Clinical Investigation Plan

CP362

Investigation of a new rectal catheter for users of transanal irrigation

April 2024 – June 2024

Master

Version 4.0

CHANGE LOG

VERSION NUMBER	ISSUED BY (INITIALS)	COMMENTS (MAJOR CHANGES SINCE LAST REVISION)
1.0	[redacted]	First approved version
2.0		Study design-picture changed, LPO changed to June 2024, section 5.3.2 has been updated, section 5.3.6 has been added, additional comment field added to Visit 1 and Visit 2 and unscheduled visit added
3.0		[redacted]
4.0		Changes made to section. 4.1, 6.2.1, 8.1, 8.2, and 14.4

SYNOPSIS OF THE CLINICAL INVESTIGATION

Title:

Investigation of a new rectal catheter for users of transanal irrigation.

Investigational device and comparator device:

The investigational device in this clinical investigation is a newly developed rectal catheter (CP362 rectal test catheter) used for transanal irrigation (TAI).

The investigational device is a rectal catheter, that will be tested [redacted] and will be used together with the CE-marked Peristeen Plus TAI system [redacted] Thus, Peristeen Plus TAI system, the CP362 rectal test catheter and Peristeen Gel comprises the investigational device.

In this clinical investigation the CE-marked Peristeen Plus rectal balloon catheter will be used as a comparator device. The Peristeen Plus rectal balloon catheter will also be used together with the Peristeen Plus TAI system.

The investigational device is not a CE-marked device, and it will be provided by Coloplast A/S. Both the comparator device and the Peristeen Gel [redacted] will also be provided by Coloplast A/S.

Intended use:

Both the investigational device and the comparator device are accessories to the Peristeen Plus TAI system. The Peristeen Plus TAI system is intended to perform TAI, which is an effective bowel management technique that empties faeces from the lower colon in a controlled manner, allowing patients to be in control of when and where they empty their bowels. The Peristeen Gel is intended to be used with the CE-marked Peristeen Anal Plug to make insertion easier. [redacted]

Objectives:

Primary objective:

The primary objective is to obtain indications that a new rectal catheter can be used for TAI.

Secondary objective:

The secondary objective will include assessment of safety [redacted]

Design of the investigation:

The clinical investigation is an exploratory, randomised controlled, open-labelled, crossover investigation. The clinical investigation will be conducted as a multi-centre clinical investigation in two different clinical investigation sites[redacted]

The aim is to randomize 20 subjects who are currently using a rectal balloon catheter for TAI procedure. Furthermore, the subjects must have been using a rectal balloon catheter for at least four weeks prior study inclusion.

The total clinical investigation duration for each subject will be up to 17 days, consisting of three site visits: Screening Visit (V0), Baseline Visit (V1) and Visit 2 (V2). [redacted]

[redacted] V0 and V1 can be performed on the same day. V1 and V2 must be scheduled on a day where the subject normally performs the TAI procedure, and V2 must furthermore be scheduled within 14 days after V1. At V1 and V2 the TAI procedure will be performed in a hospital setting.

[redacted]

Expected duration of the clinical investigation:

The clinical investigation will be conducted from:

First patient in (FPI): April 2024

Last patient out (LPO): June 2024

Database lock (DBL): June 2024

Clinical Investigation Report (CIR): November 2024

Primary endpoint:

The primary endpoint is: Was it possible to perform transanal irrigation (assessed after irrigation at V1 and V2)? (Yes/no).

Population/subjects:

As this is an exploratory clinical investigation it is assumed that 20 randomized subjects will be adequate for obtaining indications on performance and feasibility of the investigational device.

The subjects included in the clinical investigation must comply with the inclusion- and exclusion criteria listed below:

Inclusion criteria

- Has given written informed consent
- Is at least 18 years old
- Has full legal capacity
- Has used trans anal irrigation with balloon catheter for at least four weeks prior to inclusion
- Performs trans anal irrigation minimum 3 times/week
- Is able to follow study procedures assessed by investigator

Exclusion criteria

- Has known anal or colorectal stenosis
- Has active/recurrent colorectal cancer
- Is within 3 months of anal or colorectal surgery
- Is within 4 weeks of endoscopic polypectomy
- Has ischaemic colitis
- Has acute inflammatory bowel disease
- Has acute diverticulitis
- Is participating in any other clinical study that may interfere with this study assessed by investigator
- Is pregnant or breastfeeding

LIST OF ABBREBIATIONS

ABBREVIATION	WRITTEN OUT	EXPLANATION (IF APPLICABLE)
ADE	Adverse Device Effect	See section 16.2
AE	Adverse Event	See section 16.1
ASADE	Anticipated Serious Adverse Device Effect	See section 16.4.2
CIP	Clinical Investigation Plan	
CIR	Clinical Investigation Report	
CM	Clinical Manager	
CRA	Clinical Research Associate	
CRF	Case Report Form (paper or electronic)	Questionnaire to be used for data collection
DBL	Database lock	
DD	Device deficiency	
EC	Ethics Committee	
eCRF	Electronic Case Report Form	
EDC	Electronic data capturing	
FPI	First patient in	
HCP	Health care professional	
IB	**Investigator's Brochure**	Compilation of the current clinical and non-clinical information on the investigational medical device(s,) relevant to the clinical investigation.
ICF	Informed Consent Form	
IFU	Instruction For Use	
ITT	Intention to Treat	
LPO	Last patient out	
pCRF	Paper Case Report Form	
PI	Principal Investigator	Qualified person responsible for conducting the clinical investigation at an investigation site. If the clinical investigation is conducted by a team of individuals at an investigation site, the PI is the responsible leader of the team. Whether this is the responsibility of an individual or an institution can depend on national regulations.
SADE	Serious Adverse Device Effect	See section 16.4.1
SAE	Serious Adverse Event	See section 16.4
SIF	Subject Information Form	
TAI	Transanal irrigation	
USADE	Unanticipated Serious Adverse Device Effect	See section 16.4.3
VAS	Visuel analog scale	

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1. List of personnel involved in the investigation

1.1. Sponsor representatives

Coloplast A/S located at Holtedam 1-3, 3050 Humlebæk in Denmark is the Sponsor for this clinical investigation.

COORDINATING CLINICAL MANAGER	ASSOCIATE CLINICAL MANAGER
[redacted]	[redacted]
HEAD OF CLINICAL TRIAL MANAGEMENT	**SENIOR CLINICAL STRATEGY PROJECT MANAGER**
[redacted]	[redacted]
PRINCIPAL BIOSTATISTICAN	**DATA MANAGEMENT SPECIALIST**
[redacted]	[redacted]

In case of emergency, please contact the Clinical Managers (CM) from the above list of sponsor representatives.

1.2. Investigators

Details of sites and Principal Investigators (PI) are listed in the list below.

COORDINATING PRINCIPAL INVESTIGATOR	PRINCIPAL INVESTIGATOR
[redacted]	[redacted]

2. Justification for conducting the clinical investigation

This is an exploratory clinical investigation (first in human) investigating the feasibility and performance of a new rectal catheter for TAI procedure.

Based on recent consensus, TAI should be considered as a therapeutic modality for patients with bowel dysfunction failing to respond to conservative bowel management (e.g., laxative and diet), before resorting to invasive interventions (such as antegrade enemas, sacral nerve stimulation and stomas)[1-7]. This was also one of the conclusions in a meta-analysis comparing treatments for faecal incontinence[8].

The main components of the Coloplast A/S produced Peristeen Plus TAI system consist of a control unit (featuring a pneumatic bulb pump and a four-position rotary switch), a water bag (featuring a pressure relief valve) and a pre-coated rectal balloon catheter or cone catheter.

[redacted]

The data will not be used for conformity assessment; therefore, the study will be submitted to the Danish Ethical Committee (EC) under Article 82 of the Medical Device Regulation EU 2017/245.

3. Objectives

The aim of this clinical investigation is to explore the feasibility of performing TAI by using the newly developed investigational device, CP362 rectal test catheter, compared to the CE-marked Peristeen Plus rectal balloon catheter.

3.1. Objectives

Primary objective:

The primary objective is to obtain indications that a new rectal catheter can be used for TAI.

Secondary objective:

The secondary objective will include assessment of safety [redacted]

4. Investigational device and comparator device

4.1. Description of investigational device

The investigational device will be classified according to MDR EU 2017/745 and MDCG-2021-24 Guidance on classification of medical devices.

CP362 test catheter will be classified as Class I, based on rule 5:

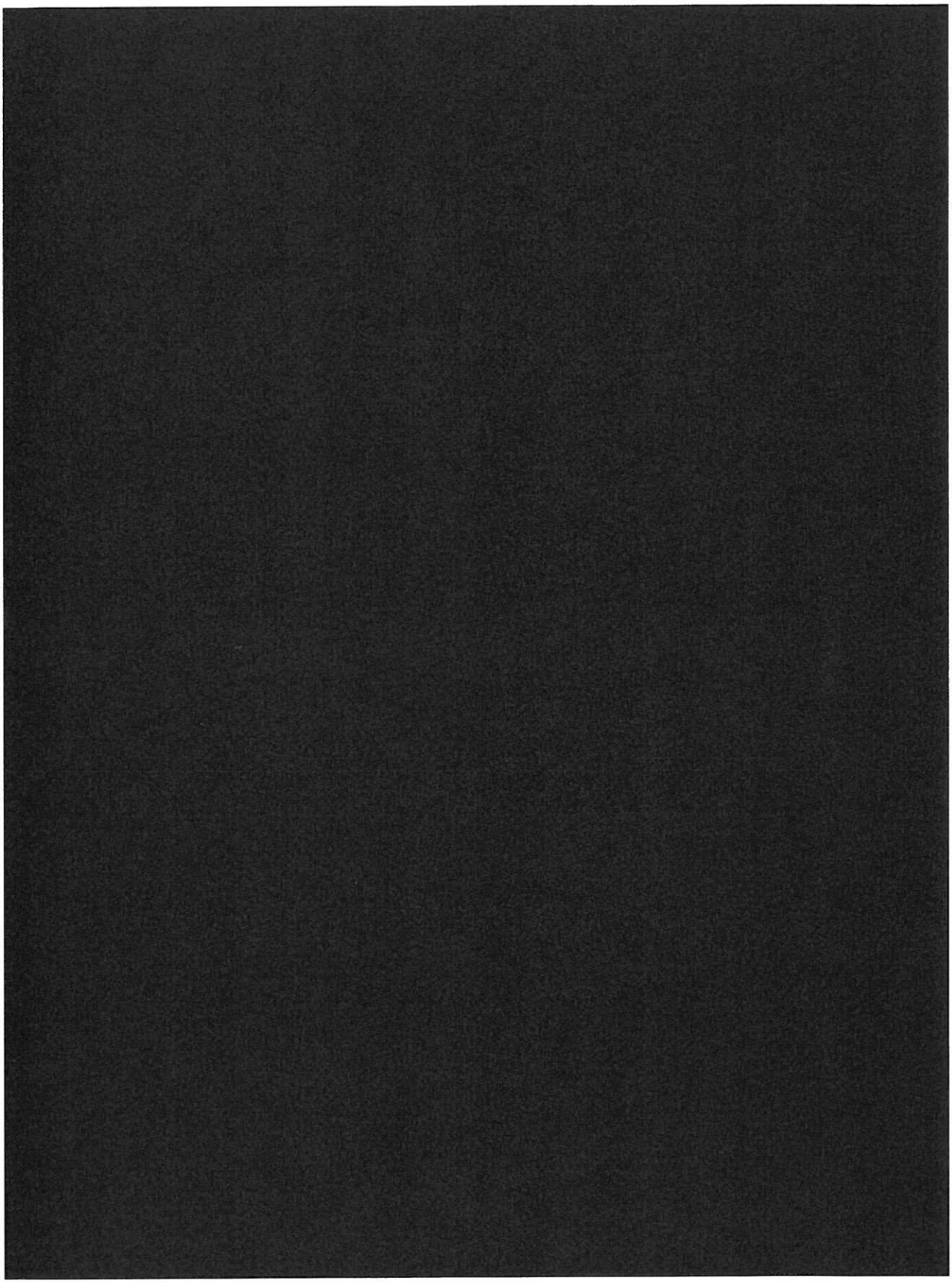
"All invasive devices with respect to body orifices, other than surgically invasive devices, which are not intended for
connection to an active medical device or which are intended for connection to a class I active device are classified
as:
- *Class I if they are intended for transient use"*

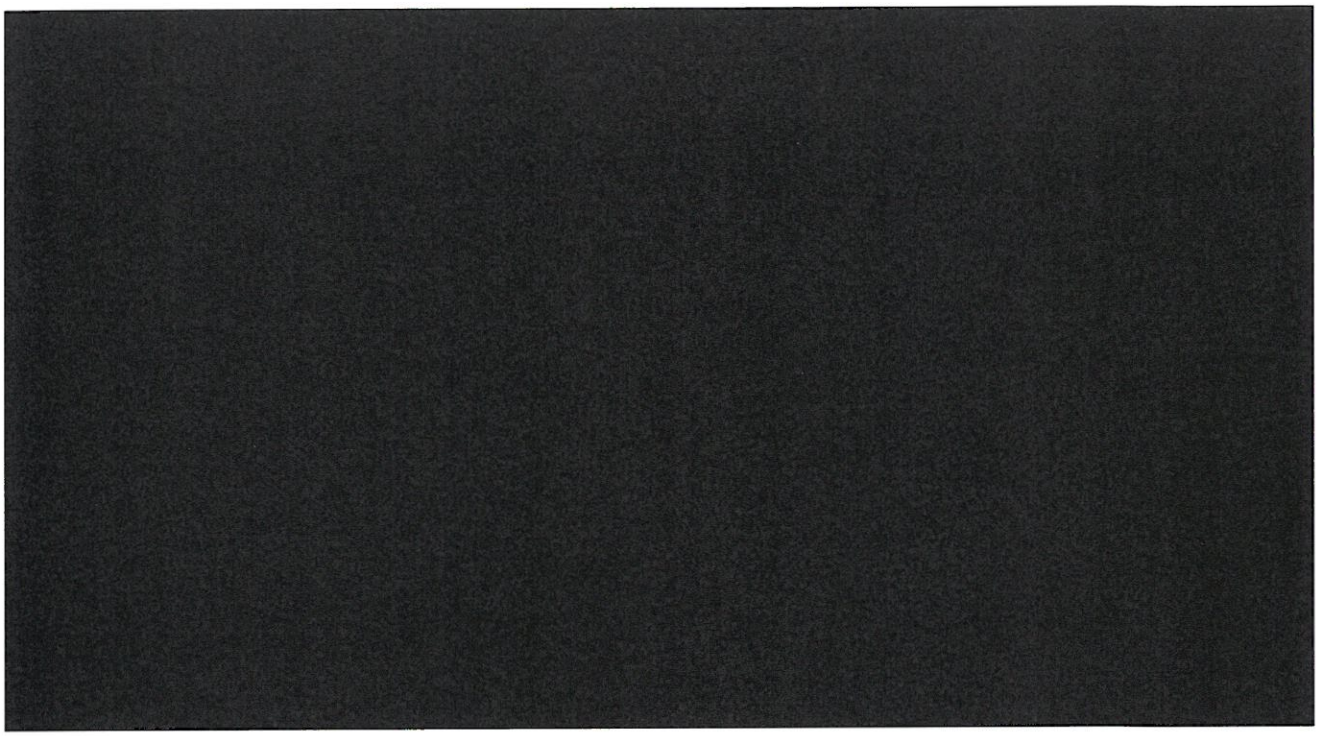
The test catheter is invasive and intended for transient use, therefore, the device is class I.

CE-marked Peristeen Plus TAI system is Class I, non-sterile, and CE-marked Peristeen Gel is Class IIb, non-sterile.

TAI procedure is performed by introducing water into the rectum using a rectal catheter. The water fills up in the large intestine and causes peristaltic movement in the bowels. After introducing the appropriate amount of water into the bowel, water and stools are emptied into the toilet, and the rectal catheter is discarded.

[redacted]





4.1.1. Manufacturing

Responsible for manufacturing the investigational device:

Coloplast A/S

[redacted]

4.2. Identification and traceability of the devices

All investigational devices are labelled as per regulations and included "exclusively for clinical investigation" on the label. The devices are also identified with a study number, device name/code, and item/lot number and is accounted for through a sponsor accountability log.

Upon EC approval, investigational devices and comparator devices will be shipped to the principal investigator or designee at sites. Additionally, all investigational devices and comparator devices will be accounted for and documented on a site accountability log. The receipt and disposition of all investigational devices and comparator devices will be verified through monitoring. All unused devices will be returned to Coloplast A/S at the conclusion of the study.

