risks

2.1 Benefits

Hakim programmable shunt system serves as the shunt system of hydrocephalus treatment. Hydrocephalus shunt operations can alleviate or eliminate hydrocephalus and improve clinical symptoms and signs. Meanwhile, retrospective collection of data and experience of clinical safety can be used as a reference for investigators and enterprises and conducive to the diagnosis and treatment of future subjects. However, such data and experience had no extra benefits for the participants in this study.

2.2 Risks

This is a retrospective study. It did not intervene in subjects' normal treatment. It objectively collected patients' clinical data. Hence, there were no additional risks associated with participating in this study.

3 Research purpose

3.1 Indications

Hakim programmable shunt system: Hakim programmable shunt system serves as the shunt system of hydrocephalus treatment.

3.2 Purpose

This study aimed to collect safety information from subjects implanted with a programmable shunt system (trade name: Hakim programmable shunt system) produced by Codman & Shurtleff, Inc. of the United States. Device safety would be assessed based on all the adverse events that occurred within one year after the subjects were implanted with the catheter.

4. Research Design

4.1 Basic design

This study was designed to be single arm, multi-center, observational and retrospective. It is designed to gather information from actual clinical practice from the clinical records of patients in relation to the one-year clinical safety to the use of operation of Hakim programmable shunt system. The treatment date would be defined as the implant date of the Hakim programmable shunt system. The study period includes a general history period that includes up to 30 days prior to the treatment date and a follow-up period of up to 365 days post implant operation. A total of 130 patients would be enrolled and adverse events would be collected for subjects enrolled within one year after the implantation of Hakim programmable shunt system from April 01, 2017 to August 31, 2019, through case review or hospital database (if any).

4.2 Data collection

The following information would be collected from subjects' medical records:

1. General condition and medical history of the subjects

2. Intraoperative condition and shunt system implantation

3. Information on the shunt system product

4. Adverse events of subjects within one year after the operation and classification of the adverse events

5. Relevant examinations in case of postoperative infection

6. Other adverse event-related information (except anticipated adverse events)

Information on adverse events would be collected. And the safety of clinical application of the product would be assessed.

5. Objectives and Endpoint

5.1. Objectives

The objective of this study is to assess the safety of the Hakim programmable shunt system.

5.2 Primary Endpoint

1. Non-infection rate of a subject within one year post implant

2. Incidence of adverse events within one year post implant

5.2 Safety indicators

The incidence of adverse events was observed in line with the IFU. Key attention should be paid to:

- Obstruction of a cerebral ventricular catheter
- Falling out of a programmable shunt system
- Poor position of a catheter
- Intestinal perforation, abdominal and pseudocysts, umbilical fistula, pseudo-acute appendicitis, infection, and ascites
- Subcutaneous twist, rupture, distal obstruction, and distal retraction from the abdominal cavity
- Failure of a programmable shunt system
- Mechanical failure
- Obstruction or infection of the shunt path
- Leakage of CSF in an implanted programmable shunt system
- Excessive drainage
- Damage of intracranial or abdominal tissue
- Fibrous adhesion

6 Study Population

6.1 Selection of subjects

Subjects who received a hydrocephalus shunting operation between April 01, 2017 and August 31, 2019 and met the inclusion criteria were enrolled. As this was a retrospective study, it would apply for the exemption of informed consent from the Ethics Committee of a center. For the centers which did not exempt informed consent, the informed consent process would be completed prior to the start of data collection, either by telephone or by anyway approved by the Ethics Committee.

6.2 Inclusion criteria

Subjects who met all of the following inclusion criteria would be enrolled:

1. The informed consent was exempted by the Ethics Committee of a research center. Or a subject or his/her legal representative signed the informed consent form (ICF) prior to the enrollment;

2. A subject had an indication suitable to use Hakim programmable shunt system;

3. A subject received a Hakim Shunt Programmable System at least one year ago.

6.3 Exclusion criteria

Subjects who met any of the following exclusion criterion were excluded:

1. A subject didn't have an indication suitable to use the product;

2. A subject was known to be allergic to a component or ingredient of the product to be implanted, including silicone tubing and other components;

3. According to the comprehensive judgment of an investigator, a subject had an infection of the implant site, when the shunt was implanted, such as ventriculitis, meningitis, peritonitis, and local implant skin infection;

4. A subject was simultaneously implanted another shunt system different from Hakim programmable shunt system;

5. A subject had a contraindication of the shunt operation;

6. A subject had uncorrected coagulopathy or any bleeding disorder.

7 Research Process

The research process included: Screening and enrollment of subjects, Days -30 to -1 before the operation, Day 0, the day of operation, and one-year follow-up (Days 1-365) after the operation.

7.1 Screening and enrollment

7.1.1 Screening of subjects

Qualified and authorized investigators or clinical study coordinators reviewed the medical records of subjects to screen subjects eligible for this study.

7.1.3 Enrollment of subjects

If a subject met all the inclusion criteria and did not meet any exclusion criterion, he/she could be included in the retrospective analysis cohort. Subjects could be considered as enrolled in this study only if they met the following requirements:

1) A subject met all the inclusion criteria and did not meet any exclusion criterion; and

2) The ICF was signed (in terms of a research center that did not waive informed consent).

7.2 Days -30 to -1 before the operation

The following information needed to be collected and recorded:

1. Demographic information and medical history of a subject before the operation: including patient age, gender, height, weight, preoperative diagnosis; past medical history, past surgical history, personal history; preoperative laboratory examination results: including white blood cells, red blood cell count, neutrophilic granulocyte count, hemoglobin content, platelet count, alanine aminotransferase (ALT), aspartate aminotransferase (AST), C-reactive protein, albumin, blood glucose, APTT, PT, and INR. If there were multiple laboratory tests before the operation, the latest results should be collected.

