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Protocol for Study H24-501

Digital Spinal Range of Motion Measurement Development

VERSION:	2.0	DATE:	05 September 2023
SPONSOR:	AbbVie Inc.*	PLANNED NUMBER OF SITES:	1
ABBVIE INVESTIGATIONAL PRODUCT:	Not Applicable	Phase	0

FULL TITLE: A Non-Drug, Exploratory Study to Demonstrate Changes in Spinal Range of Motion in Healthy Controls and Axial Spondylarthritis Patients

Incorporating Versions 1.0 and 2.0

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* Additional study contact information can be found in the Operations Manual (Appendix F).

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1 SYNOPSIS

Title: A Non-Drug, Exploratory Study to Demonstrate Changes in Spinal Range Motion in Healthy Controls and Axial Spondylarthritis Patients	
Background and Rationale:	The goal of the study is to test the measurement validity of the Bend Ease DHT (digital health technology) in measuring the angle of forward functional bend. The exploratory goal of the study is to determine if the Bend Ease DHT can be used to measure morning stiffness duration and severity in an at-home setting. The measurement of forward functional bend is important for the diagnosis and management of rheumatologic conditions of the lumbar spine. The Bend Ease DHT can be used to manage disease by clinicians, or for label claims in clinical development studies.
Objective(s) and Endpoint(s):	The primary objective of this study is to investigate the analytical validity, repeatability, and usability of the Bend Ease app to measure spinal range of motion (SRoM). This study will compare the motion sensor-based bend angle measurements collected from the Bend Ease app with the in-clinic bend activity captured at baseline via video capture. The secondary objective of this study is to investigate the objective changes in SRoM that take place during the first hour after awakening in heathy and axial spondylarthritis (axSpA) subjects. This is the first time that such as measurement will have been performed, providing novel insights into the concept of morning stiffness.
Investigator(s):	[redacted], DO
Study Site(s):	[redacted]
Study Population and Number of Subjects to be Enrolled:	20 healthy control participants, 20 patients with diagnosed axSpA, a diagnosis that is inclusive of axial spondylitis (AS) or non-radiographic axial spondylarthritis (nr-axSpA)
Investigational Plan:	This is a non-drug, exploratory study of Bend Ease, a smartphone app-based DHT to measure SRoM using smartphone accelerometry (motion-sensing) data. The accuracy and precision of Bend Ease will be determined by comparing the forward flexion (forward bend) angles generated by Bend Ease with the forward flexion angles measured directly from video capture of forward flexion bend tasks. The study will also test the ability of Bend Ease to be used as an at-home measure of morning stiffness by comparing: 1. Bend Ease angle measures with patient-reported outcomes from the BASFI and BASDAI questionnaires. 2. Changes in DHT angle measures with changes in the Ease of Bend Questionnaire between when subjects wake up and various time points after wakeup. This study will also assess the usability of the Bend Ease app with the App Usability Survey.

Key Eligibility Criteria:	Volunteers older than 18 years of age that do not have balance issues that would prohibit them from performing a forward flexion (forward bend) task.
Study Drug and Duration of Treatment:	No study drug will be administered.
Date of Protocol Synopsis:	05 September 2023

2 INTRODUCTION

2.1 Background and Rationale

Why Is This Study Being Conducted?

Spinal mobility is a meaningful aspect of health and well-being, as it affects posture, movement, and pain. Spinal mobility, or SRoM, is impaired in axSpA, a spectrum of chronic inflammatory diseases primarily affecting the axial skeleton. SRoM impairment is at its peak for axSpA patients directly upon waking, commonly categorized as morning stiffness, and this stiffness improves with time and movement. However, morning stiffness is not objectively measured in a clinical setting, instead relying on subjective questionnaire recall. As a result, it is currently unknown the extent to which objective changes in SRoM occur during the alleviation of morning stiffness and whether this is different between healthy and axSpA populations. Addressing this measurement limitation has the potential to improve criteria for disease diagnosis; provide 'treat-to-target' goals for remote therapeutic monitoring; and create a differentiating clinical trial endpoint.

This study will determine the extent to which a smartphone app-based digital measurement tool, Bend Ease, can accurately measure functional forward bend movement with an acceptable variance when self-administered by study participants. The study will then investigate the changes in objectively measured bend angle over the course of one hour after awakening in an at-home setting. Bend Ease uses accelerometry (motion sensing) to measure bend angles and thus does not require an independent evaluator, and the sensors required for measurement are relatively ubiquitous and reliable in consumer smartphone technology. These features of Bend Ease may enable accurate and frequent self-measurement of SRoM where and when it has not previously been possible, providing a better understanding of axSpA symptom presentation for clinical care and clinical research.