4.3. Intended use of the device in the clinical investigation

The investigational device is intended to perform TAI procedures together with the CE-marked Peristeen Plus TAI system. TAI is an effective bowel management technique that empties faeces from the lower colon in a controlled manner, allowing patients to be in control of when and where they empty their bowels. [redacted]

Contraindications for use are identical to the contraindications for the Peristeen Plus rectal balloon catheter. The contraindications are: Known anal or colorectal stenosis, active or recurrent colorectal cancer, anal or colorectal surgery within three month, endoscopic polypectomy within four weeks, ischaemic colitis, acute inflammatory bowel disease or acute diverticulitis.

4.4. Intended population for the device

The intended population for the new CP362 rectal test catheter is adults who are currently using a rectal balloon catheter for TAI procedure.

4.5. Handling of the investigational device

The handling of the investigational device is described in detail in the Instruction for Use (IFU) (see appendix A), which is included in all boxes with the investigational device. It is stated in the IFU that the investigational device is for single-use only. Reprocessing, washing, disinfection, and sterilisation may compromise device characteristics, causing additional risk of physical harm to or infection of the user. [redacted]

All PIs and designees will receive training by the sponsor in the handling and correct use of the investigational device. All training will be documented. For further details regarding the investigational device, please see the Investigators Brochure (IB)[redacted]

4.6. Total number of devices intended for the clinical investigation

Approximately 20 randomized subjects will be included in this clinical investigation and have a TAI procedure performed at V1 and V2 with the investigational device or the comparator device in a randomized order. Following number of investigational devices, comparator devices and Peristeen Plus TAI systems intended for the clinical investigation will be needed:

- 560 investigational devices (140 [redacted] Multiple factors are unknown and the sum of these are driving for a high buffer when estimating the total number of the investigational devices needed for this clinical investigation.
- 28 Peristeen Plus rectal balloon catheters [redacted]
- 64 Peristeen Plus TAI systems.

4.7. Description of the comparator device

In this clinical investigation the CE-marked Peristeen Plus rectal balloon catheter is used as a comparator device. The Peristeen Plus rectal balloon catheter will be used together with the CE-marked Peristeen Plus TAI system.

As the comparator device is already on the market and will be used within the intended use in this investigation, it is not considered as an investigational device according to ISO 14155:2020 and is thus not described in further details here.

Coloplast A/S will provide comparator devices to sites. To ensure that the site has enough supplies, more comparator devices than needed will be provided by Coloplast A/S.

4.8. Device accountability

All access to the investigational devices and comparator devices used in this clinical investigation is controlled by storage procedures and device accountability logs as described below. The investigational devices and comparator devices must only be used in this clinical investigation and only as stated in the clinical investigation plan (CIP).

Sponsor keeps a device accountability log that states the physical location of all investigational devices from shipment of investigations devices to the investigational sites until return of or disposal.

The PI or delegate keeps records documenting the receipt, use and return, and disposal of the investigational devices, which includes:

- Name of device

- Date of receipt
- Number of devices/retail boxes received
- Identification of each investigational device (LOT number and item number)
- The expiry date
- The date(s) of use
- Subject identification
- The date of return unused, expired or malfunctioning investigational devices.

5. Design of the clinical investigation

5.1. General

The clinical investigation is an exploratory, randomised controlled, open-labelled, crossover investigation (see figure 5). The clinical investigation will be conducted as a multi-centre clinical investigation in two different clinical investigation sites [redacted]

The total clinical investigation duration for each subject will be up to 17 days, consisting of three site visits: Screening Visit (V0), Baseline Visit (V1) and Visit 2 (V2). [redacted] V0 and V1 can be performed on the same day. V1 and V2 must be scheduled on a day where the subject normally performs the TAI procedure, and V2 must furthermore be scheduled within 14 days after V1. At V1 and V2 the TAI procedure will be performed in a hospital setting.

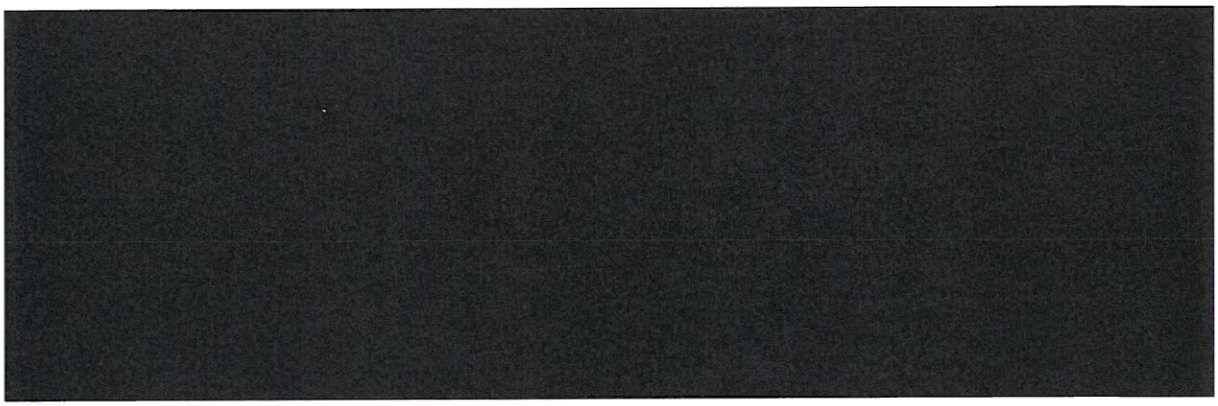
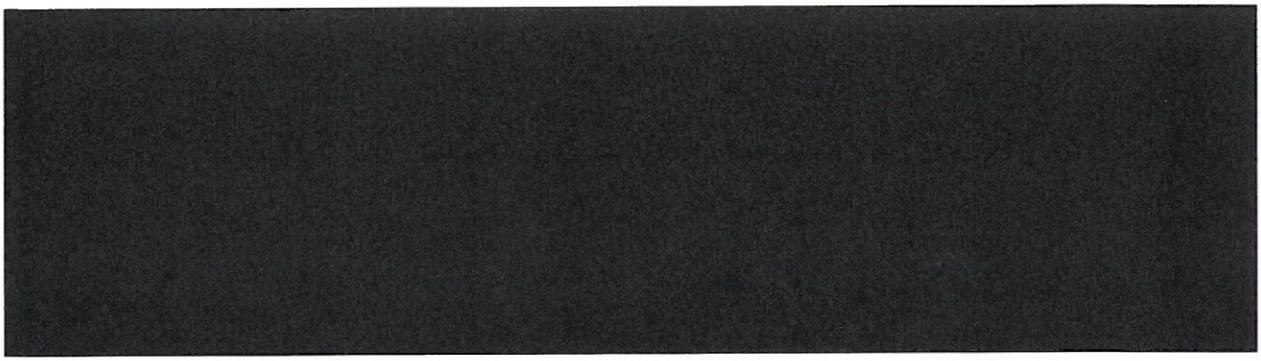


Figure 5: Design of the clinical investigation

5.2. Primary endpoint

The primary endpoint is: Was it possible to perform transanal irrigation (assessed after irrigation at V1 and V2)? (Yes/no).

5.3. Assessments



[redacted]

5.3.4. Safety

- Adverse events
- Device deficiency.

[redacted]

[redacted]

5.4. Rationale for selection and measurement of endpoints

The endpoints and assessment have been selected to support the aim of the investigation exploring the feasibility of performing TAI with the investigational device.

The primary endpoint has been selected to evaluate if it is feasible to use investigational device for TAI to fulfil its intended purpose. Irrigation is defined according to the IFU and must be done with the regular volume of water used by the subject.

[redacted]

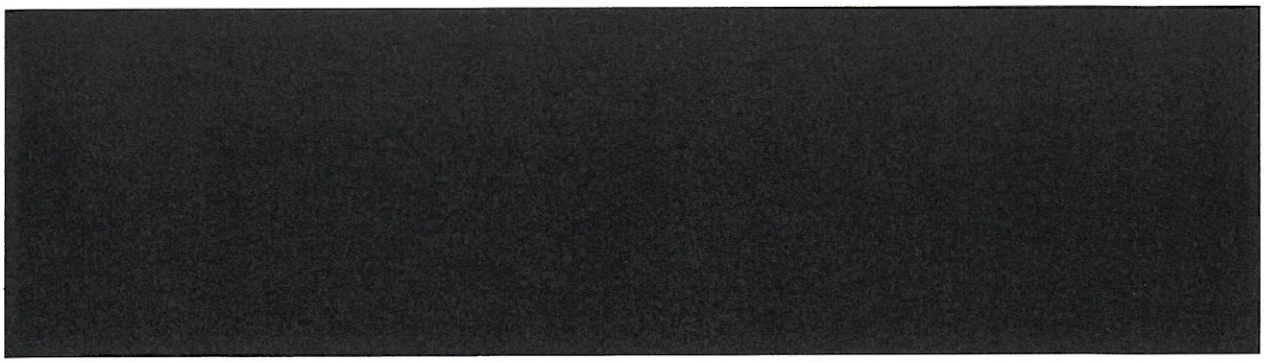
5.5. Demography and potential compromising factors

The following baseline data will be collected and reported at V1 by the PI or delegate:

Demographic information:

- Age at time of enrolment: Years
- Sex: Male, female
- Height: cm
- Weight: kg.

[redacted]



5.7. Randomisation Procedure

All subjects that have given informed consent and meet the inclusion and exclusion criteria will be randomised to one of two treatment sequences:

- First sequence: Investigational device at V1 and comparator device at V2
- Second sequence: Comparator device at V1 and investigational device V2.

The Rave RTSM™ from Dassault Systèmes/Medidata is a validated computer randomization solution, that will be used for the randomization in this investigation. A randomization will be implemented, in which, subjects are to be randomly assigned to one of two sequences in block sizes of 4.

5.8. Blinding

Subjects and HCP will not be blinded in this investigation. Furthermore, since this is an exploratory investigation, Coloplast A/S personnel (e.g., CMs, Data Management Specialist, Biostatistican) will also not be blinded.

5.9. Total expected duration of the clinical investigation

The dates below are approximate, and no subjects will be enrolled before all required approvals have been obtained. If changes are required, applicable EC will be notified.

First patient in (FPI): April 2024

Last patient out (LPO): June 2024

Database lock (DBL): June 2024

Clinical Investigation Report (CIR): November 2024.

6. Clinical Investigation population

The clinical investigation will be conducted in approximately 20 randomized subjects enrolled in two clinical investigation sites [redacted]

6.1. Eligibility criteria

To be included in the investigation, the subjects must comply with the selection criteria described below:

6.1.1. Inclusion criteria

For an eligible subject, all inclusion **criteria described below must be answered** "yes":

Table 1: Inclusion criteria

Inclusion criteria	Justification for inclusion criteria
1. Has given written informed consent	To meet the Helsinki declaration
2. Is at least 18 years old	To meet the Helsinki declaration
3. Has full legal capacity	To meet the Helsinki declaration
4. Has used TAI irrigation with balloon catheter for at least 4 weeks prior to inclusion	To ensure subjects can use TAI and is familiar with the sensation of a balloon catheter to be able to compare with the new rectal catheter
5. Performs TAI minimum 3 times/week	To ensure a homogenous population that performs TAI on a regular basis for comparability within a relative small sample size
6. Is able to follow study procedures assessed by investigator	To ensure study completion of subjects

6.1.2. Exclusion criteria

For an eligible subject, all exclusion criteria **described below must be answered** "no":

Table 2: Exclusion criteria

Exclusion criteria	Justification for inclusion criteria
1. Has known anal or colorectal stenosis	IFU contraindication for TAI with Peristeen/Peristeen Plus
2. Has active/recurrent colorectal cancer	IFU contraindication for TAI with Peristeen/Peristeen Plus
3. Is within 3 month of anal or colorectal surgery	IFU contraindication for TAI with Peristeen/Peristeen Plus
4. Is within 4 weeks of endoscopic polypectomy	IFU contraindication for TAI with Peristeen/Peristeen Plus
5. Has ischaemic colitis	IFU contraindication for TAI with Peristeen/Peristeen Plus
6. Has acute inflammatory bowel disease	IFU contraindication for TAI with Peristeen/Peristeen Plus
7. Has acute diverticulitis	IFU contraindication for TAI with Peristeen/Peristeen Plus
8. Is participating in any other clinical study that may interfere with this study (assessed by investigator)	To ensure the scientific integrity of the study
9. Is pregnant or breastfeeding	IFU caution for TAI with Peristeen/Peristeen Plus

6.1.3. Pregnancy and breastfeeding

For female subjects with childbearing potential (they have had at least one period during the last 12 months), a urine pregnancy test will be performed at the Baseline Visit, to ensure the subject is not pregnant. The urine pregnancy test will be performed by dip-stick at the clinical investigational site. Furthermore, the female subjects should not be breastfeeding, when participating in the clinical investigation. If the subject becomes pregnant during the investigation, it is important, that the subject informs the PI or delegate representative immediately. The medical adviser will then consider whether she should continue in the investigation.

6.2. Recruitment and enrolment

The recruitment of potential subjects will only commence once authorisation and approval from EC. The recruitment period from first subject enrolled to last subject enrolled is expected to be approximately two month.

Table 3: Overview of the recruitment process

Recruitment method	Sites	Coloplast database
Potential candidates	[redacted]	
First contact		
Screenings visit (V0)	At the scheduled Screening Visit (V0) the Principal Investigator or delegate will introduce the investigation and review the inclusion and exclusion criteria. If the subject wishes to reconsider his/her participation at V0, the subject has the right to wait a minimum of 24 hours before deciding on participation. If the subject hereafter decides to participate in the clinical investigation, a Baseline Visit (V1) will be scheduled unless performed the same day as the screening visit. The screening can be performed at the site or as a phone call. If the subject does not meet the inclusion criteria or meets the exclusion criteria, this will be registered at the Subject Pre-Screening Log.	
Baseline visit (V1)	If the subject decides to participate and it is certain that it is understood what the investigation entails, the subject will be asked to sign the SIF/ICF. When the SIF/ICF is signed, the subject is considered included in the investigation.	

6.2.1. Informed consent process

Written informed consent is obtained from all subjects participating in the investigation after thorough written and verbal information. The information is given by the PI or designee in the subjects' native non-technical language. Each subject will be fully informed about the aim of the investigation, procedures, potential risks, or inconveniences and/or expected benefits, and all anticipated adverse device effects. The subject will receive both written and verbal information to ensure that the subject understands what was read and explained and can freely agree to participate in the investigation. The subject will, beforehand, also be informed about the possibility of bringing a companion to any subsequent visits. The verbal information must be given in reasonable quite surroundings.

The subject has the right to wait a minimum of 24 hours before deciding on participation and will be informed that their participation is voluntary and that they may leave the investigation at any time, without this having any influence on their further treatment.

The informed consent signature form includes personally dated signatures of the subject and the PI or designee (must be a medical doctor by profession) will be responsible for conducting the informed consent process. A copy will be provided to the subject.

If new information is to be given during the investigation, sponsor will inform the PIs, and the new information is given to the subjects by the PI. If new information becomes available that can significantly affect a subject's future health and medical care that information will be provided to the subject in written form. The CM is responsible for writing the information and providing the approved Subject Information and Consent Form to PIs that will further provide it to the subjects. If applicable, all affected subjects shall be asked to confirm their continuing informed consent in writing.

This procedure also applies to informed consent obtained from a subject's legal representative. The procedure cannot waive the subjects' legal rights.

6.2.2. Point of enrolment

A subject is considered enrolled in the investigation at the time of consent. Prior to any clinical investigation related procedures are undertaken, the subject signs and dates the informed consent form. The expected duration for each subject is described in section 5.1.

6.2.3. Subject screening and randomization failures

Subjects that have signed the informed consent form but fail to comply with the eligibility criteria are considered screening failures. A screening failure will be replaced by a new subject if the subject is not randomized.

If a subject is randomized by mistake (e.g., if the PI realizes that the subject is not eligible after the subjects has been randomized), this is considered a randomization failure. If the subject has not been treated and has no data registered on the primary endpoint the subjects can be replaced by a new subject if the new subject can complete the investigation within timelines (before last subjects last visit and within visit windows).

6.2.4. Subject withdrawal criteria

The subject is allowed to withdraw from the investigation at any time for whatever reason without any consequences for their future treatment outside the clinical investigation. The Investigator may withdraw a subject from the investigation at any time if they judge it to be the subject's interest.