2. Concomitant medication: Only the administration of antibiotics within seven days prior to the operation was recorded.

7.3 Operation period (Day 0, the day of operation):

The following information needed to be collected and recorded:

1. Operation: date of surgery, surgeon, surgical procedure, start and stop time of the operation, blood loss during the operation, medications, intraoperative complications, intraoperative shunt, and combined treatment;

2. Record of devices used during the operation: type, No. and batch No. of the cerebral ventricular shunt catheter; type, No. and batch No. of the pressure regulating valve; and type, No. and batch No. of shunt catheters at the abdominal cavity/the lumbar cistern/ the atria.

7.4 Postoperative follow-up period: Days 1-365

An adverse event (except an anticipated adverse event) discovered during the review of postoperative history or hospital database (if any) should be recorded:

The date, description, concomitant therapy, and outcome of an adverse event, information related to the operation and the product, not matter the implanted part was taken out due to an adverse event, and concomitant medication and treatment should be recorded.

Additional records were required for the following special adverse events:

1. Infection: Infection site which is usually classified into intracranial, skin, and abdominal infections. For intracranial infection, date of infection, white blood cell count, red blood cell count, neutrophilic granulocyte count, hemoglobin content, alanine aminotransferase (ALT), aspartate aminotransferase (AST), C-reactive protein, blood glucose, traits and color of CSF, cell count, Pan's test results, contents of protein, sugar, and chloride in CSF, bacterial culture type, and bacterial susceptibility to rifampicin and clindamycin should be recorded. For skin infection and abdominal infection: white blood cell

count, red blood cell count, neutrophilic granulocyte count, bacterial culture type, and bacterial susceptibility to rifampicin and clindamycin should be recorded.

2. Obstruction of catheter: site, reason (judged by an investigator), and nature of obstruction should be recorded.

3. Leakage of CSF: date and position of leakage should be recorded.

4. Mechanical failure: type of mechanical failure should be recorded, including falling out, displacement, twisting, and rupture.

A patient who died within one year was still considered as a complete case. The form of SAE should be completed. And the death should be specified in this study endpoint table.

8 Adverse Event Reporting

8.1 Adverse events

8.1.1 Adverse events

Adverse event (AE) refers to any adverse medical event of a subject, no matter if it is related to this study or a research-related device.

During the assessment of a subject enrolled to this clinical study, an investigator should each time determine whether there was an AE and collect information, including date, severity, treatment, prognosis, and analysis of the AE, and research-related device, operation, or drug, in as detailed a way as possible.

Information of all AEs, research-related device failures, and other product issues should be as much as possible collected from existing medical records, and entered into CRFs.

8.1.2 Anticipated operation-related adverse events

Anticipated AE refers to an event that occurred after the operation during hospitalization (relative to the baseline change of a subject), which was an anticipated consequence of the operation. If an anticipated AE occurred, it would not be reported to the sponsor.

Currently, postoperative anticipated AEs known include:

- Wound pain within 48 hours followed by agitation
- Fever lower than 38.5°C within 48h
- Abdominal distension and constipation within 48h
- A small amount of wound exudation within 48h
- Mild anemia (hemoglobin > 90g/L)
- Increase in white blood cells within 48h

8.2 Unanticipated adverse device effect

Unanticipated adverse device effect (UADE) refers to a serious adverse effect, a life-threatening issue, or death caused by or related to the devices, or a serious and unanticipated issue related to the rights, safety, or health of a subject and the devices. In addition, the nature, severity, or frequency of such an event was not specified in the study proposal, IFU, and clinical trial instructions.

8.3 Serious Adverse Events

Serious adverse event (SAE) refers to any of the following adverse events:

1) Cause Death,

2) Serious deterioration of a subject's health, including:

   a. A life-threatening illness or injury,

   b. Permanent damage of the body structure or a body function,

   c. Hospitalization or extension of the current hospital stay:

   d. Medical or surgical intervention required to avoid a life-threatening disease or prevent permanent damage to the body structure or a body function,

3) Fetal distress, fetal death, congenital malformation, or birth defects.

In this retrospective study, planned hospitalization or medical intervention due to a disease existing before the operation not followed by serious deterioration of health was not regarded as a serious adverse event.

8.4 Duration of follow-up after an adverse event

As this is a retrospective study, it did not intervene in subjects' normal treatment. Therefore, all adverse events were properly evaluated by an investigator based on medical requirements. And no additional follow-up would be performed.

8.5 Adverse event reporting

Within one year after the shunt operation of a subject, all the adverse events (except anticipated adverse events) recorded in the medical records or hospital database (if any) should be reported. An investigator reported AEs to the sponsor via CRF.

An investigator should record the nature, severity, treatment and prognosis of an AE and determine the correlation with the devices, medication, or operation involved in this clinical study.

An investigator must report SAEs and UADEs to the sponsor (or a designated person) within 24h after their occurrence, and report them to the Ethics Committee in a timely manner. In the event of any request by the sponsor, additional information should be provided. The investigator should judge the time associated with the research product. The research center should report them to a local medical device adverse event monitoring organization. Death should be reported within 7 days, after it was known. A serious injury or an event that might result in death or a serious injury should be reported within 20 days after it was known. The sponsor would report to NMPA and/or a local medical device adverse event monitoring organization in line with the same requirements as those of the research

center. If the adverse event had existed or been reported in the previous reporting system, it would be unnecessary to report it repeatedly.

The sponsor should regularly inform all the clinical investigators of this study of all SAEs and UADEs.

8.5.1 Severity criteria

The severity of an adverse event could be classified as mild, moderate, and severe according to the following criteria.