The investigator must withdraw a subject from the investigation due to:

- Noncompliance with the CIP impacting the scientific integrity of the investigation.
- If subject's safety and wellbeing is compromised by further participation.
- Subjects lost to follow-up. At least three documented attempts will be made to verify subjects lost to follow-up. If, after these attempts are made, and there is still no response, the subject will be withdrawn from the clinical investigation.

6.2.5. Subject Identification and Confidentiality

Subjects will be identified on the Case Report Form (CRF), and any other document transmitted to the sponsor by the PI or clinical site staff, by a unique identification number.

The PI for each clinical investigation site will maintain, as part of the investigational file, a list identifying all subjects entered the clinical investigation.

7. Procedures

7.1. Transanal irrigation set-up

Subjects are allowed to lay down during the insertion of the rectal catheter (both the investigational device and the comparator device). After insertion the rectal catheter the subjects should move to a toilet chair to complete the TAI procedure. When the TAI procedure is completed the subjects can move to the toilet to empty their bowel.

7.2. Clinical investigation-related procedures

Visit 0 – Screening visit and study information:

- Introduction to the investigation and review of Subject Information Form/Informed Consent Form
- Scheduling V1 unless performed the same day as V0
- Register the potential subject on the pre-screening log.

Visit 1 – Inclusion and TAI procedure

- Introduction to the investigation reviewed and confirmed by subject
- Sign Informed Consent Form
- Allocation of subject ID number
- For female subjects of childbearing potential urine pregnancy dipstick must be done
- Check of inclusion and exclusion criteria
- Obtain relevant medical history (assessed by PI)
- Collection of baseline data (see section 5.5)
- Randomization electronically in [redacted]
- Was it possible to perform the TAI procedure? [redacted]
- Complete adverse events, device deficiencies, vigilance or protocol deviation forms, if applicable (see section 5.3.4)
- Complete Electronic Case Report Form (eCRF) incl. additional comments in comment field (if relevant)
- Schedule V2 (up to 14 days after V1) [redacted]

Visit 2 – TAI procedure

Ensure the subjects well-being and that the subject is still comfortable to participate in the clinical investigation.

- Review for safety adverse events/serious adverse events/adverse device effects/protocol deviations/device deficiency

[redacted]

- Was it possible to perform the TAI procedure?

[redacted]

- Complete adverse events, device deficiencies, vigilance form or protocol deviation forms, if applicable
- Complete eCRF, including termination form and additional comments in comment field (if relevant)

[redacted]

Unscheduled visit/call

If an unscheduled visit/call is needed the unscheduled form in the eCRF must be completed.

7.3. Flow-chart

Table 4: Connection between visits and assessments

Visit (V)	V0	V1	V2
Timing of visit (weeks)	0	0	1-14 days after V0
Activity			
Introduction to investigation and review of Subject Information Form/Informed Consent Form	X		
Signed Informed Consent		X	
Allocation of subject number		X	
Check of in- and exclusion criteria		X	
Pregnancy test (urine dipstick) – for subjects of childbearing potential only		X	
Baseline information		X	
Randomization		X	
[redacted]		X	X
		X	X
		X	X
			X
Assessment of subject's wellbeing and compliance with CIP		X	X
AEs/ADEs/SAEs/SADEs/DD		X	X
Protocol deviations		X	X
Complete eCRF		X	X
Termination form			X

7.4. Concomitant treatment

There is no specific requirement to concomitant medication.

7.5. Case report forms

All assessments and observations throughout the investigation for each subject must be carefully recorded in the eCRF.

CRFs will be filled in by the principal investigator and/or delegated site personal, who have signed the Site Personnel Signature and Delegation List and Clinical Investigation Training Log.

The delegated site personal will be required to complete e-learning prior to system access. Delegated personal will receive credentials.

It is the responsibility of the principal investigator that all data are entered promptly and correctly.

8. Risk – benefit analysis and ethical considerations

8.1. Risk-benefit analysis of the investigational device

A risk management process has been performed in accordance with the requirements stated in ISO 14971 Application of risk management to medical devices and in accordance with internal Coloplast A/S procedures, including design verification, validated test methods, risk analysis and completion of a biological evaluation report for the investigational device.

There is a series of ISO standards "ISO 10993 - Biological Evaluation of medical devices" that dictates how to ensure that medical devices are safe and biocompatible for use in humans. For the investigational devices in CP362 we have followed this series, and performed the required testing, thus we are able to state the above. This is standard procedure for ensuring biocompatibility and safety in medical devices.

It is concluded that the investigational device is safe and biocompatible, when used according to the intended purpose of the device.

8.2. Risk-benefit for subjects participating in the clinical investigation

The clinical investigation is conducted in accordance with current law and applicable standards (see section 14). The rights, safety and well-being of human subjects shall prevail over the interest of science of society.

The study population will not include any vulnerable test subject such as children, pregnant or nursing women, or people with inability. MDR states a list of General Safety and Performance Requirements (GSPR) to be in compliance with. All GSPR are fulfilled for CP362 test catheter, except for those investigated in the clinical investigation. Relevant GSPRs for the clinical investigation can be found in Investigator's Brochure (Appendix 3). GSPR for CE-marked Peristeen Plus system are covered. Peristeen Gel is CE-marked under Medical Device Directive (MDD) under Peristeen Anal Plug certification and MDD extension (not under MDR), thus in compliance with MDD requirements.

[redacted]

To mitigate and reduce these risks, investigator/designees will be trained, according to the IFU, in correct handling of the investigator and comparator device. Furthermore, CP362 test catheters will be inserted by the study personnel and not the test subject. Test subjects will only use the test products for limited duration of time and under full supervision of the study personnel on site of the clinical investigation, and the test subjects will stay in hospital setting during the visit days. No test products will be handed out to the test subjects for independent use.

The transanal irrigation of subjects, with both investigational device and the comparator device will be performed by experienced HCP at investigational sites with many years of experience in conducting bowel management and with previous experience in working with clinical investigations.

The investigational setting is not expected to result in increased frequency or severity of the known risks associated with transanal irrigation. There are no direct benefits for the subjects involved; but, by participating in this investigation, the subjects will contribute with important information for developing improved solutions for bowel management that in turn may benefit individuals who are dependent on rectal catheters for bowel management. The subjects will be compensated for the time spent (see section 15).

8.3. Risk analysis for the conduct of the clinical investigation

A risk assessment of the clinical investigation will be conducted initially prior to the first subject enrolment and periodically re-assessed based on any new risks identified through the process. This assessment will be completed throughout the duration of the investigation, as defined by the investigational team. A risk-based monitoring strategy may be implemented including on-site remote, and central monitoring. Details of the strategy are defined in the monitoring plan.

8.4. Delegation of responsibility

Before initiation of the clinical investigation, sponsor must be provided with key personnel signed and dated curriculum vitae (not more than 2 years old) to verify their qualifications. Key site personnel are those, who treat or evaluate subject data in the clinical investigation. Also, the sponsor will ensure that all site personnel are trained in the investigation procedures, how to complete the eCRFs, procedure for reporting an adverse event (AE) or serious adverse event (SAE) (how, when, to whom), and who to contact in case of emergency related to the investigational device.

9. Monitoring Plan

The sponsor is responsible for ensuring appropriate monitoring of the clinical investigation activities.

The monitors will be the primary contact for the principal investigator and clinical investigation site personnel.

In this clinical investigation the sponsors CMs will be allocated as monitors. The monitoring will be conducted periodically at all sites by qualified personnel, to ensure that the investigation will comply with the approved CIP.

Monitoring activities are mandatory as per good clinical practice, however the extend and depth of these activities depend on the criticality of the clinical investigation, speed of enrolment, the experience of the clinical investigation site personnel in carrying out clinical investigations and specific study designs.

The data collected throughout the investigation and the conduct of the investigation, will be monitored according to the Monitoring Plan to ensure and verify, that the rights and well-being of the subjects are protected, that the data are accurate, complete and verifiable from source documents and that conduct of the investigation complies with the approved CIP, subsequent amendments (if any), ISO14155:2020 and the applicable regulatory requirements.

The investigator must be available for and agrees to cooperate with Coloplast A/S CMs during their visits and ensure, that they have direct access to all documents required, including directs access to subjects' files, to ensure thorough monitoring.

The investigation can be subject to internal audits, if relevant. All monitoring visits and possible audits will be followed by internal reports and corrective actions, if needed. Follow-up letters will be forwarded to sites after all visits and any findings should be addressed by the investigator or designee.

To ensure proper conduct of the investigation the following on site or as remote visits will be performed during the investigation:

- Site selection visit
- Site initiation visit
- Periodic monitoring visits
- Close out visit.

9.1. Site selection visit

The feasibility of the requirements and qualifications of PI and investigational site shall be verified and documented as part of the site selection process. A site selection visit can be replaced by one or more phone calls if the sponsor has prior experience working with the PI or investigational site.

9.2. Initiation visit

All clinical investigation sites will complete an initiation visit during which full training on all aspects of the clinical investigation will be provided.

Training in use of the equipment used for measuring the assessment related to the secondary objective will be performed at sites.

9.3. Monitoring visit(s)

The site dedicated monitor is to ensure adherence to the clinical investigation plan, the safety of the subjects, accurate data recording on the e-CRFs and to monitor recruitment rates and adherence to follow-up schedules. During the clinical investigation, monitors shall check that appropriate written informed consents have been obtained. The PI shall permit and assist the monitor to carry out verification of completed eCRFs against data in the source documents.

The sponsor shall determine the extent and nature of monitoring appropriate for the clinical investigation based on the risk assessment. The sponsor shall ensure, through oversight of the clinical investigation and timely adverse event reporting, that unanticipated adverse device effects are identified and investigated rapidly so that, where necessary, additional risk control measures can be implemented.

The PI can delegate tasks to his/her collaborators, however the roles and responsibilities as time of involvement for each clinical site personnel must be documented on the Site Personnel signature and Delegation list as well as training received before getting involved with the clinical investigation must be documented in the Clinical Investigation Training Log.

The monitor shall inform the sponsor about any problems relating to facilities, technical equipment, or personnel at the clinical investigation site. The monitor shall also be responsible for notifying such deficiencies in writing to the PI and convene with the clinical investigation site personnel appropriate and timely corrective actions.

The sponsor, or delegate, will provide clinical monitoring, including review of eCRF with verification to the source documentation, as described below:

- All available data in the eCRF must be monitored including verification of all fields in the eCRF.
- Within 4 weeks after a subject has completed/terminated the investigation, all data should be monitored and all queries related to the subject must be resolved and closed Fourteen days before planned LPO, the monitoring and verification of all available data in the eCRF must be finalised and all available queries must be resolved and closed.
- For subjects terminating the investigation within 14 days before planned LPO, monitoring and verification of data must be finalized within 2 days after the subject's termination visit.
- After LPO, monitoring and verification of data must be finalized within two days after LPO.
- Queries raised after LPO must be resolved within two days.
- At the Monitoring Visits before the planned LPO, the monitor must ensure PI readiness for signing the eCRF (has completed relevant eLearning in the eCRF) and is available for signature after LPO. In addition, ensure site personnel is available for query resolution after LPO, if raised.

The monitor shall make written reports to the sponsor, including documentation of any deviations after each visit. Follow-up letters will be forwarded to sites after all visits and any findings should be addressed by the PI or designee.

9.4. Remote monitoring

Remote (source data verification) and/or centralized (data review) monitoring is carried out by sponsor personnel or representatives (e.g., data management personnel, statisticians, or clinical monitors) at a location other than the site(s) at which the clinical investigation is being conducted (evaluation without visiting the investigation site). Remote monitoring processes can provide many of the capabilities of on-site monitoring as well as additional capabilities.

In addition to onsite monitoring visits, remote monitoring of the data entered in the eCRF system could be used to achieve the following:

- Conduct activities such as: standard checks of range, consistency, and completeness of data and checks for unusual distribution of data, such as too little variance).
- Special attention will be given in case of frequent data anomalies or errors, protocol deviations or excessive dropouts.
- Augment on-site monitoring by performing monitoring activities that can only be accomplished using centralized processes (e.g., statistical analyses to identify data trends not easily detected by on-site monitoring).
- Monitor data quality through routine review of submitted data in real-time to identify missing data, inconsistent data, data outliers, and potential protocol deviations that may be indicative of systemic and/or significant errors in data collection and reporting at the site.
- Verify source data remotely, provided that both source data and CRFs can be accessed remotely.
- Conduct aggregate statistical analyses of investigational data to identify subject data that are outliers relative to others and to evaluate individual subject data for plausibility and completeness.
- Conduct analyses of site characteristics, performance metrics (e.g., high screen failure rates, high frequency of eligibility deviations, and delays in reporting data), and clinical data to identify early on corrective actions needed for characteristics correlated with poor performance or noncompliance.

9.5. Source data verification

Source data is all information in original records, certified copies of original records of clinical findings, observations, or other activities in the clinical investigation, necessary for the reconstruction and evaluation of the clinical investigation. This includes source data initially recorded in an electronic format.

All documents and data related to the clinical investigation handled by site personnel, shall be produced, and maintained in a way that assures reliability, integrity, control, and traceability, and shall be appropriately stored to provide a complete history.

The PI shall assure the accuracy, attribution, completeness, legibility, and timeliness of the data reported to the sponsor in the eCRFs and in all required reports. All printed copies of electronic source documents shall be certified, as indicated by a dated signature by the investigational site personnel at the time the document is printed. Special requirements should be applied to the capture, review, and retention of electronic source data, to ensure reliability, quality, integrity, and traceability.

The data reported in the eCRFs shall be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. The eCRF can serve as the source document and this must be documented on the Source Data Specification Form. The Source Data Specification Form must be completed at the initiation visit detailing the location of the source data for each data point agreed upon by the PI. Only the PI, relevant site personnel, and the sponsor representatives will have access to all the eCRFs.

10. Statistical considerations

The primary objective will be evaluated by analyzing the primary endpoint [redacted]

The secondary objective will be evaluated based on [redacted], adverse events and device deficiency, [redacted]

[redacted]

10.1. Statistical design, method and analytical procedures

Definition of analysis populations:

Intention to Treat (ITT) and Safety populations will be defined at a formal data review meeting before database lock. As a minimum, the data manager, the clinical manager and the statistician will be involved in the classification of subjects.

The ITT population (full analysis set) will be constituted by all subjects with valid informed consent who have been exposed to at least one Test product, with information on at least one endpoint or assessments used to evaluate the primary or secondary objective.

The Safety population will constitute by subjects who have given informed consent.

All evaluations of endpoint and assessments will be based upon the ITT population whereas adverse events and device deficiencies will be assessed based on the safety population. Invalid individual data points may be omitted from evaluations even though the corresponding subject is part of the ITT population. Any exclusion of data points will be documented.

Considering the data obtained it might be considered to make additional explorative analyses based on a subset of the ITT population.

Evaluation of endpoints and assessments:

All baseline measurements, endpoint and assessments will be summarized by descriptive statistics and/or listed. Endpoint and assessments will be summarized by product, if relevant.

Descriptive statistics for continuous variables are presented with N, Mean, SD (standard deviation), Median, Min and Max, where N denotes the number of subjects contributing with non-missing data. For discrete variables, descriptive statistics are presented with N and percentage, where percentage is based on the total number of subjects/observations with non-missing data.

As an exploratory analysis to support the aim of the investigation the proportion of successful irrigations will be compared for the two type of devices by a one-sided Fisher's Exact Test testing if the proportion with the investigational device is lower than with the Comparator device. The test will be performed on a 5% test level.

Other summaries and analyses can be made, if relevant.

As it is an exploratory clinical investigation no adjustment for multiple testing will be applied if statistical analyses are performed.

All statistical analyses and summaries are made with SAS version 9.4 (SAS Institute Inc., Cary, NC) /Enterprise Guide version 7.1.

10.2. Sample size

As this is an exploratory clinical investigation no formal sample size calculation has been performed. It is assumed that 20 randomized subjects will be adequate for obtaining indications on performance and feasibility, and we aim to have an equal distribution between neurogenic and functional subjects.

10.3. Level of significance and power

For Fisher's Exact Test a one-side 5% test level will be applied. As this is an exploratory investigation no power has been applied, when evaluating the sample size. If other explorative statistical analyses are performed a significance level of 5% will be applied.

10.4. Pass/fail criteria

No formal success criteria are applied in this explorative clinical investigation.

10.5. Interim analysis

There is no planned interim analysis in this clinical investigation.

10.6. Statistical reason for termination of investigation

There will be no interim analysis and therefore no reason to terminate the investigation based on statistical considerations.

10.7. Deviations from statistical design, method or analytical procedures

Any deviations from the statistical plan will be documented in the clinical investigation report.