- Mild: It was transient and mild with no influence on daily life, and no special measures or treatment was required.
- Moderate: It had a slight impact on daily life. Measures or treatments were needed, if necessary.
- Severe: It had a serious impact on daily life. Special measures or treatment must be taken, and hospitalization was required, if necessary.

8.5.2 Determination of causal relationship

The relevance between any adverse event and a research-related device should be judged, according to the following criteria, including unrelated, possibly unrelated, possibly related, probably related, and definitely related. If an AE was judged to be possibly related, probably related, or definitely related to a research-related device, such an AE was related to the devices.

- Unrelated: An AE was not related to the devices.
- Possibly unrelated: An adverse event was more likely to be related to other factors, such as concomitant medication or disease. Or the timing of the AE indicated that it was unlikely to be caused by a research-related device.
- Possibly related: An AE might be caused by a research-related device. Other reasons were not excluded, such as concomitant medication or disease. When the occurrence of an AE and the use of a research-related device had a reasonable time sequence, the causal relationship between the event and a research-related device could not be excluded.
- Probably related: An AE was probably caused by a research-related device. An AE and the use of a research-related device had a reasonable time sequence. For example, the causal relationship was proved after the device was taken out. There was unlikely to be another explanation, such as concomitant medication or disease.
- Definitely related: The type of an AE was identified as a side effect of a research-related device, which could not be explained by other reasons, such as concomitant medication and disease. The time of an AE strongly implied a causal relationship (e.g. reaction after the removal and re-implantation of a device).

9 Early Termination of the Study

9.1 Reason of early termination

Possible reasons of early termination include, but are not limited to, the following:

- Withdrawal of informed consent: (For a research center which required its subjects to sign the ICF) a subject decided to withdraw from this study. The decision must be "determined by the subject himself/herself" and recorded in the subject's research file;

- Early termination of this study: The sponsor might decide to suspend this study in advance for any reason.

9.2 Early termination of this study by a subject

For a research center which required its subjects to sign the ICF, if a subject terminated this study in advance, the reason must be recorded in the source document and the file of the research center and submitted via CRF.

A subject who terminated this study in advance could not be replaced, and his/her data would be included in the results analysis, unless the subject submitted a written request to withdraw the data.

9.3 Early termination of this study by the sponsor

The sponsor had the right to temporarily suspend or terminate in advance the research of a single research center, multiple research centers, or all the research centers at any time. The reasons include, but are not limited to: Security or ethical issues, inaccurate or incomplete data records, non-compliance, or unsatisfactory quantity or quality of enrollment.

If this study was terminated or suspended, the sponsor or its representative should follow applicable regulatory requirements to inform investigators/their organizations and regulatory authorities of the reason. The sponsor or investigators/their organizations should comply with applicable regulatory requirements to notify the Ethics Committees and submit the reason.

10 Statistical Methods

10.1 Primary endpoint

The primary endpoint of the study is:

Non-CSF infection within one year post implant.

Incidence of adverse events within one year post implant, which includes:

- Obstruction of a cerebral ventricular catheter

- programmable shunt system slipping

- Poor position of a catheter

- Intestinal perforation, abdominal and pseudocysts, umbilical fistula, pseudo-acute appendicitis, infection, and ascites caused by catheter

- Subcutaneous twist, rupture, distal obstruction, and distal retraction from the abdominal cavity

- Failure of a programmable shunt system

- Mechanical failure
- Obstruction or infection of the shunt path
- Leakage of CSF in an implanted programmable shunt system
- Excessive drainage
- Damage of intracranial or abdominal tissue
- Fibrous adhesion related to distal catheter

10.2 General considerations

The primary analysis will be descriptive in nature and will be based on information in the data collection form.

The extraction of the data from the medical records will be done by the investigators who care for the patients; in this way, the possible limitation of the study that is normally observed in other studies of review of clinical histories in which the information can be interpreted incorrectly is minimized.

10.3 Sample size

This study will provide infection free survival at 1 year for Hakim programmable shunt system and ensure 95% confidence bounds acceptable (half width < 5%). If N_0 is the number of enrolled subjects, the number of infection free subjects after *t* years will be approximately:

$$N(t) = N_0 e^{-(r1+r2)t}$$

where r1 and r2 are the infection rate and the dropout rate respectively.

Following the Peto method, parameter estimation (e.g., infection free survival) in survival analysis will be performed. Defined S(t) as the survival rate at t years post operation, the Kaplan-Meier half 95% confidence width for the survival rate is given by:

$$margin = 1.96\sqrt{[S(t)]^2[1-S(t)]/N(t)}.$$

Based on published data, the annual infection rate of a normal shunt system is assumed to be 7.2%[5], then the 1-year infection free rate is 92.8%. With an enrollment of 130 patients and a dropout rate of 10%, by using the aforementioned formula, the sample size for infection free survival at one year post operation is given by:

$$N(1) = N_0 e^{-(r1+r2)} = 130 * e^{-(0.072+0.1)} = 109.$$

The half 95% confidence width of the survival given by:

$$margin = 1.96\sqrt{[92.8\%]^2[1-92.8\%]/109} = 4.7\%.$$

The precision of 4.7% is less than 5% and is considered acceptable.

10.4 Criteria of qualification/disqualification of the trial results

This study is to collect post-marketing safety data on the Chinese population implanted Hakim programmable shunt system, according to product registration requirements. The occurrence, type, severity, frequency, of all AEs occurring during the study period, as well as the correlation between AEs and the product will be collected and presented. Hence, criteria of qualification/disqualification were not applicable.

10.5 Interim analysis

No interim analysis is planned for this study.

10.6 Analysis plan

All study data collected in this study will be presented in subject data listings. Statistical analyses will be performed using SAS 9.3 or later version. Other valid software might also be used as appropriate.