11. Data management

Data management of all measurements described in this protocol are carried out by Clinical Operations, Coloplast A/S.

Data will be collected through an electronic data capturing (EDC) system on eCRF, a secure, internet-based case report form.

The EDC system used is [redacted]
The system is designed to be compliant with the FDA requirements of 21 CFR part 11. It is a validated data management system, with restricted role-based access control, allowing only qualified and trained personnel to enter the system. The system has full audit trail and electronic signature.

The PI and delegate(s), and investigation monitor(s) must be trained in the system prior to getting access. The training is web-based (eLearning) and must be completed before access to the investigation is granted. The web-based training will be documented in the data management system. In addition, the data management specialist will demonstrate the system on a virtual/physical meeting. This training will be documented in the Clinical Investigation Training Log. The sponsor will be responsible for training the investigator, delegate(s) and the monitor(s).

Only the principal investigator, or delegate(s), who have completed the relevant eLearning, signed the Site Personnel Signature and Delegation List and Clinical Investigation Training Log will be authorised to enter data in the eCRF.

The eCRF will be completed by the PI, or delegate, that will perform primary data collection directly into the eCRF or drawn from source-documents. The eCRF will be completed on a continuous basis starting from the point of enrolling the subject to final follow up. In addition, the PI, using his/her personal login information, will be authorised to, and must, sign each eCRF. It will also be the responsibility of the PI to ensure that all measurements and observations are correctly noted in the eCRF.

The PI will keep a separate list of the subjects' ID numbers, names, and addresses in a locked room/cabinet.

The monitor, using his/her personal login information shall verify all data points and issue electronic queries for the authorised clinical site personnel to respond, as defined in the monitoring section (and monitoring plan, if created).

The Data Validation Plan describes which edit checks, range checks, and other consistence checks that will be done on the clinical data during conduct of the investigation. The Data Validation Plan will be developed in collaboration with the Clinical Manager and the Statistician and will be aligned with the monitoring section (and monitoring plan, if created).

A critical quality control will be performed by the data management team and queries issued where needed. Such queries must be resolved by the site personnel. Automated, real-time access to the data enable control on study compliance and safety assessments. A full audit trail ensures, that each user's (site personnel, monitor, sponsor, data manager) access to and actions in the system is tracked.

At the end of the study formal data review meeting(s) will be performed before the database will be locked.

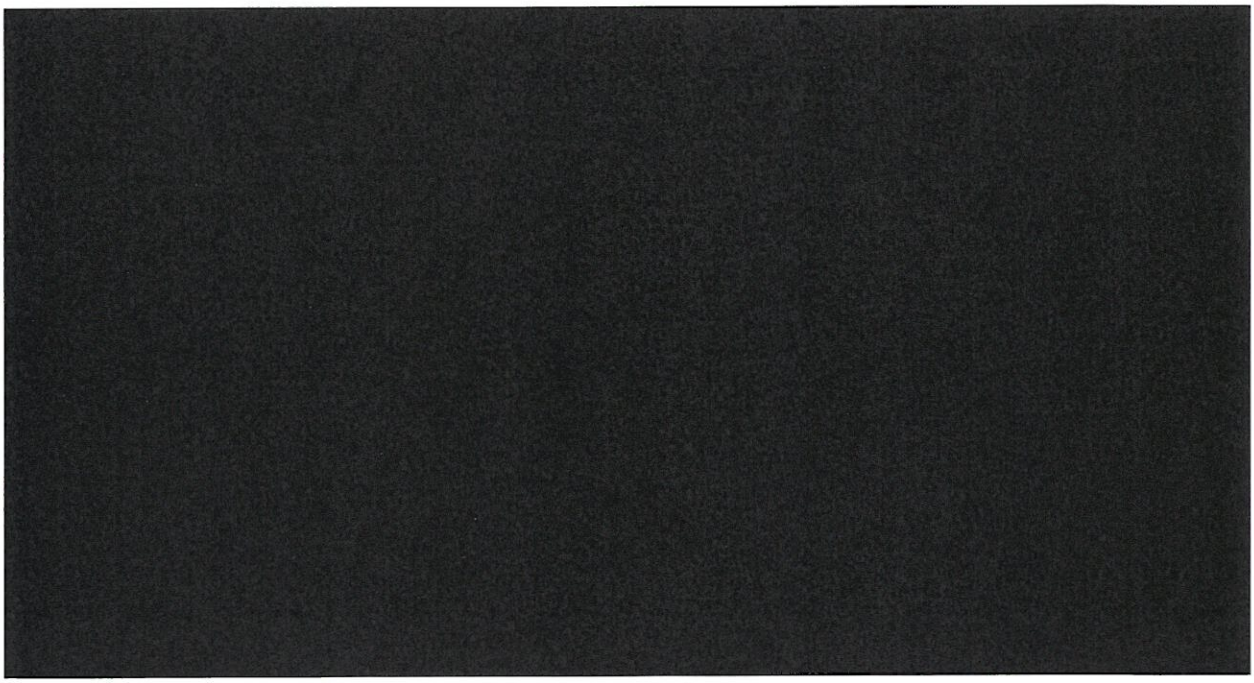
The Data Management procedures are further described in the Data Management instructions.

11.1. Data collection procedure

All assessments and observations throughout the investigation for each subject must be carefully recorded in an eCRF or in a paper CRF (pCRF) during the visit or immediately after. The eCRF makes it possible to enter data right away when they are obtained. This is the preferred way of collecting data. In case this is not possible the data should be entered no later than seven days after the visit / procedure.

When subject and PI is required to complete different sections in the CRF, it will be specified which sections the subject will fill in (using paper CRF or app solution) and which sections the investigator will fill in.

In the unforeseen situation, where site cannot establish connection to the EDC system, a paper CRF (pCRF) has been printed and supplied by sponsor.



Other:

The remaining endpoints, assessment and baseline information can be entered directly into the eCRF.

11.2. Data retention

The Investigator file must be archived for a minimum period of 10 years after the final clinical investigation report has been signed.

12. Amendments to the Clinical Investigation Plan

No changes in the clinical investigation procedures shall be affected without mutual agreement between the principal investigator and the sponsor. The agreement of the changes must be documented by signing the corresponding clinical investigation plan amendments and registered in the Change Log.

All significant changes require notification to the EC/ and applicable regulatory authority. Substantial changes may require approval from the EC and applicable regulatory authority prior to implementation.

13. Deviations from the Clinical Investigation Plan

Deviations to the Clinical Investigation Plan occurs when the activities during the clinical investigation do not comply with the EC approved investigation plan.

The PI is not allowed to deviate from the Clinical Investigation Plan unless, under emergency circumstances or to protect the rights, safety, and welfare of the subject(s).

If a situation occurs, that affect the rights, safety and well-being of the subject(s), the PI is obliged to deviate from the CIP, and other regulations to protect the subject. The PI must inform the monitor immediately, and the Monitor will report and inform the Clinical Manager or designee immediately. Documentation with all relevant details will be completed to document the deviation and must be reported to the EC by the CM as required by local regulations.

The site will complete a protocol deviation eCRF form for all subject-related deviations and all deviations that are **not** related to a subject (for example, an untrained nurse performing investigational procedures) are reported in the Deviation Log by the PI.

If any deviations to the investigation plan are detected during the monitoring visit, the Monitor shall ensure the site reports all subject-related deviations in the eCRF and non-subject related deviations on the Deviation log in the Investigator Site File. Additionally, the monitor must report any deviation noted during the visit in the Periodic Monitoring Report.

14. Statement of compliance

The clinical investigation is conducted in accordance with:

- Ethical principles that have their origin in the Declaration of Helsinki, 1964, Last amended at the 59th WMA General Assembly, Brazil, October 2013.
- MDR (EU) 2017/745
- ISO 14155:2020 "Clinical Investigation of medical devices for human subjects – Good clinical practices".
- Any applicable regional or national regulations will be specified in the country specific CIP.

14.1. Ethics committee and regulatory authorities

The CIP and/or other relevant documents are submitted to the appropriate EC and regulatory authorities. This clinical investigation will not begin until the required approval from the EC and regulatory authorities have been obtained. Any amendment to the protocol will be submitted to the same EC and regulatory authority.

Sponsor will notify the relevant regulatory authority and EC concerned of the end of the clinical investigation.

14.2. Data protection

As part of the investigation, Coloplast A/S [redacted] ("Coloplast") will collect and process the personal information the subject provides for the investigation ("subject personal data"). This includes identification and contact information (which may be anonymized depending on the nature of the investigation) as well as information about product usage experience and your health (sensitive data). Coloplast will comply with the EU General Data Protection Regulation (GDPR) and the Danish act on data protection ("databeskyttelsesloven"), including in connection with transfer of data to third countries, cf. chapter V of GDPR, Coloplast will only process the subjects' personal data:

1. To conduct the investigation and carry out related research based on subject voluntary consent (primary use), cf. articles 6(1)(a), cf. articles 9(2)(a) The EU´s personal data regulation of GDPR.
2. To comply with applicable legal obligations, which is the responsibility of Coloplast to e.g., ensure reliability and safety when processing clinical data, cf. article 6(1)(c) in conjunction with article 9(1)(i) of GDPR, and
3. If separate consent is given for secondary use of subject personal data, cf. articles 6(1)(a) and 9(2)(a) of GDPR – carry out research outside the clinical protocol to improve Coloplast's products and services, and for use in education.

Part of Coloplast's processing is carried out on third-party platforms (clinical trial databases) and certain third parties are assisting Coloplast in the data processing (e.g., the PI). Such cases will imply a transfer of your personal data to the third parties (data processor), but solely for process data, for the specified purposes and with the third parties acting on instruction from Coloplast. Data may be collected and processed across the Coloplast network, which may entail processing of personal data outside the EU/EEA area. In such cases, an adequate level of protection will be ensured by the third parties being subject to the standard contractual clauses on data protection adopted by the EU or to an EU-approved certification mechanism on data protection. For further information about this please the subject can always consult Coloplast's data protection officer (details below).

Subject personal data will be kept as long as required under applicable laws and regulations. The EU Medical Device Regulation obligates Coloplast to keep the data for a period of at least ten years after the investigation is completed, or, if the device is subsequently placed on the market, at least ten years after the last device has been placed on the market. Subject personal data will be deleted at the end of the mandatory retention period.

If the subject has questions or queries regarding Coloplast's handling of personal information, the subject can always contact Coloplast's Data Protection Officer at [redacted] Complaints related to Coloplast's handling of subject personal information may similarly be sent to the Data Protection Officer, and the subject is also entitled to file a complaint with the relevant supervisory authority, which in the case of Denmark is the Danish Data Protection Agency (www.datatilsynet.dk).

The subject can write to [redacted] at any time to request:

- Access to personal data.
- Correction of errors in personal data or to erase personal data.
- Limit what can be done with personal data.
- To receive personal data in machine-readable format (data portability).
- Withdrawal of consents the subject has given Coloplast to process personal data.

14.3. Indemnity

All subjects are fully covered by Coloplast A/S insurance throughout the investigation: XL Insurance Company SE, policy number DK00000300LI23A.

14.4. Financial conditions

Coloplast A/S will compensate all investigators involved in the clinical investigation for their time and resources spent on the investigation. All financial agreements with the investigation sites involved in the clinical investigation will be specified in a sponsor investigator agreement. None of the investigators has any financial relationship with sponsor outside the task of the clinical investigation activities.

15. Subject compensation

15.1. Compensation in case of injury

Product liability and No-Fault Clinical Investigation Insurance covering the duration of the clinical investigation are in place, to enable compensation in the event of an injury to a participating subject (see 15.3).

15.2. Disadvantage compensation for participating in the clinical investigation

Subjects will be compensated with a voucher per visit, paid by Coloplast A/S with the value as described in the Subject Information Form and in the table below:

Table 5: Disadvantage compensation

Visit	Disadvantage compensation
Visit 1 (V1)	[redacted]
Visit 2 (V2)	

This is to compensate for any inconvenience caused during the TAI procedure and time used. There is no medical benefits for the subjects to participate in this clinical investigation, and even though subject are currently TAI users, there can still be some discomfort and pain. Travel expenses will be accounted separately. The vouchers are taxable (B-income), and it is the responsibility of the subject to declare this to SKAT.

16. Adverse events, adverse device effects and device deficiencies

16.1. Adverse events

An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, whether related to the investigational medical device(s) or the comparator(s), or the procedures involved. The adverse event shall be marked with the intensity mild, moderate or severe. This could include events such as headache or dizziness.

16.2. Adverse device effect (ADE)

An adverse event, which is related to the use of the investigational medical device, is an adverse device effect, and should be marked as unlikely related, possible related, probable related or with causal relationship on the adverse event form.

The definition of an adverse device effect includes any event resulting from insufficiencies or inadequacies in the instruction for use, deployment, implantation, installation and operation, or any malfunction of the medical device, as well as any event resulting from use error or from intentional misuse of the device.

If any adverse device effects occur for CE-marked Coloplast products the incident shall be stated in the Vigilance Form in the eCRF.

16.3. Device deficiency (DD)

A device deficiency is the inadequacy of the investigational medical device or comparator with respect to its identity, quality, durability, reliability, usability, safety or performance. This includes malfunctions, use errors and inadequacy in the information supplied by the manufacturer including labelling.

If any Device Deficiencies occur for CE-marked Coloplast products the incident shall be stated in the Vigilance Form in the eCRF.

Table 6: Examples of device deficiency

Examples of device deficiency
[redacted]

16.4. Serious adverse events (SAEs)

A serious adverse event is an adverse event that:

1. Led to death,
2. Led to a serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:
    - a life-threatening illness or injury, or
    - a permanent impairment of a body structure or a body function including chronic diseases, or
    - in-patient or prolonged hospitalization, or
    - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
3. Led to foetal distress, foetal death, a congenital abnormality, or birth defect including physical or mental impairment.

This includes device deficiencies that might have led to a serious adverse event if:

1. Suitable action had not been taken, or
2. Intervention had not been made, or
3. Circumstances had been less fortunate.

These are handled under the serious adverse event reporting.

Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

16.4.1. Serious adverse device effect (SADE)

A serious adverse device effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

16.4.2. Anticipated serious adverse device effect (ASADE)

There is no anticipated serious adverse device effect.

16.4.3. Unanticipated serious adverse device effect (USADE)

An unanticipated serious adverse device effect is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

16.5. Medical care of subjects

Principal investigator shall ensure that adequate medical care is provided, during and after participation in the clinical investigation, to a subject experiencing an adverse event. All ongoing ADEs, SAEs, SADEs and DDs that could have led to a SAE at subject termination will be followed according to the Risk Benefit analysis (see section 8.2). An ongoing adverse event at subject termination visit is documented as the current status for the adverse event and will not be followed up.

The subjects shall be informed of any new significant findings occurring during the clinical investigation, including the need for additional medical care that can be required, and of the nature and possible cause of any adverse events experienced.

16.6. Reporting and timelines

16.7. Investigator's reporting responsibilities

- PI at each site must assess all (S)AEs that occur at his/her site.
- All serious adverse events and serious adverse device effects must be reported to sponsor within 24 hours of the site becoming aware of the event.
- A device deficiency that could have led to a serious adverse event but did not because suitable action was taken, intervention had been made or because of fortunate circumstances should be reported to sponsor within 24 hours of the site becoming aware of the event.
- New findings and/or updates in relation to already reported serious events should also be reported to sponsor within 24 hours of the site becoming aware of the event.
- Device deficiencies and all adverse device effects related to CE-marked Coloplast investigational product and/or comparator must be reported to sponsor within 24 hours of becoming aware of the event.

When reporting the SAE, the relationship to the test material shall be described whether the event is considered:

- **Not related**, the event has no temporal relationship with the use of the test material or the procedures.
- **Unlikely related,** the relationship with the use of the test material seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- **Possible related,** the relationship with the use of the test material is weak but cannot be ruled out completely. Alternative causes are also possible (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed or no information has been obtained should also be classified as possible.
- **Probable related,** the relationship with the use of the test material seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
- **Definitely related/Causal relationship,** the event has a temporal relationship with the test material use/application or procedures.

And the intensity of the event should be considered, as such:

- **Mild,** the intensity of the event is mild with no further action or intervention.
- **Moderate,** the intensity of the event will lead to an action or intervention to solve the event.
- **Severe,** the intensity of the event will lead to follow up on the action or intervention, as the effect of the action or intervention may not decrease the symptoms.

All above events must be reported by use of the relevant adverse event/serious adverse event/device deficiency form.