Data analysis will be carried out primarily using descriptive statistics. In general, mean, standard deviation, median, minimum and maximum will be calculated for continuous variables, and frequencies and percentages will be presented for categorical variables. If necessary, additional descriptive statistics may be calculated.

Analysis population

The primary analysis population for this study is the Per Protocol (PP) populations. The PP population will include all subjects who meet the inclusion/exclusion criteria

Subgroup analyses

The main subgroups that will be analyzed, in addition to the total population per protocol, will be adults and children.

Endpoint analysis

The primary endpoint of1-year infection free survival rate will be estimated by the Kaplan-Meier method, the 95% confidence width for the survival rate will be estimated by the Peto method. The Kaplan-Meier survival curve will be presented.

10.7 Report

After the data of all subjects were completely collected (within one year after the operation), a clinical study report would be compiled and submitted to NMPA for review as material supporting the extension of product registration.

11 Research Management and Administration

11.1 Responsibilities of investigators and the sponsor

11.1.1 Responsibilities of investigators

An investigator should ensure that all the work and services herein or incidental matters of all the work and services herein were implemented in accordance with the highest standards of medical and clinical study practice. An investigator should perform his/her duties according to all applicable laws and regulations. An investigator should provide a copy of the current study proposal to all assistant investigators or research staff of other research centers in charge of research implementation, and ensure all research staff are qualified, trained, and competent.

An investigator should submit the progress report, the safety report required by local regulations or national regulatory requirements, and study completion notice to the EC within the specified time limit.

11.1.2 Responsibilities of the sponsor

The sponsor should be solely responsible for the implementation of this study. The sponsors should ensure compliance with all applicable regulations and guidelines during this study.

The sponsor should properly monitor clinical study centers, obtain subjects' informed consent, provided quality data in compliance with regulations, notify investigators, ECs, and regulatory authorities of AEs, revocation of ethical approval, a list of current investigators (if necessary), and relevant safety issues, in accordance with international and local guidelines, and describe proposal deviation, as appropriate. The sponsor should write the safety report, the progress report, and the final clinical study report.

11.2 Assessment, initiation, monitoring, and close of visits

11.2.1 Assessment visits

The main requirements for which a research center and an investigator are selected and continue to participate in this study include: They have sufficient experience in relevant research areas and all research operations, and adhere to safety commitments and the study proposal. The number of subjects should also be consistent with what is specified in the study proposal. The sponsor and its designated personnel should select qualified investigators, obtain a copy of signed research agreement from the latter, and provide the latter with the information necessary to implement this study, including any amendment or update to the research information specific to this study.

11.2.2 Initiation visits

At the beginning of this study, the monitor designated by the sponsor would visit research centers to confirm that all investigators personnel and research-related items were in place. The monitor would offer research-related training to investigators, including study proposals, informed consent procedures (if applicable), complaint of adverse events and research-related devices, completion of CRF, maintenance of research documents, responsibility of immediate notification to the sponsor of investigator changes, monitoring process, and GCP. During the initiation of visits, all preparations for subjects enrolled should be carried out.

11.2.3 Monitoring visits

At all research centers, the monitoring of this study should be carried out by the sponsor or personnel designated by the sponsor. Monitoring should ensure:

- Rights and health of subjects were protected;
- This study was conducted in accordance with all applicable regulations and guidelines;
- The study proposal and corresponding amendments were complied with;
- The accuracy of data recorded should be confirmed by verifying source documents.

Throughout the clinical study period, all effective research centers should be regularly monitored and visited to ensure that investigators fulfilled their obligations. These visits were to ensure that the research centers met requirements for facilities, follow the study proposal and all amendments, informed their ECs of changes to the proposal as required, maintain complete records, report to the sponsor and their ECs appropriately and in a timely manner, and that investigators were implementing all agreed matters.

11.2.4 Closing visiting of research centers

At the completion of the clinical study (Data were completely collected from all subjects enrolled. All CRFs were completed. And all data queries were resolved), the sponsor or designated personnel should inform research centers to end this study and close their visit to the centers.

At the last visit to research centers, all unused research materials should be collected and returned to the sponsor or destroyed at research centers. The monitor and investigator should ensure that the investigator folder and other research-related materials were up-to-date and complete, and that all outstanding issues of previous visits were resolved. During this visit, others issues to be reviewed included: storage of research materials, possibility of audit of research centers, open policies, and notice to ECs about the end of this study.

If a research center failed to enroll any subject for any reason, and the sponsor decided that the research center should stop further participation in this study, before the end of this clinical study, the last visit to the research center could be planned. In this case, the sponsor should instruct investigators to complete the notification to the EC of the participation of the research center in this study and prepare the final documents required by the sponsor.

11.3 Documents required

Before enrolling subjects, at least the following documents should be submitted to the sponsor or designated personnel:

- The confidentiality agreement;
- Signed signature page of the study proposal;
- CVs of primary investigators and assistant investigators recently signed and dated; The CVs should clearly describe the qualifications and experience of research personnel;
- A copy of the written approval of the study proposal by ECs (including version number and date) and informed consent (including version and date) (if applicable);

- A list of current EC members, including name, title, occupation, and name of any organization of each member;
- Signed research contract.

11.3.1 Source documents

Regulations state that investigator should maintain the information in subjects' medical records (i.e., source documents). Such information could verify the data collected in CRFs. In order to comply with these regulatory requirements, the following information should be stored and available upon request by the monitor and/or inspectors of regulators:

- Information on medical history/physical condition of a subject that could prove the subject met the inclusion criteria of this study before participating in this study;
- Records on the informed consent process (if applicable);
- Description of implantation;
- All exam results and follow-up information;
- Dated and signed exam reports (e.g., X-ray);
- Description of an adverse event (description, severity, date, and duration of the adverse event, correlation with a research-related device, prognosis and treatment of the adverse event, and concomitant medication);
- Condition of a subject at the completion of or withdrawal from this study.

Source documents of a subject should include at least but not be limited to the above information.

11.3.2 Source data verification (SDV)

During visits, the monitor should check all the following key items in accordance with CRF entries of 100% of the subjects: all inclusion/exclusion criteria, the ICF (if applicable), demographic information of a subject, all events that met the criteria of reporting of adverse events (the inducing factor that indicated the occurrence of an event), safety and efficacy endpoints, use of devices, re-operation, and all device failure/complaint reports. The monitor should check the other data of 50% of the subjects. For complete and details of verification of source data, please refer to the monitoring plan.

During a visit by the monitor, a research coordinator and/or an investigator should be present. The research coordinator or the investigator should ensure that the monitor could review source documents and provide the latter with an appropriate environment to review relevant documents. All inconsistencies should be identified and discussed with the investigator or designated personnel for resolution.

11.3.3 Case Record Form (CRF)

The CRF of each subject should be completed by an authorized investigator or another authorized personnel of research center. All the data on subjects required must be collected in CRFs. CRFs could not be used as a source document. The monitor should check completed CRFs at a research center to confirm the accuracy of the data collected in CRFs. All corrections to CRFs should be carried out by an authorized investigator or another authorized personnel of research center.to CRFs should be carried

out by an authorized investigator or other authorized personnel of the research center. The investigator /assistant investigator must sign and date at a specific part of CRF to prove that he/she had reviewed the data and ensured the data were complete and accurate.

A investigator should complete CRFs as soon as possible after a subject was screened or relevant information was collected. This would facilitate timely monitoring visits.

11.3.4 Archive and data retention

After being informed of the end of all research, an investigator should keep all research records, reports, and source documents supporting the completion of CRFs for at least ten years and could continue to keep the data in line with the local and international guidelines specified in the clinical study agreement.

Investigators should be able to provide the document records at the request of regulators and the sponsor (designated personnel). Before the transfer of the documents, the sponsor or designated personnel must approve in writing the filing or transfer of the documents so as to relocate the documents. Investigators must notify the sponsor in writing of the location of the transfer and duration and procedures of reviewing the documents. Before destroying any records and reports related to this study, an investigator must contact the sponsor or designated personnel to confirm that the records and reports were no longer to be retained.

If an investigator no longer shouldered the main responsibility of storage of research records due to retirement, relocation, or other reasons, the investigator must transfer in writing the right of storage to the sponsor or designate personnel and indicate the name and address of the person with the primary responsibility.

11.3.5 Audit and inspection

In the case of an audit initiated by the sponsor (or its designated personnel), or a regulator, an investigator should ensure that auditors and inspectors had access to the original medical records during their audit or inspection and provide all necessary information. In the case of an audit initiated by a regulator, an investigator should notify the sponsor immediately.

11.4 Data Collection and Management Responsibilities

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site Investigator. The Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

The recruitment of the study centers and the extraction of data from patients' medical records will be closely monitored to reach the proposed sample sizes. The study investigators will be asked to extract the data from the medical records of all patients implanted with Hakim programmable shunt system for the study in their respective centers. Integra Clinical Operations will follow up with the centers during the data collection process when appropriate to ensure a rapid completion of the data collection process.

Hardcopies of the study visit CRFs will be provided for use to collect data for each subject enrolled in the study. Data recorded in the CRFs derived from any source documents should be consistent with the data recorded on those source documents.

Clinical data (including AEs), concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into Microsoft Access database by Sponsor by double data

entry. The data will be reviewed and validated. Queries for any missing, inconsistent or illogical data points will be forwarded to the research center for resolution. After all data queries are resolved, the data will be transferred to a biostatistician for analysis.

12 Ethical and Regulatory Requirements

12.1 Ethics Committee

Before enrolling subjects, a research center should submit the study proposal, the ICF (if applicable), and other applicable documents related to this study to its EC, obtain a written approval from the latter, and submit the approval to the sponsor or designated personnel.

An investigator should immediately report any change to the appointment of primary investigator s and all unanticipated issues related to risk of subjects. Without the consent of the EC, an investigator was not allowed to alter the study proposal, excluding necessary changes to eliminate immediate hazards to subjects. Amendments involving significant risks or changes requiring EC approval and the written approval by an EC must be submitted to the sponsor or designated personnel.

12.2 Informed consent

If informed consent was not exempted by a research center, before any research-related action outside of routine treatment or nursing was implemented, each subject (or their legally authorized representative) must complete the informed consent process in line with the requirements of the EC of a research center, after having the nature of this study fully explained to them. At a research center which did not exempt informed consent, for a subject younger than 18 years old, an investigator should obtain a signed ICF from either of the parents or the statutory guardian. A subject aged between 6 and 18 should also sign a relevant version of an ICF in person.

The voluntary process of informed consent demonstrated that a subject (or his or her statutory guardian) was willing to participate in this study. Before an ICF was signed, an investigator must explain all aspects of this study to and answer all questions raised by a subject (or his/her statutory guardian). An investigator and/or a designated personnel must clearly document the process of obtaining informed consent in a subject's clinical record. An investigator should ensure that the informed consent process was implemented in accordance with all applicable regulations and requirements of the EC.

12.3 Subject confidentiality

Throughout the clinical study period, all data should be traceable to the original records; and subject data should be kept confidential. To this end, unique subject identification numbers (research center number and subject number) were used, via which all data reported on each subject could be identified.

If data were encrypted and subjects' privacy was protected, information related to this study could be used by third parties (e.g. regulatory authorities during inspection).

12.4 Revision of the study proposal

Changes to the study proposal could be submitted by the sponsor or designate personnel to an investigator or by an assist investigator to his/her EC. Before any change to the study process was implemented, all major amendments must be approved by the EC of a research center.