Please report to:

[redacted] OR [redacted]

AND [redacted]

16.8. Sponsors reporting responsibilities

It is the responsibility of sponsor to ensure that the following are reported to national regulatory authorities immediately, but no later than 7 calendar days following the date of awareness by sponsor:

- All SAEs.
- All SADEs.
- All device deficiencies that could have led to serious adverse events but did not because suitable action was taken, intervention had been made or because of fortunate circumstances.
- New findings and/or updates in relation to already reported events.

If the serious adverse event results in imminent risk of death, serious injury, or serious illness that requires prompt remedial action for other subjects, users or other persons or a new finding to such a serious adverse event, sponsor must immediately but no later than two calendar days after awareness by sponsor report the event to national regulatory authorities.

It is the responsibility of sponsor to inform all investigators in writing within 10 working days if device deficiencies, adverse events, adverse device effects, near-incidents, serious adverse events, serious adverse device effects or unanticipated serious adverse device effects lead to corrective actions (e.g., change of IFU).

17. Suspension or premature termination of the clinical investigation

Sponsor may suspend or prematurely terminate an investigation site or the entire clinical investigation for documented significant reasons.

If a suspicion of an unacceptable risk to subjects develops during the clinical investigation, sponsor will suspend the investigation while the risk is assessed. Sponsor will terminate the investigation if an unacceptable risk is confirmed. Sponsor will ensure that the premature termination will be justified in writing and will promptly inform the regulatory authorities and EC. If monitoring or auditing of the clinical investigation identifies serious or repeated deviations at one of the participating investigation sites, sponsor will suspend or terminate the particular investigational site. The sponsor or investigator will inform the regulatory authority as appropriate and notify the EC about the termination of the site.

18. Clinical Investigation Report

At completion of the investigation sponsor is responsible for writing the clinical investigation report. The report is retained on file. The report contains a critical evaluation of all data, which have been collected during the investigation. The report describes the methodology and design and a data analysis, including statistical preparation and conclusion.

Sponsor and coordinating investigator must sign the final version of the clinical investigation report or an affidavit, indicating their agreement with the contents. If no coordinating investigator is appointed, then the signatures of the principal investigator(s) should be obtained.

The clinical investigation report must be submitted to EC.

19. Publication policy

In accordance with the Declaration of Helsinki, a description of the clinical investigation will be registered in a publicly accessible database (www.clinicaltrials.gov) before the start of any recruitment activities. The content of the registration will be registered throughout the conduct of the clinical investigation, and the results will be entered at completion (i.e., within one year after last patient out) of the clinical investigation.

The results of the investigation, positive as well as negative, may be communicated by publications, abstracts, posters, or oral presentations. **In all cases, the subject's identity will remain confidential.** The terms of publication between sponsor and PIs and delegates are agreed in separate Sponsor Investigator Agreements.

No preliminary results from the clinical investigation will be published. Data from the investigation is considered confidential until it is published.

20. Suspension/termination of the clinical investigation

Sponsor will withdraw from sponsorship of the clinical investigation if:

- Major non-adherence to the clinical investigation plan is occurring.
- It is anticipated that the subject recruitment will not be adequate to meet the investigation objectives (at least 75% of the subjects should be entered within the recruitment time).

In case sponsor withdraws, sponsorship for the subjects already recruited into the clinical investigation will continue.

21. Bibliography

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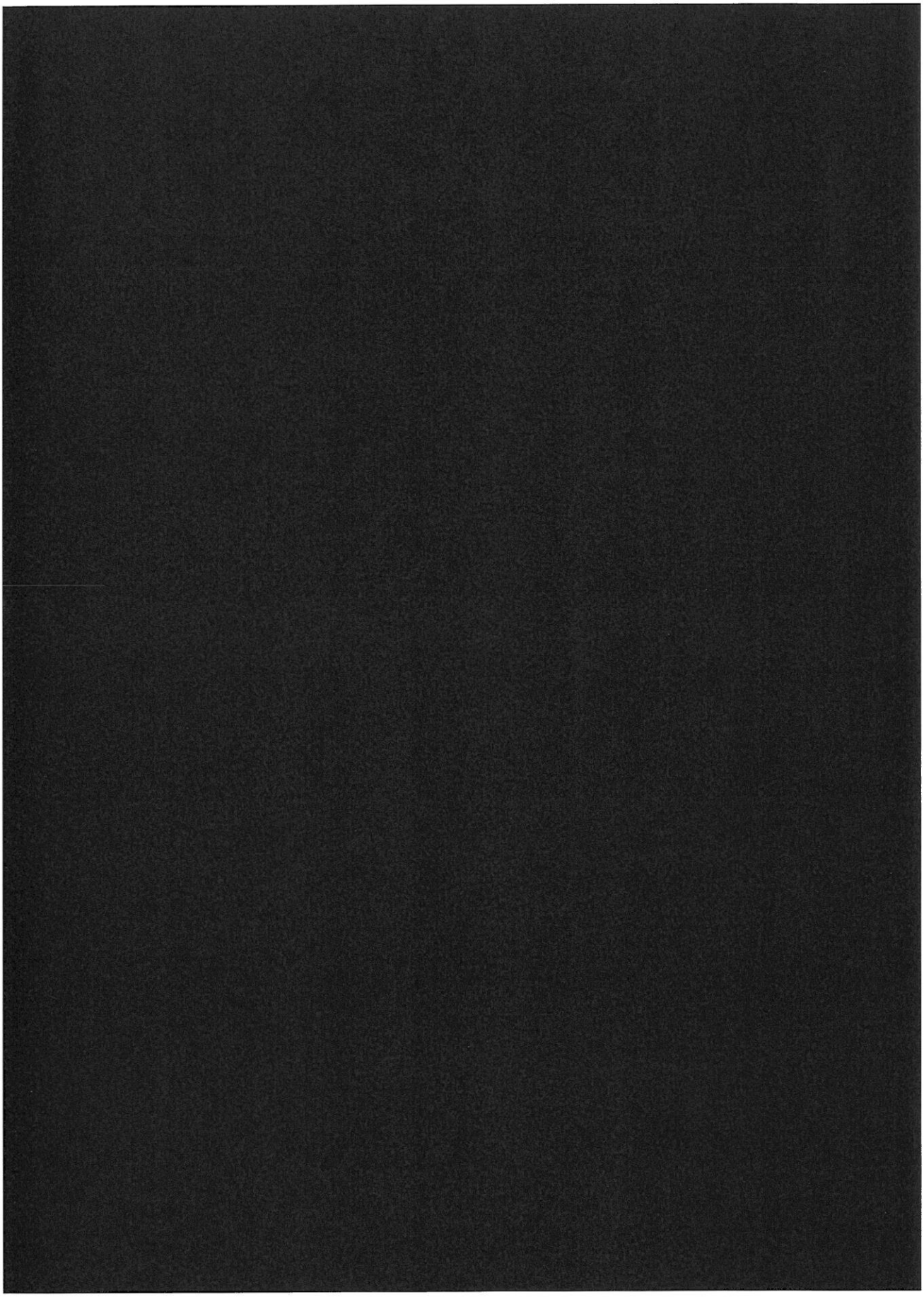
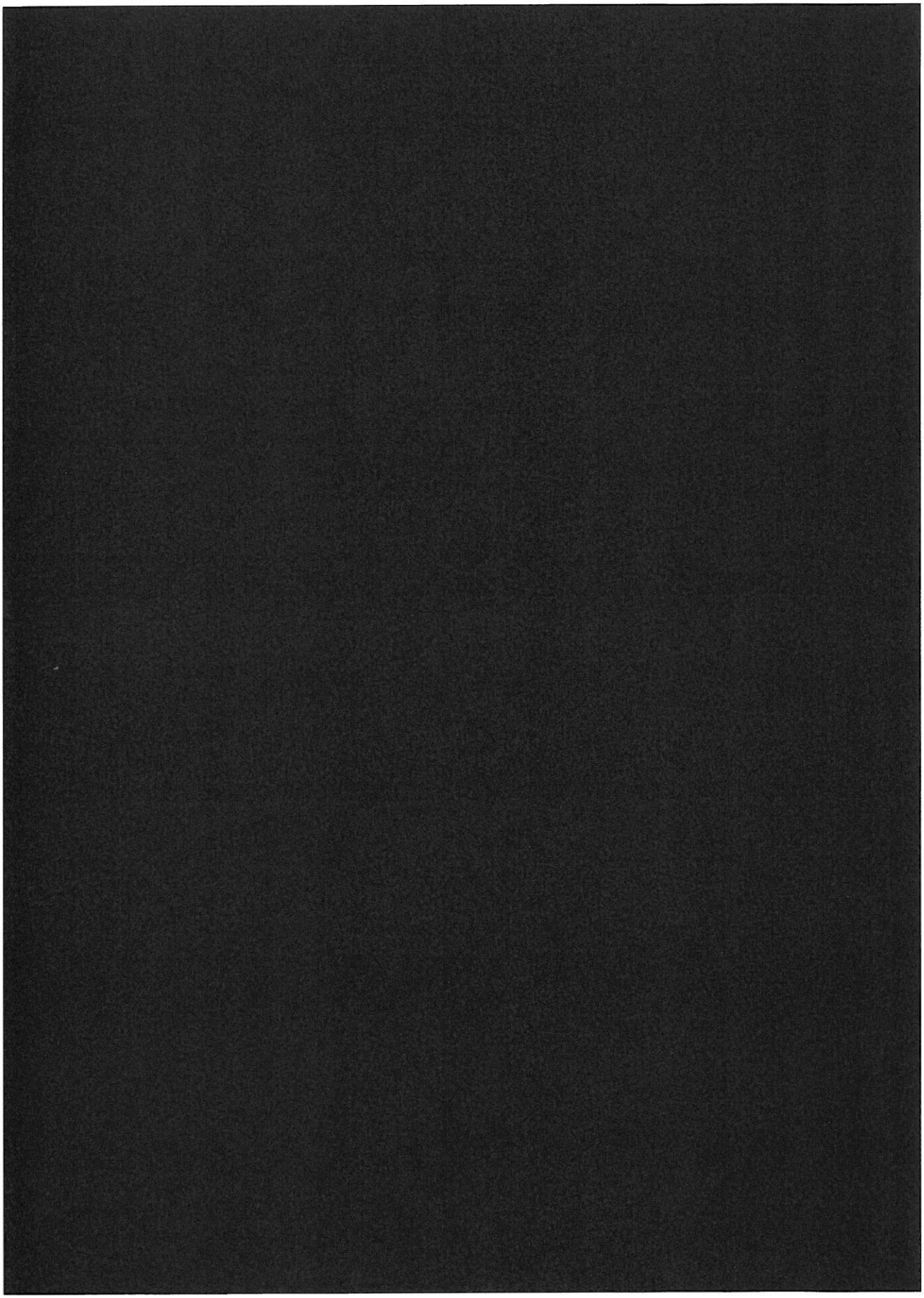
Appendix A

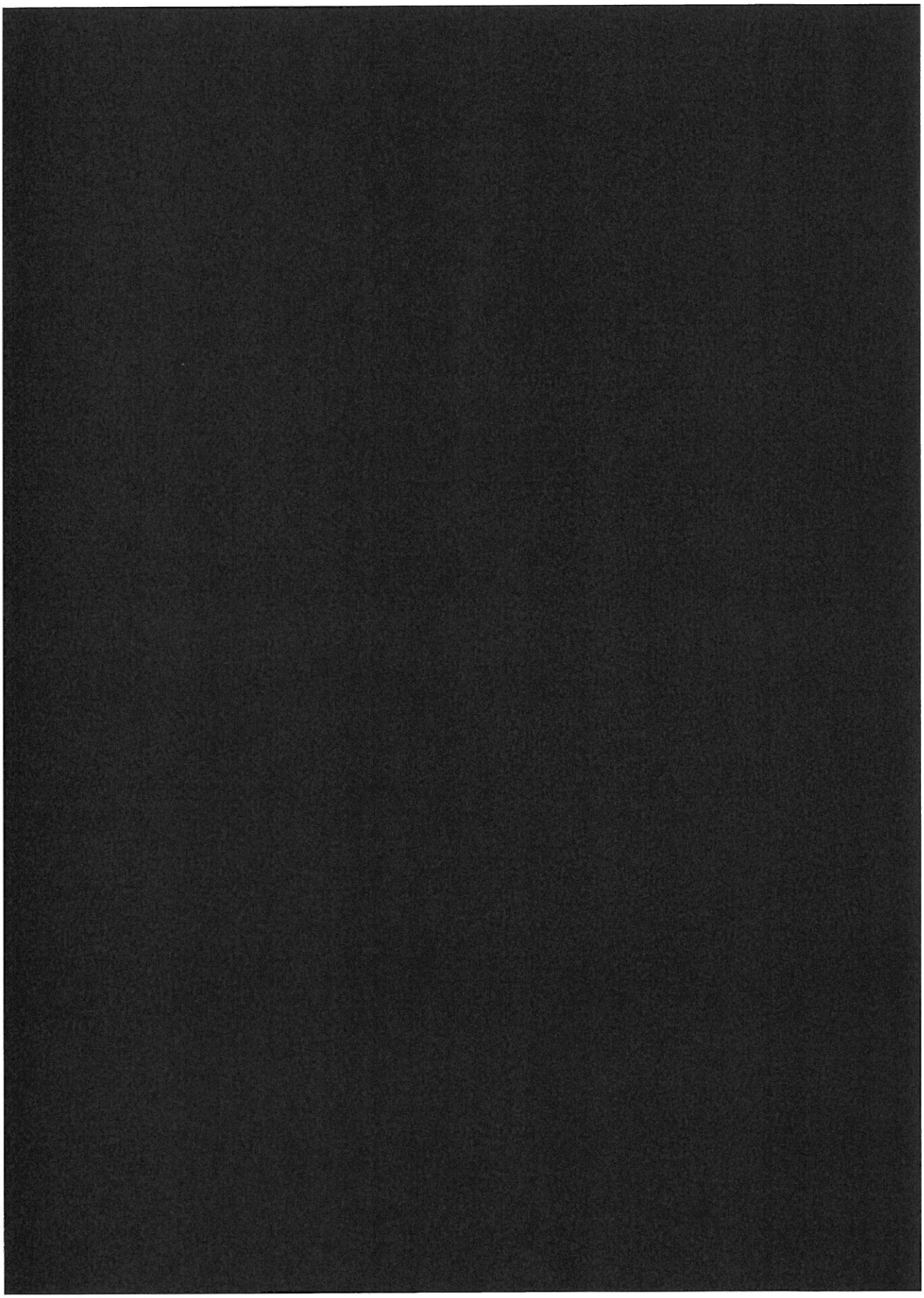
CP362 Clinical Investigation
Peristeen® Plus Transanal Irrigation System with CP362 test catheter

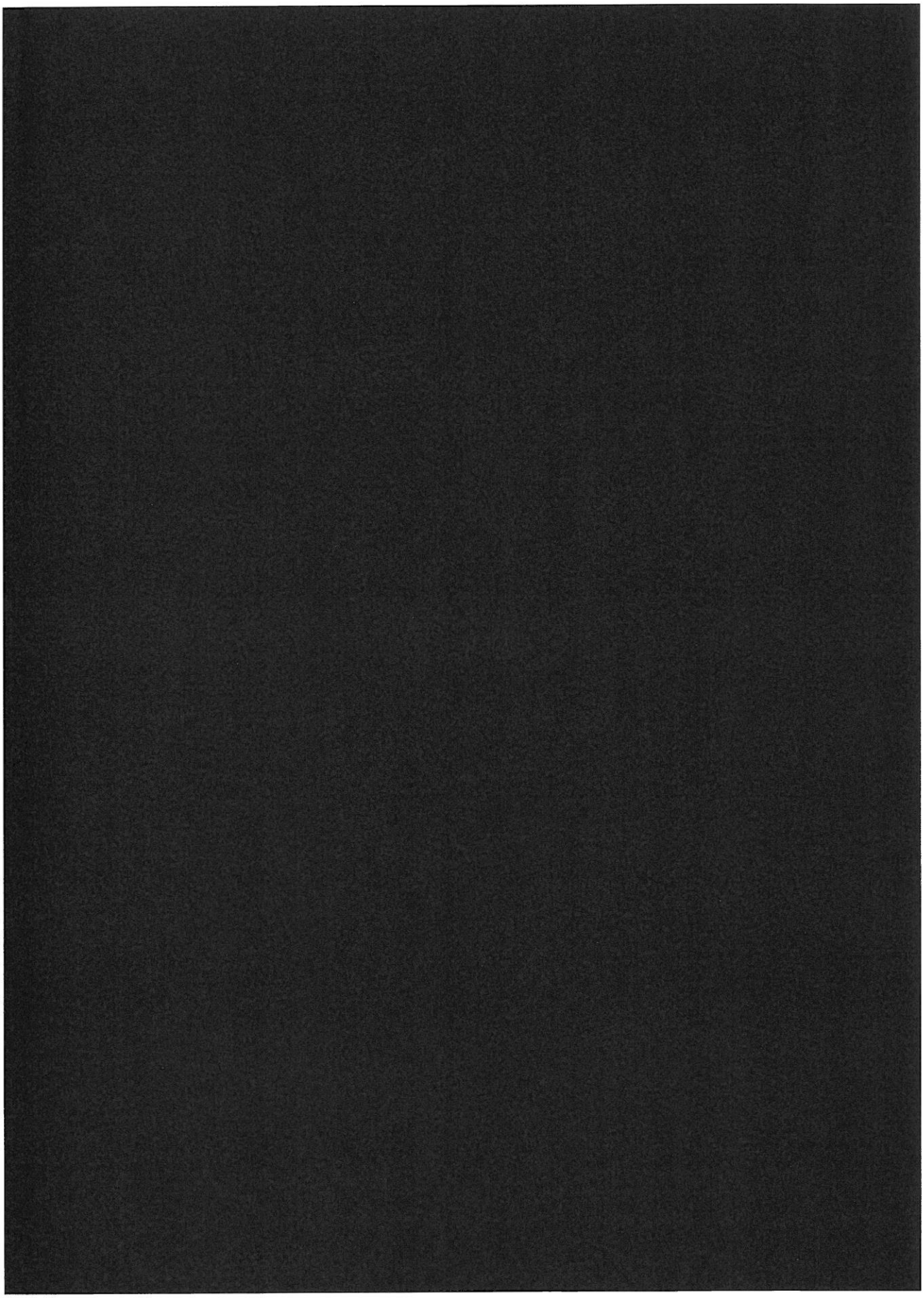
CP362 Clinical Investigation consists of a Peristeen® Plus Transanal Irrigation System together with a CP362 test catheter. Please read all the instructions provided here before using the CP362 test system for the first time.