If it was likely to significantly impact the following items, an amendment would be a major

amendment:

- The safety or physical or mental health of a subject;
- Scientific value of the trial;
- Implementation or management of the trial;
- Quality or safety of equipment used in the trial.

12.5 Protocol deviation

Protocol deviation stands for the deviation of actual implementation of the study protocol from a particular part of the study protocol (e.g. non-compliance with inclusion/exclusion criteria). This study only retrospectively collected data. An exam item required in the protocol yet missing was not regarded as a protocol violation.

No matter if it was medically sound, or if a violation was made to protect a subject in an emergency, the violation should be reported to the sponsor. An investigator should follow procedures as well as reporting policies and requirements of the EC of the research center to report a violation to the EC.

Relevant regulations required an investigator 's records should be accurate, complete, and up-to-date, including documentation recording the date and cause of each protocol violation.

Protocol violation could be classified into primary protocol violation and secondary protocol violation. A violation related to inclusion/exclusion criteria or informed consent (if applicable) or affecting the endpoint would be regarded as a primary protocol violation. Other violations other than primary protocol violations were secondary protocol violations.

The final confirmation of a protocol violation should be agreed by an investigator, a data analyst, and the sponsor.

13 Publication Policies

At the end of this study, an article reflecting the results of the multi-center study would be published in prestigious scientific journals. Prior to the compilation and publication of the multi-center study results, any main results of any single research center in this study were not allowed to be published. Exceptions to this rule were subject to prior approval by the sponsor and the primary investigator. Other pre-defined and non-pre-defined endpoint analysis would be implemented by the data management department. Secondary analysis and other proposed research studies were subject to the approval by the primary investigator and the sponsor. In order to promptly extract and publish statements, secondary publication would be delegated to a relevant main author. The final analysis and review of all multi-center data should be approved by the primary investigator and the sponsor.

The results of the study may be published in scientific literature and may also be used in submissions to regulatory authorities. It is the intent of the Sponsor to publish or present the study results together with study results from the other sites, unless specific written permission is obtained in advance from the Sponsor to publish separate results. The Investigator will ensure that any site and/or Sponsor personnel making a significant contribution to the study or development of a manuscript are recognized as co-authors in any publication according to guidelines set forth by the International Committee of

Medical Journal Editors (ICJME).

All information received by the Investigator concerning the Sponsor's business operations (such as patent applications, product design, formulae, manufacturing processes, basic scientific data, or characterization or formulation information supplied to the Investigator and not previously published) is considered confidential by the Sponsor and shall remain the sole property of the Sponsor. The Investigator agrees not to use it for any purpose other than conduct of the study without the prior written consent of Sponsor.

It is understood by the Investigator that the Sponsor will use the information developed in this clinical trial ("Study Data") in connection with the development of the Hakim programmable shunt system. Therefore, Study Data may be disclosed to other Investigators or appropriate regulatory authorities. By agreeing to participate in this clinical trial, the Investigator understands that he/she has an obligation to provide the Sponsor with complete and accurate Study Data.

Publication and Disclosure: Because this is a multi-center trial, Investigators and/or their academic Institutions shall not independently publish, publicly disclose, present or discuss any Study Data or other information pertaining to their respective activities conducted under this study protocol until a multi-center publication is released under Sponsor's direction, unless otherwise agreed upon in the study agreement.

14 Devices

14.1 Count of research-related devices

This is a retrospective study. Devices were implanted. Hence, this entry does not apply.

14.2 Return of research-related devices

This is a retrospective study. Devices were implanted. Hence, this entry does not apply.

14.3 Complaint about devices

An investigator should immediately notify the sponsor or designated personnel of an issue regarding authenticity, identification, quality, and performance of the research product.

14.3.1 Complaint about devices

Relevant personnel of the sponsor must report the complaint to the email of the Custom Service China of Integra LifeSciences (Shanghai) Co., Ltd.within 24 hours after receiving a complaint about the research product:

custsvcchina@integralife.com

References

1. Chinese Medical Doctor Association, *Specialist Consensus on the Standardized Treatment of Hydrocephalus in China* (2013 edition).

2. Aschoff A., Kremer P., Hashemi B. et al. The Scientific History of Hydrocephalus and its Treatment. Neurosurg Rev, 1999, 22: 67-93.

3. Song Ming, Zhan Xiangxin et al., Common Complications and Countermeasures of Ventriculo-peritoneal Shunt, Chinese Journal of Neurosurgery, 2011, 27(4): 428-430.

4. Vinchon M. & Dhellemmes P. The Transition from Child to Adult in Neurosurgery. Adv Tech Stand Neurosurg 32:3-24, 2007.

5. Natalie C. Edwards, Luella Engelhart et al. Cost-consequence Analysis of Antibiotic-impregnated Shunts and External Ventricular Drains in Hydrocephalus. J Neurosurg 122:139-147, 2015.

Appendix 1: Table of Product Specifications and Models

Model	EN Description
161015	ELSBERG VENTRICULAR CANNULA 5F
161016	ELSBERG VENTRICULAR CANNULA 7F
161017	ELSBERG VENTRICULAR CANNULA 9F
161055	DISPOSABLE SCOTT CANNULA 8CM
161056	DISPOSABLE SCOTT CANNULA 10CM
161057	ICP LUER CONNECTOR ASSY
451020	TOUHY NEEDLE
821201	ACCU-FLO*VENT CATH BA
821203	ACCU-FLO* VENT CATH 30CM
821221	ACCU-FLO VENT CATH DOTTED
821231	ACCU-FLO* VENT CATH RA 5
821232	ACCU-FLO* VENT CATH RA 7
821233	ACCU-FLO* VENT CATH RA 9
821234	ACCU-FLO* VENT CATH RA 11
821301	ACCU-FLO DIST CATH BA36L
821302	ACCU-FLO*DIST CATH BA36M
821303	ACCU-FLO*DIST CATH BA36H
821380	ACCU-FLO*DIST CATH OPEN
821401	ACCU-FLO*RESV 14MM
821411	ACCU-FLO*RESV SING FLAT
821501	ACCU-FLO* CONNECT STRGHT METAL
821504	ACCU-FLO* PL STR CONN
821507	ACCU-FLO* PL RT ANG CONN
821511	ACCU-FLO* CONNECT RT ANG
821515	DISPOSABLE CATH PASSER 36CM
821516	DISPOSABLE CATH PASSER 55CM
821517	DISPOSABLE CATH PASSER 65CM
821520	ACCU-FLO* PL 3-WAY CONN
821521	ACCU-FLO* 3 WAY CONN
821615	HOLTER* RICKHAM RESV PLAS
821616	HOLTER*RICKHAM RES,LGPLAS
821617	HOLTER*SALMON RICKHAM LP
821618	HOLTER*SELKER RES,SM,PLAS
821619	HOLTER*SELKER RESV LGPLAS
821621	VENT RES TR RICKHAM ST BA
821623	VENT RES TR RICKHAM LG BA
821625	VENT RES TR SAL-RIC ST BA
821630	CEREBRAL CATHETER BAI 3CM
821632	CEREBRAL CATHETER BAI 4CM
821634	CEREBRAL CATH RES BAI 5CM
821636	CEREBRAL CATH RES BAI 6CM

821638	CEREBRAL CATH RES BAI 7CM
821640	CEREBRAL CATH RES BAI 8CM
821642	CEREBRAL CATH RES BAI 9CM
821650	VENTRIC CATH BAR STR 15CM
821652	VENTRIC CATH BAR RA 3CM
821654	VENTRIC CATH BAR RA 4CM
821656	HOLTER* VENTRICULAR CATHETER R
821658	VENTRIC CATH BAR RA 6CM
821660	VENTRICULAR, CATHETER, RA
821662	VENTRIC CATH BAR RA 8CM
821664	HOLTER* VENTRICULAR CATHETER R
821666	HOLTER* VENTRICULAR CATHETER R
821670	ATRIAL CATH BAR TYPE A
821676	ATRIAL CATH BAR TYPE E
821682	PERIT CATH BA TYPE A 90CM
821684	PERIT CATH BA SALMON 90CM
821692	SALMON TUBE PASSER MDFD
821693	PERIT CATH PLACEMENT TOOL
821694	TYPE A CONNECTORS
821695	TYPE B CONNECTORS
821696	#N/A
821697	SHUNT FILTER
821715	HOFFMAN SHUNT PASS SHORT
821716	HOFFMAN SHUNT PASS LONG
823001	HAKIM PRECISION VALVE SYSTEM
823002	HAKIM PRECISION VALVE SYSTEM
823003	HAKIM PRECISION VALVE SYSTEM
823004	HAKIM PRECISION VALVE SYSTEM
823005	HAKIM PRECISION VALVE SYSTEM
823006	STD PV PRECHAMBER UNITIZED VL
823007	STD PV PRECHAMBER UNITIZED L
823008	STD PV PRECHAMBER UNITIZED ML
823009	STD PV PRECHAMBER UNITIZED MH
823010	STD PV PRECHAMBER UNITIZED H
823011	HAKIM PREC VALV W/PC - VL
823012	HAKIM PREC VALV W/PC - LO
823013	HAKIM PREC VALV W/PC - ML
823014	HAKIM PREC VALV W/PC - MH
823015	HAKIM PREC VALV W/PC - HI.
823016	INFANT HAKIM PRECISION VALVE
823017	INFANT HAKIM PRECISION VALVE
823018	INFANT HAKIM PRECISION VALVE
823019	INFANT HAKIM PRECISION VALVE
823020	INFANT HAKIM PRECISION VALVE
823021	MICRO PV W RICKHAM UNITIZED VL

823022	MICRO PV W RICKHAM UNITIZED L
823023	MICRO PV W RICKHAM UNITIZED M
823024	MICRO PV W RICKHAM UNITIZED MH
823025	MICRO PV W RICKHAM UNITIZED H
823026	MIRCO VLV, PREC, NO CATH, V LO
823027	MIRCO VLV, PREC, NO CATH, LOW
823028	MIRCO VLV, PREC, NO CATH, MED
823029	MIRCO VLV, PREC, NO CATH, M HI
823030	MIRCO VLV, PREC, NO CATH, HIGH
823035	MICRO PV UNITIZED VL
823036	MICRO PV UNITIZED L.
823037	MICRO PV UNITIZED M
823038	MICRO PV UNITZED MH
823039	MICRO PV UNITIZED H
823041	HAKIM VENTRICULAR CATH
823044	HAKIM ATRIAL CATH, 46CM
823045	HAKIM PERITON CATH,120CM
823048	HAKIM STR CONN S/S
823049	CODMAN*-MEDOS* RTANG CONNECTOR
823052	ACCESSORIES MEDOS
823053	Shunt Connector Titanium Strl
823055	HAKIM VALVE INTROD/PLAST
823082	HAKIM PREC, VL INTRD, PL CNNCT
823083	HAKIM PREC, L INTRD, PL CNNCT
823084	HAKIM PREC,ML INTRD, PL CNNCT
823085	HAKIM PREC,MH INTRD, PL CNNCT
823086	HAKIM PREC, H INTRD, PL CNNCT
823090	SIPHONGUARD, CSF FLD CONTRL DV
823095	MICRO PV W RICKHAM VL
823096	MICRO PV W RICKHAM L
823097	MICRO PV W RICKHAM ML
823098	MICRO PV W RICKHAM MH
823099	MICRO PV W RICKHAM H
823100	HAKIM PROGRAMMABLE VALVE
823101	MEDOS* PROG INFANT VALVESYSTEM
823110	PROG VALVE CLYNDRICAL W PRECHA
823111	STD CHPV W PRECHAMBER UNITIZED
823112	PROG VALVE MICRO
823113	MICRO CHPV W RICKHAM UNITIZED
823114	MICRO CHPV UNITIZED
823115	PROG VALVE CLYNDRICAL
823116	PROG VAVLE MICRO W RICKHAM
823136	PROG VALVE RIGHT ANGLE W SG
823146	CHPV RT ANG RES W SG UNITIZED
823148	CHPV RT ANG RESERVOIR UNITIZED