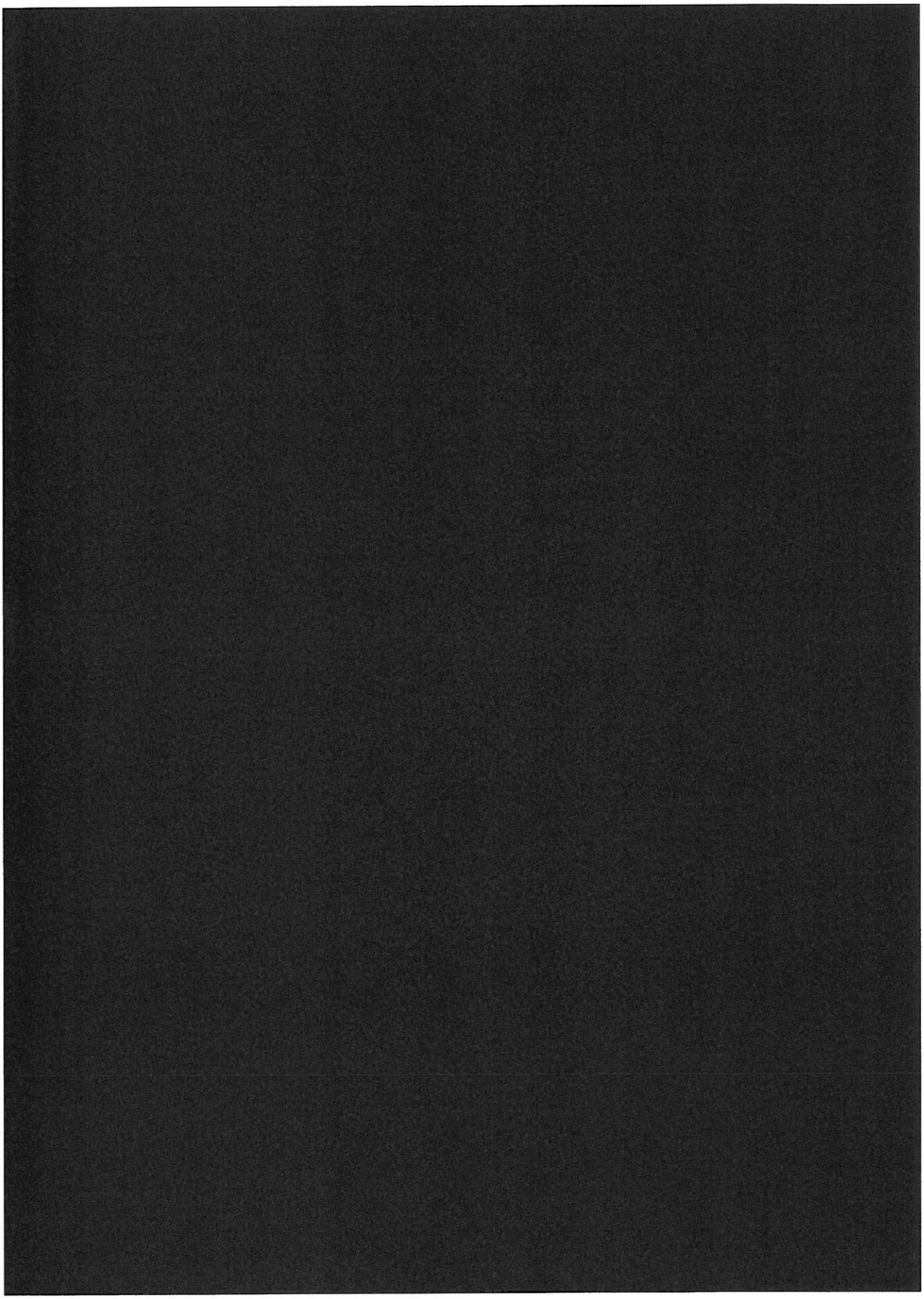
IFU Master CP362 Version 1 - **Exclusively for Clinical Investigation**