823162	PROG VALVE INLINE W SG
823164	PROG VALVE INLINE
823182	PROG VALVE RIGHT ANGLE W SG
823184	PROG VALVE RIGHT ANGLE
823261	PREC RT ANG RES UNTZ SG VL
823262	PREC RT ANG RES UNTZ SG L
823263	PREC RT ANG RES UNTZ SG M
823264	PREC RT ANG RES UNTZ SG MH
823265	PREC RT ANG RES UNTZ SG H
823281	PREC RT ANG RES UNTZ VL
823282	PREC RT ANG RES UNTZ L
823283	PREC RT ANG RES UNTZ M
823284	PREC RT ANG RES UNTZ MH
823285	PREC RT ANG RES UNTZ H
823361	PRECISION VALVE SYSTEM RIGHT
823362	PRECISION VALVE SYSTEM RIGHT
823363	PRECISION VALVE SYSTEM RIGHT
823364	PRECISION VALVE SYSTEM RIGHT
823365	PRECISION VALVE SYSTEM RIGHT
823801	SYST VALVE NP VL ANGL INT
823802	SYST VALVE NP L ANGL INT
823803	SYST VALVE NP M ANGL INT
823804	SYST VALVE NP MH ANGLE INT
823805	SYST VALVE NP H ANGL INT
823806	PV INLIN UNIT INTGRL CON VL
823807	PV INLIN UNIT INTEGRAL CON L
823808	PV INLIN UNIT INTEGRL CON ML
823809	PV INLIN UNIT INTEGRL CON MH
823810	PV INLIN UNIT INTEGRL CON H
823811	SYST VALVE NP VL LINE ASD
823812	SYST VALVE NP L LINE ASD
823813	SYST VALVE NP M LINE ASD
823814	SYST VALVE NP MU LINE ASD
823815	SYST VALVE NP H LINE ASD
823816	SYST VALVE NP VL LINE INT
823817	SYST VALVE NP L LINE INT
823818	SYST VALVE NP M LINE INT
823819	SYST VALVE NP MH LINE INT
823820	SYST VALVE NP H LINE INT
823821	PV INLIN W SG INTGRAL CON VL
823822	PV INLIN W SG INTGRAL CON L
823823	PV INLIN W SG INTGRAL CON ML
823824	PV INLIN W SG INTGRAL CON MH
823825	PV INLIN W/SG INTGRAL CON H
823832	PROG VALVE INLINE W SG

823834	PROG VAVLE INLINE
823838	PROG VALVE RIGHT ANGLE
823842	CHPV INLIN/SG INTEGRAL CON
823844	PROGRAMMABLE VALVE INLINE UNTZ
824095	DISPOSABLE SPLIT TROCAR
825461	IN LINE PRECISION VAVLE SG VL
825462	IN LINE PRECISION VAVLE SG L
825463	IN LINE PRECISION VAVLE SG M
825464	IN LINE PRECISION VAVLE SG MH
825465	IN LINE PRECISION VAVLE SG H
825471	IN LINE PRECISION VAVLE VL
825472	IN LINE PRECISION VAVLE L
825473	IN LINE PRECISION VAVLE M
825474	IN LINE PRECISION VAVLE MH
825475	IN LINE PRECISION VAVLE H
825481	RT ANGLE PRECISION VALVE SG VL
825482	RT ANGLE PRECISION VALVE SG L
825483	RT ANGLE PRECISION VALVE SG M
825484	RT ANGLE PRECISION VALVE SG MH
825485	RT ANGLE PRECISION VALVE SG H
825491	RT ANGLE PRECISION VALVE VL
825492	RT ANGLE PRECISION VALVE L
825493	RT ANGLE PRECISION VALVE M
825494	RT ANGLE PRECISION VALVE MH
825495	RT ANGLE PRECISION VALVE H
826001	#N/A
826010	ACCU-FLO*BURRHOLE BUTTONS
826025	ACCU-FLO* SIL COVER 3/8
826100	ACCU-FLO* CSF RESV 14 MM
826101	ACCU-FLO* CSF RESV 24 MM
826200	JAMES L-P SHUNT 25CM
826201	JAMES L-P SHUNT 50CM
826202	JAMES L-P SHUNT 80CM
828501	UNI-SHUNT*W/RES 53CM 2-5
828502	UNI-SHUNT*W/RES 53CM 5-9
828511	UNI-SHUNT*W/RES 62CM 2-5
828512	UNI-SHUNT*W/RES 62CM 5-9
828521	UNI-SHUNT*W/RES 78CM 2-5
828522	UNI-SHUNT*W/RES 78CM 5-9
828531	UNI-SHUNT*W/RES 90CM 2-5
828532	UNI-SHUNT*W/RES 90CM 5-9
828533	UNI-SHUNT*W/RES 90CM 9-14
828541	UNI-SHUNT*W/RES 102CM 2-5
828542	UNI-SHUNT*W/RES 102CM 5-9
828543	UNI-SHUNT*/RES 102CM9-14

828591	UNI-SHUNT*W/RESV ANCH.CL.
831371	#N/A