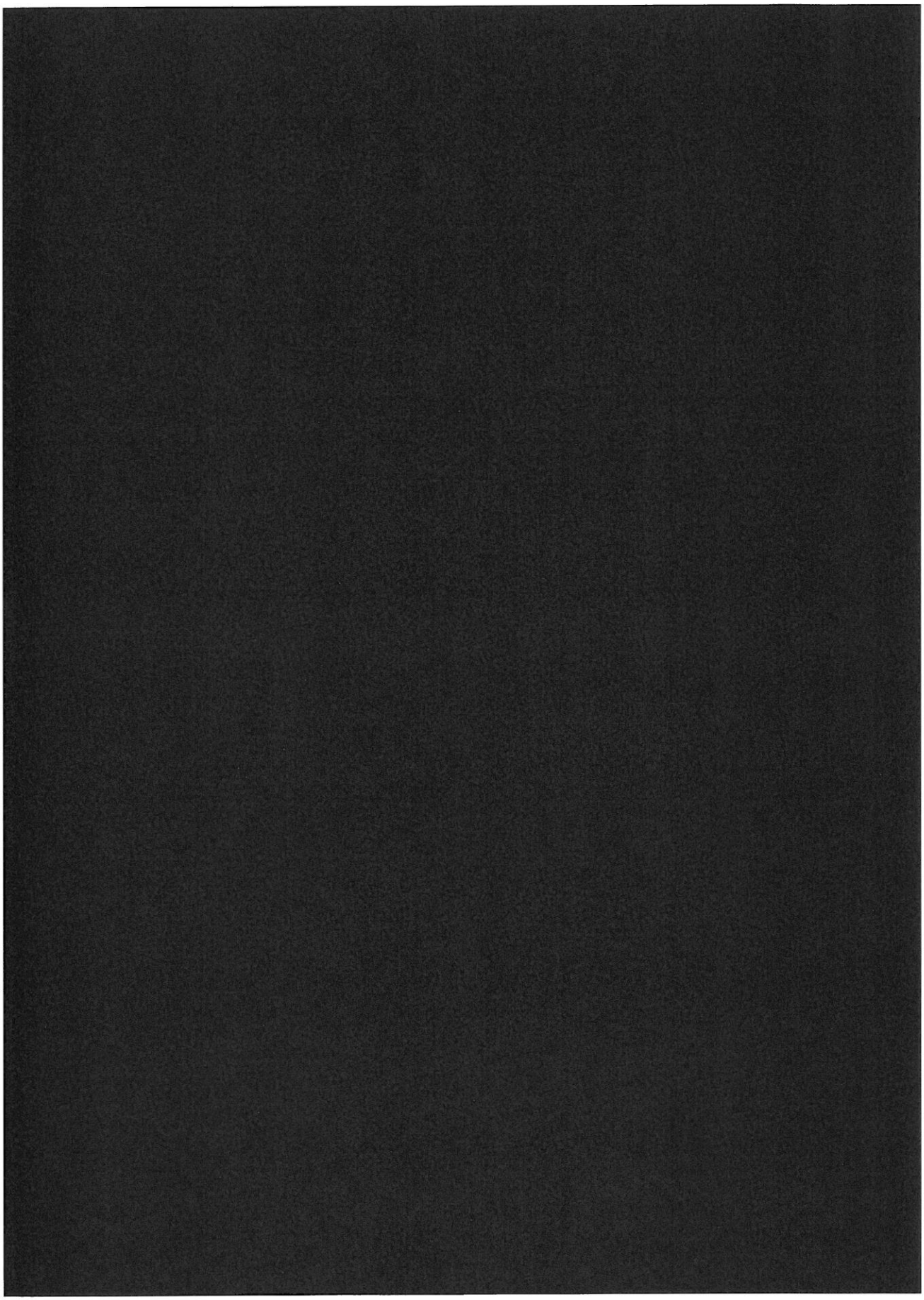


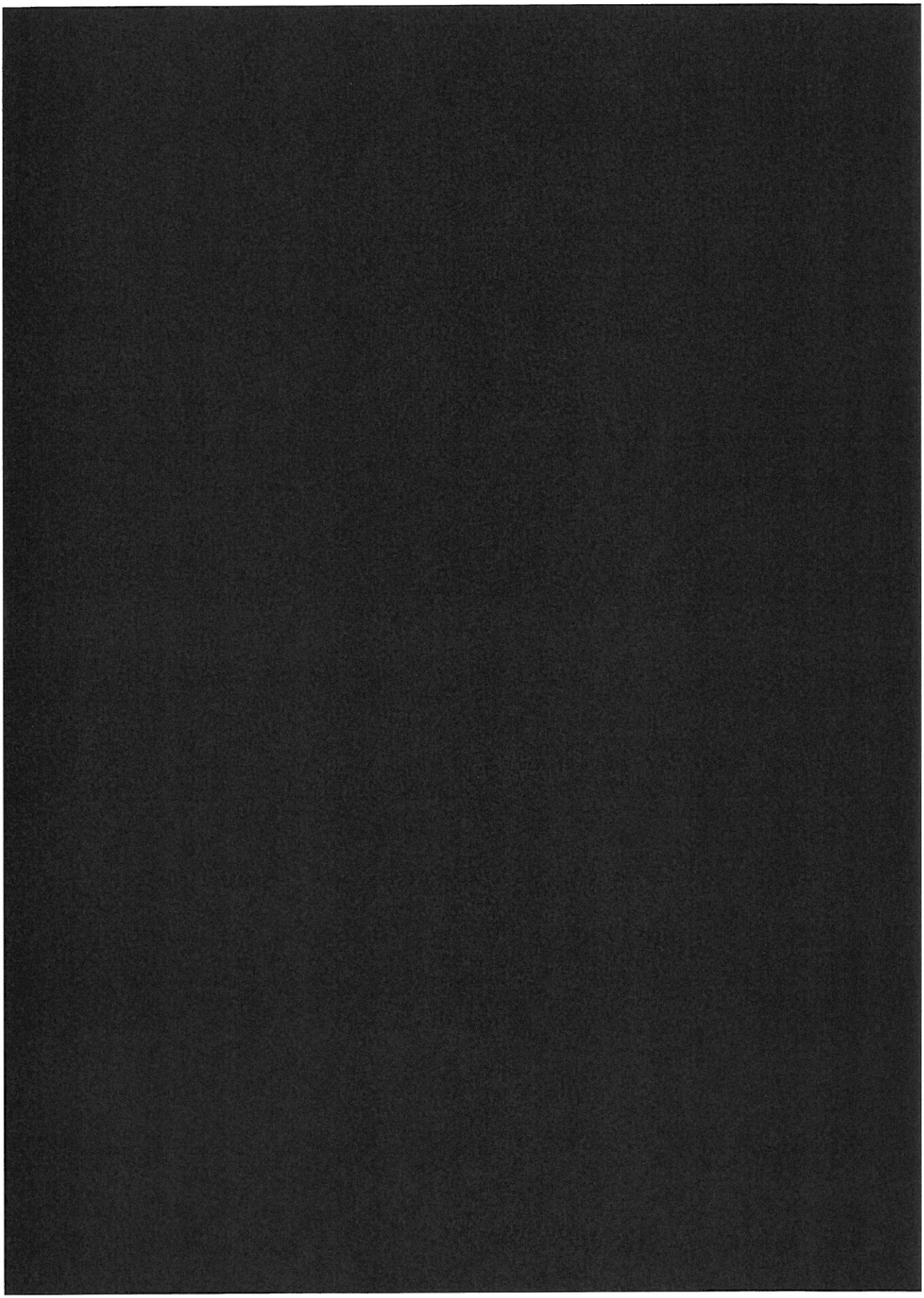


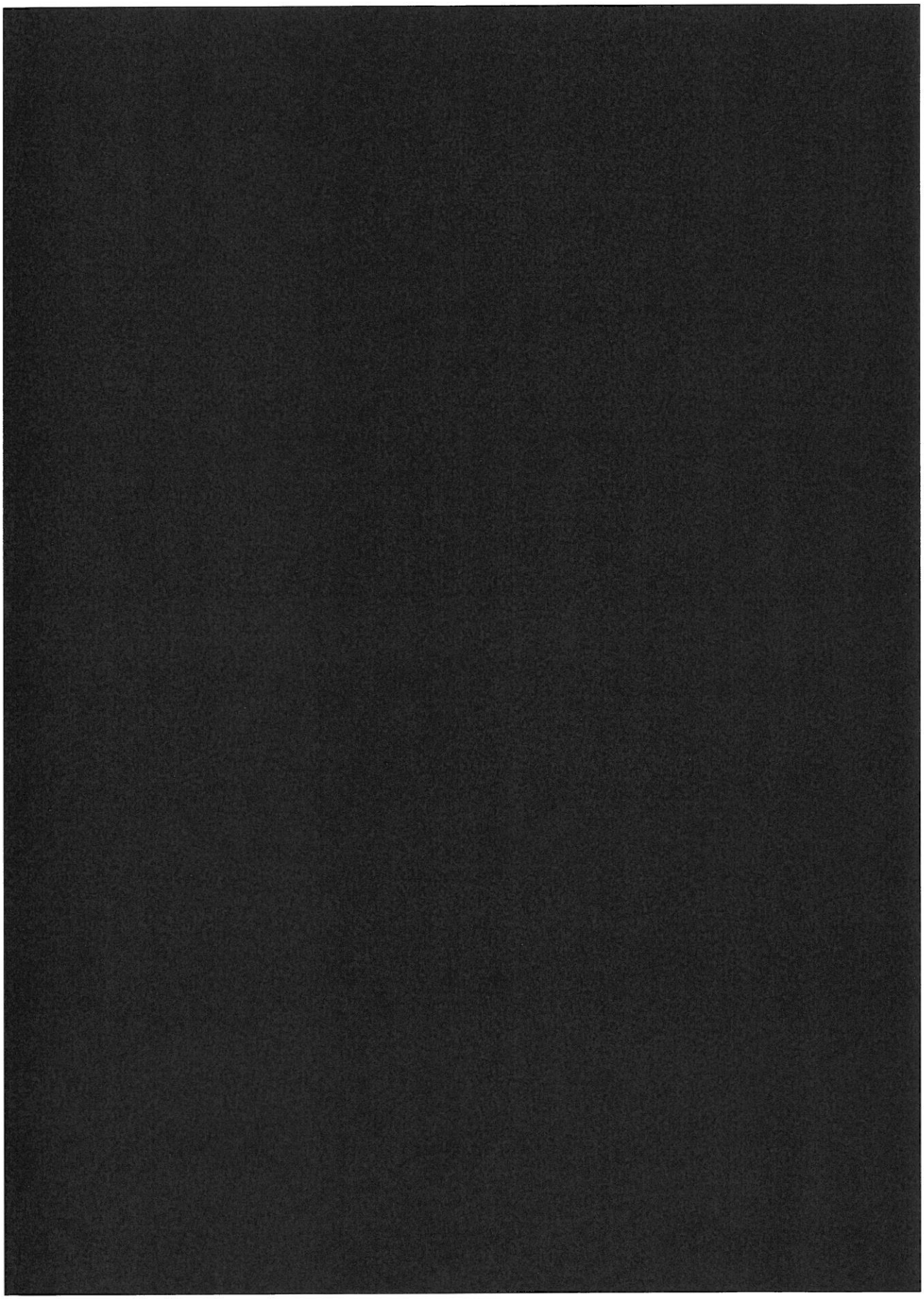


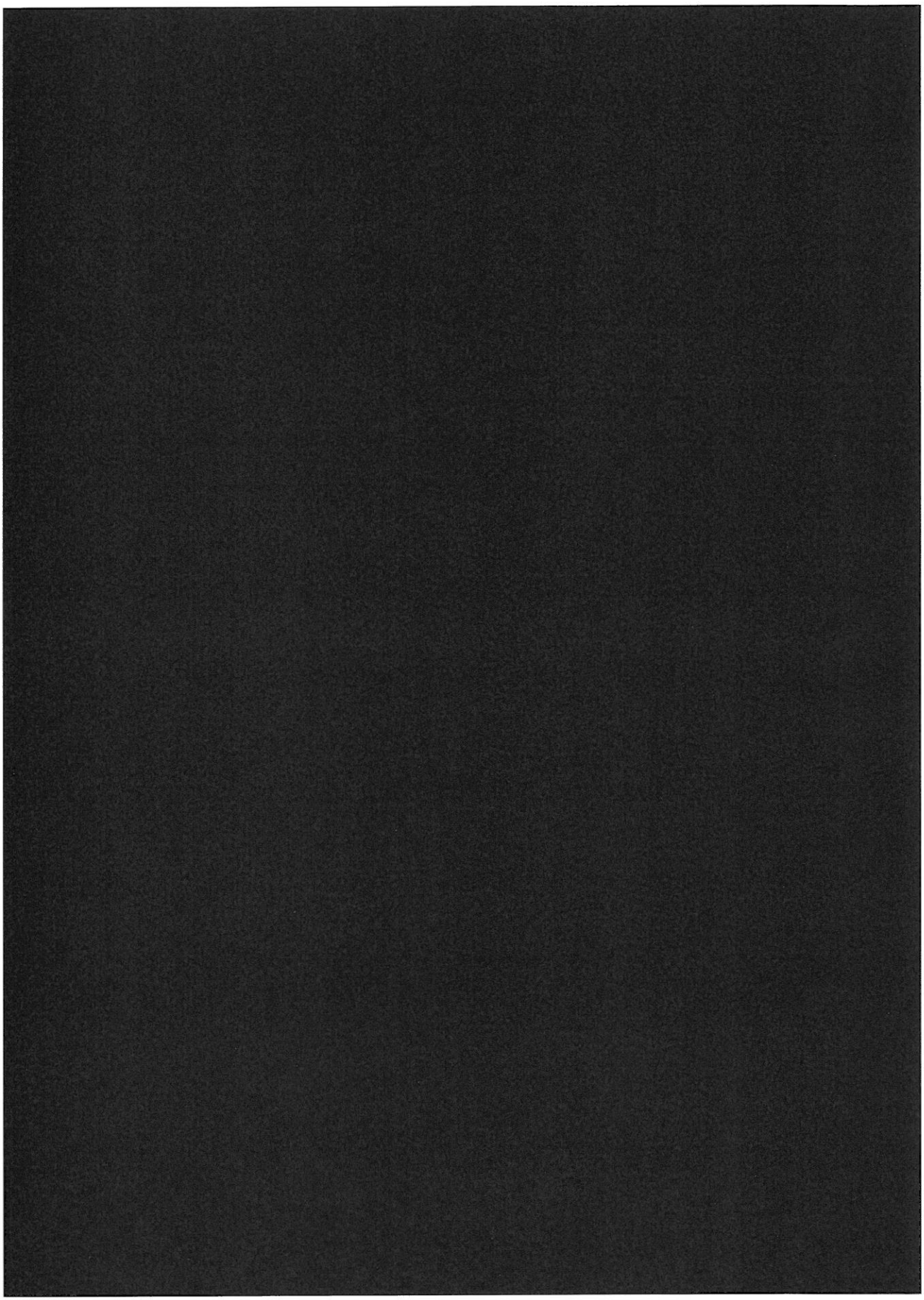


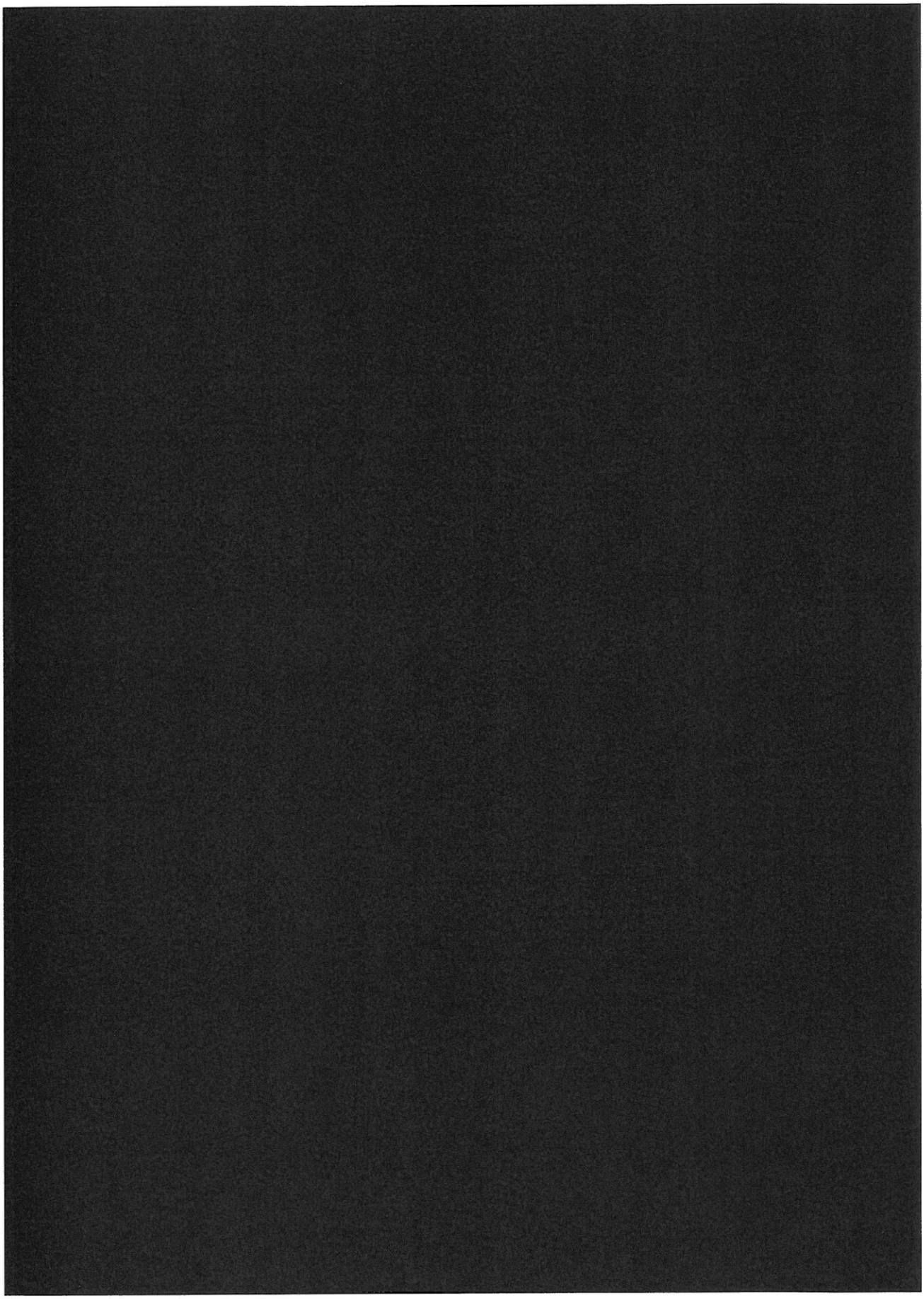


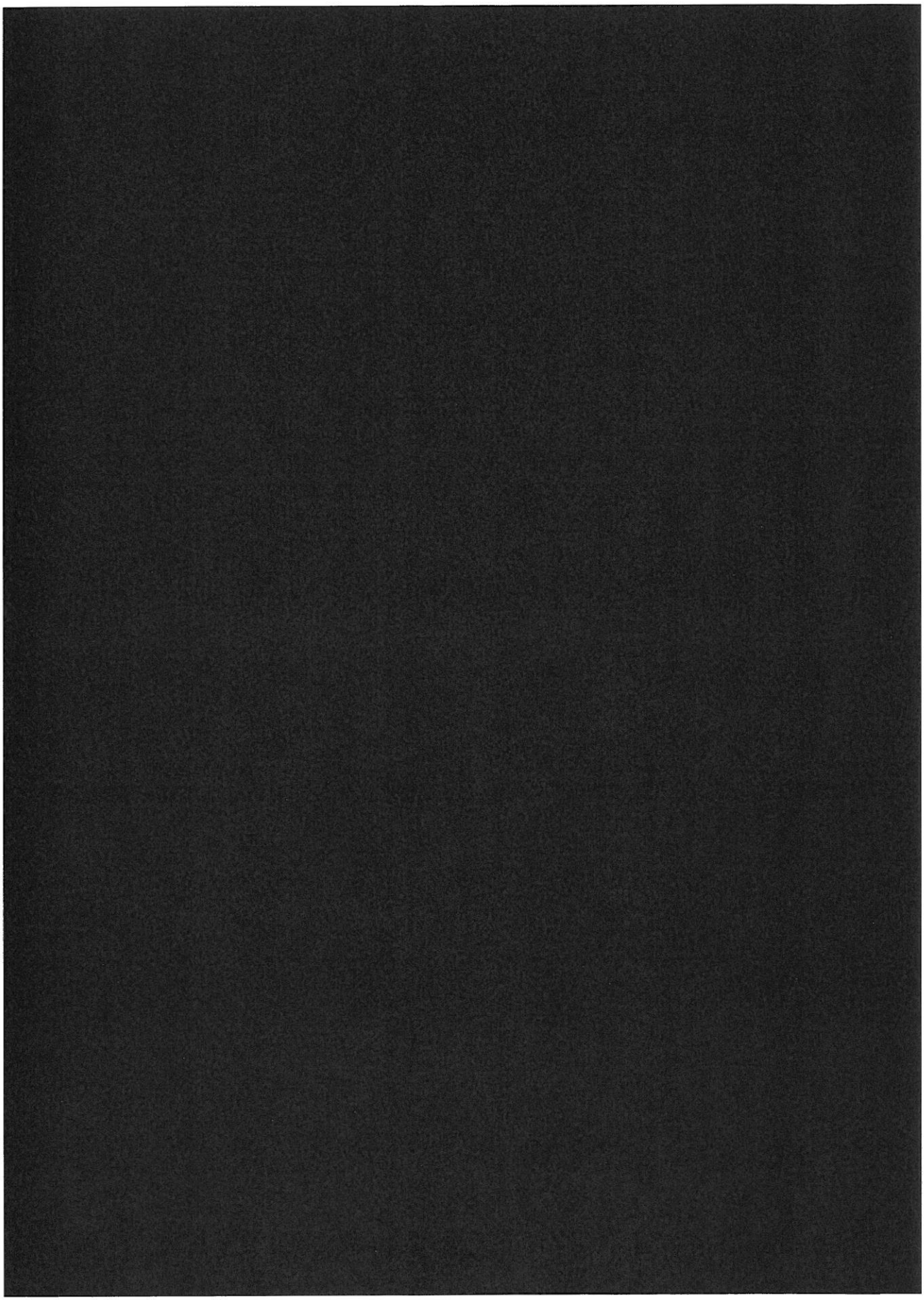


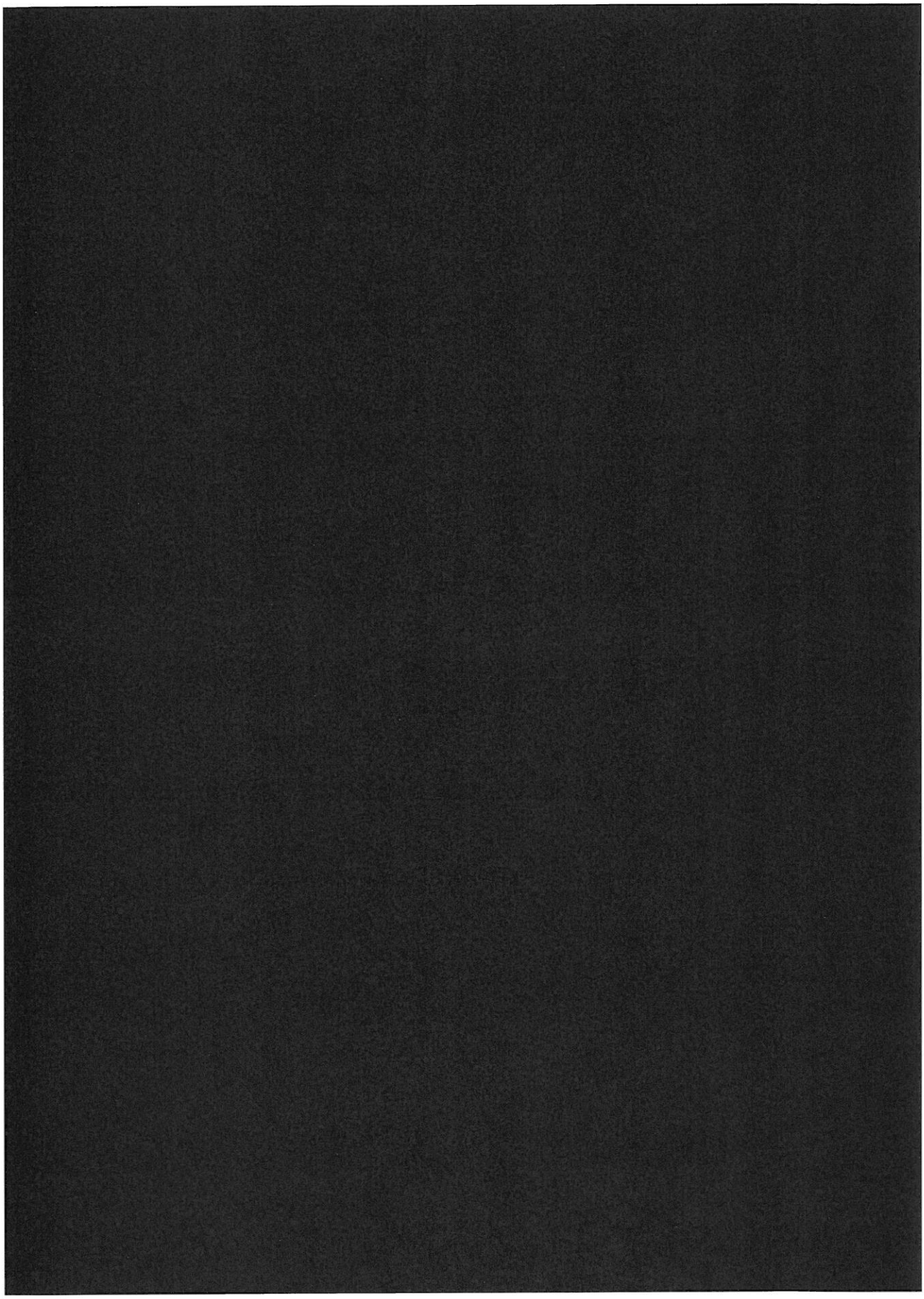




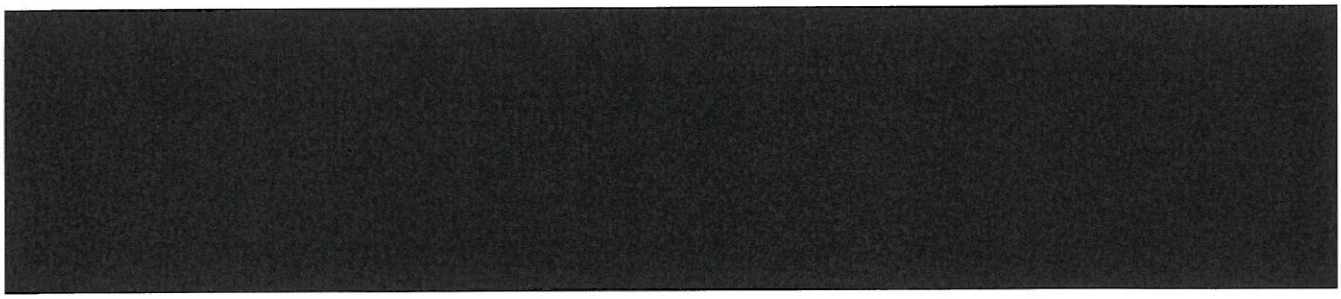


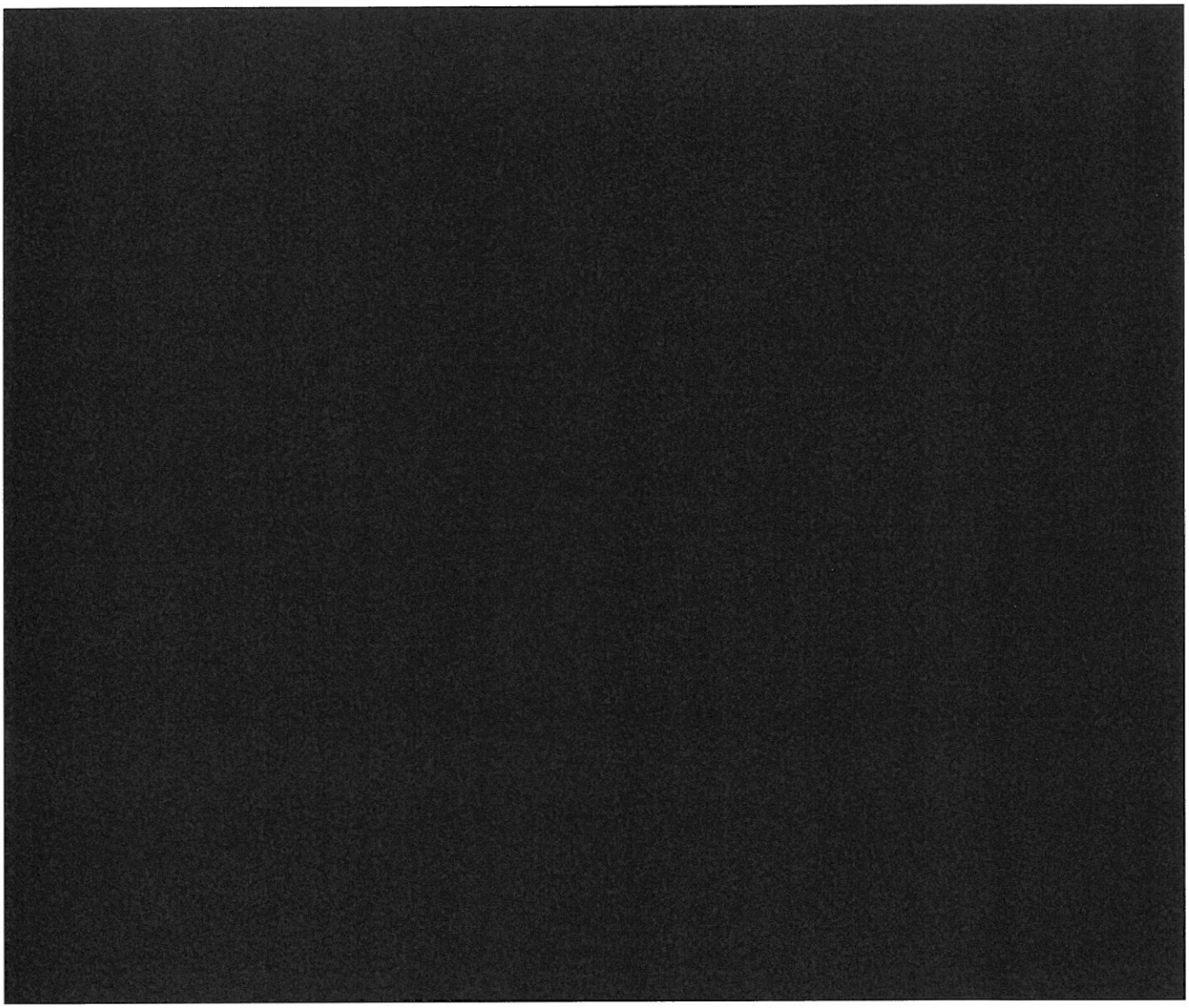


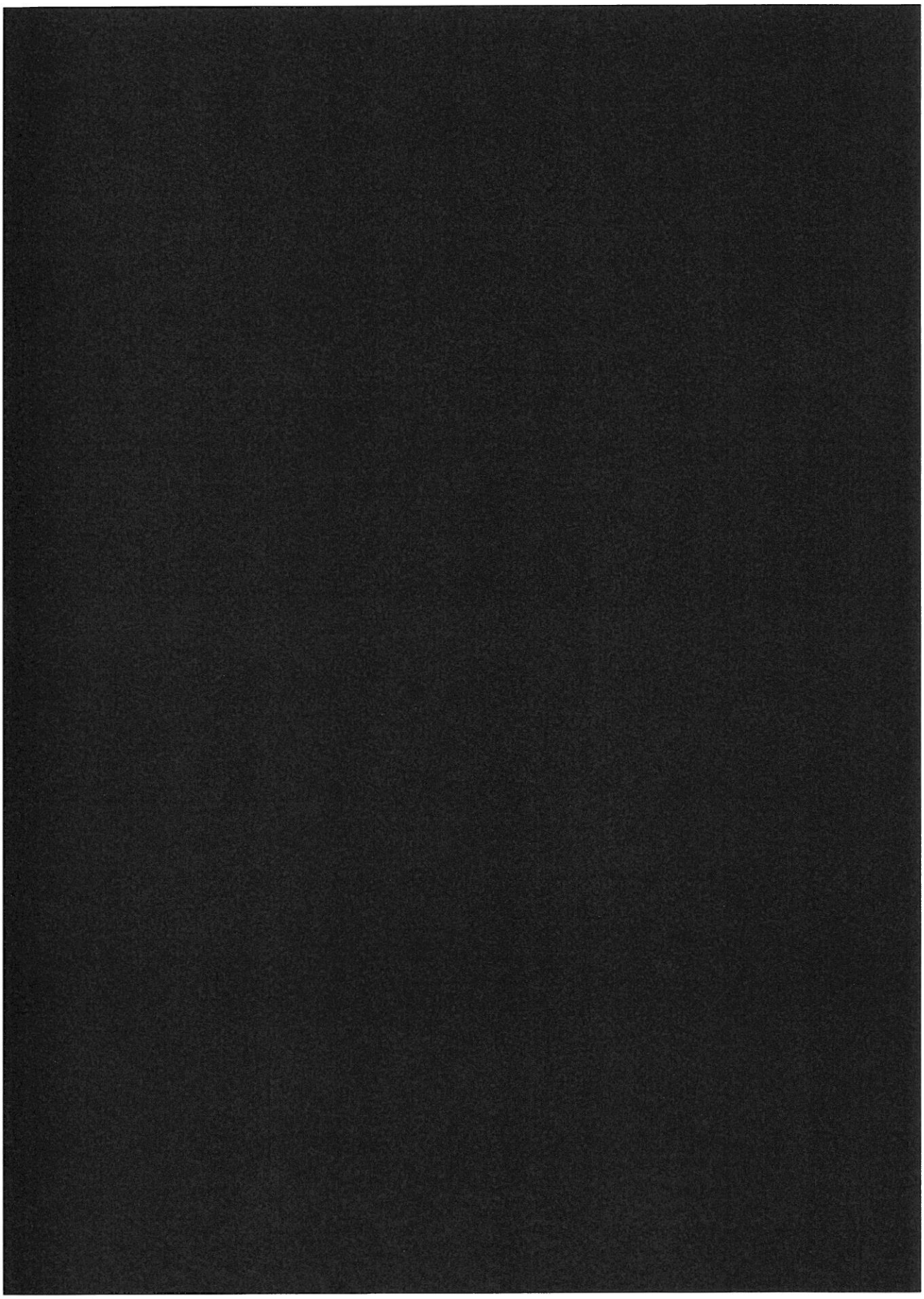


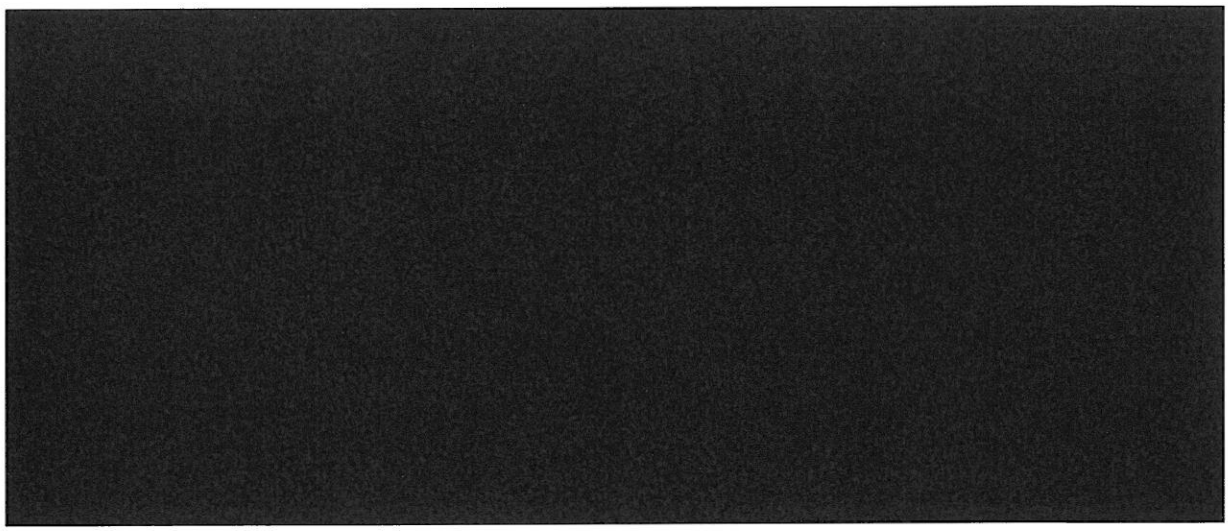


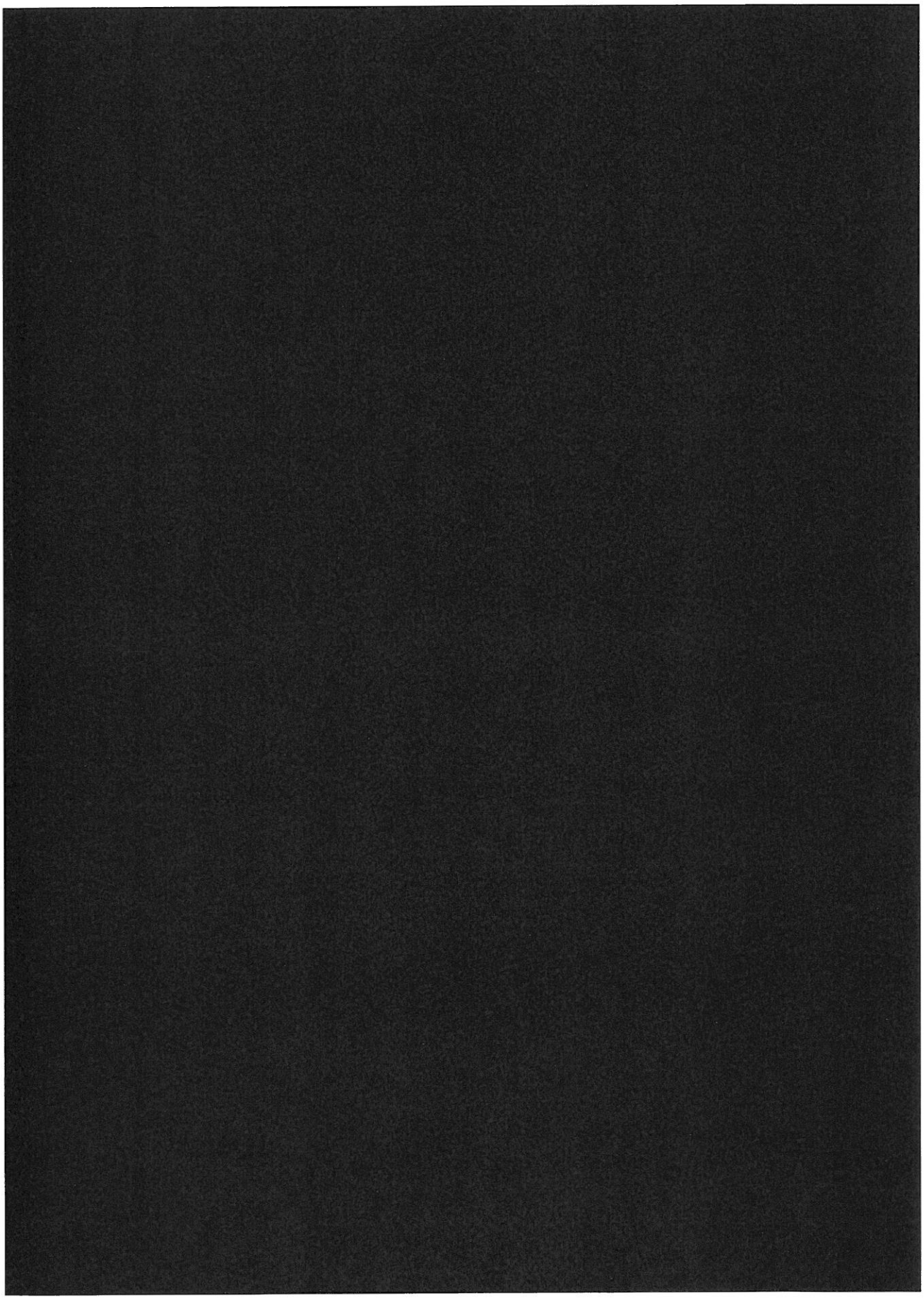
Appendix B

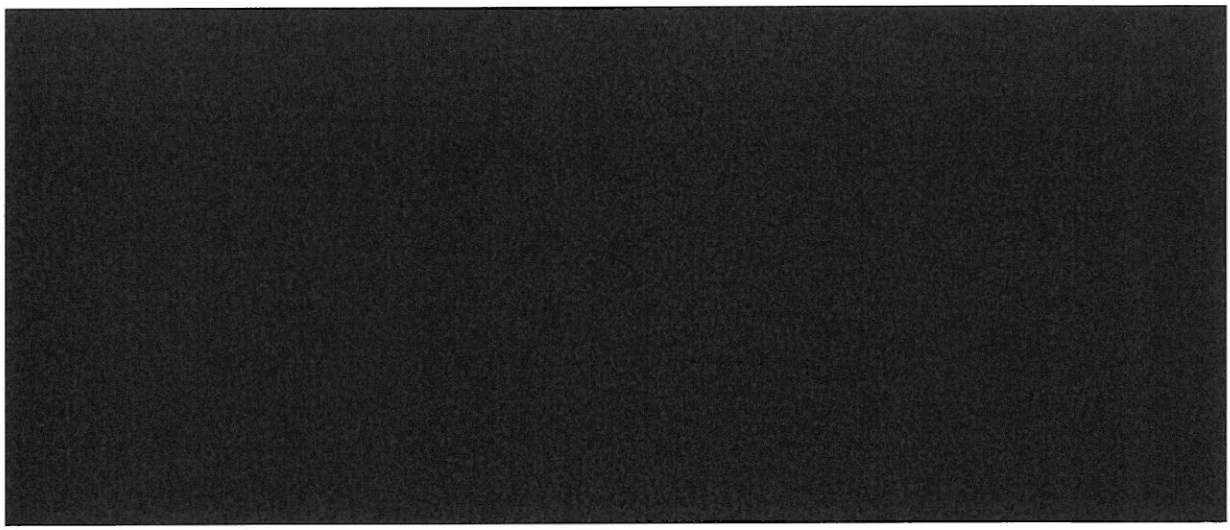












7. Document References

Refer-ence No.	Document Title and Version and Document No.
1	CP362 Clinical Investigation Plan, [redacted]
2	
3	
4	

8. Change Log

Version No.	Initials Issue Date (Month Year)	Short description of and reason for change
1.0	[redacted] Feb 2022	New document based on template "Formative Usability Test Protocol" version 2.0.

Signature Page for [redacted]

Reason for signing: Approved	Name: [redacted] Role: Approver Date of signature: 04-Apr-2024 14:02:15 GMT+0000
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