2.2 Benefits and Risks to Subjects

There are no expected direct benefits for subjects who enroll in this study. The investigational DHT may be associated with adverse effects as detailed in the subject ICF(s). Subjects may experience minor discomfort or inconvenience related to study procedures.

3 OBJECTIVES AND ENDPOINTS

3.1 Objective(s)

The primary objective of this study is to investigate the analytical validity, repeatability, and usability of the Bend Ease app to measure SRoM. This study will compare the motion sensor-based bend angle measurements collected from the Bend Ease app with the in-clinic bend activity captured at baseline via video capture.

The secondary objective of this study is to investigate the objective changes in SRoM that take place during the first hour after awakening in both healthy and axSpA subjects. This is the first time that such

a measurement will have been performed, providing novel insights into the concept of morning stiffness.

3.2 Primary Endpoints

The primary endpoint of this study will be the level of agreement, measured by concordance correlation coefficient, between angular measurement of forward flexion derived from the Bend Ease app and angular measurement of forward flexion as measured by video capture in a clinical setting.

3.3 Additional Endpoints

- Test-Retest reliability of clinically performed Bend Ease measurements over the course of 7 days.
- Comparison of angular measurement of forward flexion performed in the clinical setting from the Bend Ease app with the BASFI patient-reported outcome questionnaire administered at the baseline visit.
- Comparison of angular measurement of forward flexion performed in the at-home setting from the Bend Ease app with the BASDAI Operations Manual (Appendix F) question 5 and question 6 (questions relating to morning stiffness magnitude and duration) patient-reported outcome questionnaire administered at the baseline visit.
- Comparison between changes in a patient questionnaire of functional bend difficulty from wake-up to 'wake-up + 1 hour' and the change in digital bend angle from wakeup to 'wake-up + 1 hour.'
- Comparison between average daily change in digital bend angle from wake-up to 'wake-up + 1 hour' with the BASDAI question 5 and question 6 administered at the end of study clinical visit.
- Descriptive time course analysis of average digital bend angle change from wake-up to 'wake-up + 30 min.' to 'wake-up + 1 hour' compared between healthy control subjects and axSpA subjects.
- Descriptive analysis of patient impressions of Bend Ease's overall usability as measured by the system usability scale.

3.4 Safety Endpoints

Safety evaluations will include AE monitoring.

4 INVESTIGATIONAL PLAN

4.1 Overall Study Design and Plan

This is a non-drug, exploratory study of Bend Ease, a smartphone app-based DHT to measure SRoM using smartphone accelerometry (motion-sensing) data. The accuracy and precision of Bend Ease will be

determined by comparing the forward flexion (forward bend) angles generated by Bend Ease with the forward flexion angles measured directly from video capture of forward flexion bend tasks. The study will also compare Bend Ease angle measures with patient-reported outcomes from the BASFI and BASDAI questionnaires and will compare changes in Bend Ease angle measures with changes in self-reported functional bend difficulty. This study will also assess the usability of the Bend Ease app with the System Usability Scale.

The study is planned to enroll approximately 40 subjects, 20 healthy control participants and 20 patients with a confirmed diagnosis of axSpA.

Bend Ease uses smartphone accelerometry data and a proprietary algorithm to calculate an angle of forward flexion achieved during a forward bend activity. While Bend Ease is running, subjects will hold the iPhone against their chest, press "Start," perform a forward bend to a comfortable limit of their mobility and return upright before pressing "Stop." The DHT will be used to measure bend in clinical and at-home settings.

For this study, subjects will complete both in-clinic and at-home activities to assess the measurement validity and system usability of Bend Ease. Prior to performing a measurement, subjects will be briefly trained with an in-app video module (SRoM Assessment Task Training) and the practice task on how to perform a forward flexion bend while using Bend Ease. Subjects will perform 3 forward flexion bends using Bend Ease. In the clinic on Day 1, a video will be captured of each bend event. For each of the 3 bends, forward flexion bend angles will be measured by Bend Ease and ground-truth angles will be measured using captured video. After a subject completes their bends, they will complete an in-person BASFI and BASDAI questionnaire to measure their functional impairment. This will be followed by completing the App Usability Survey Questionnaire to provide feedback on the technical and ergonomic function of Bend Ease.

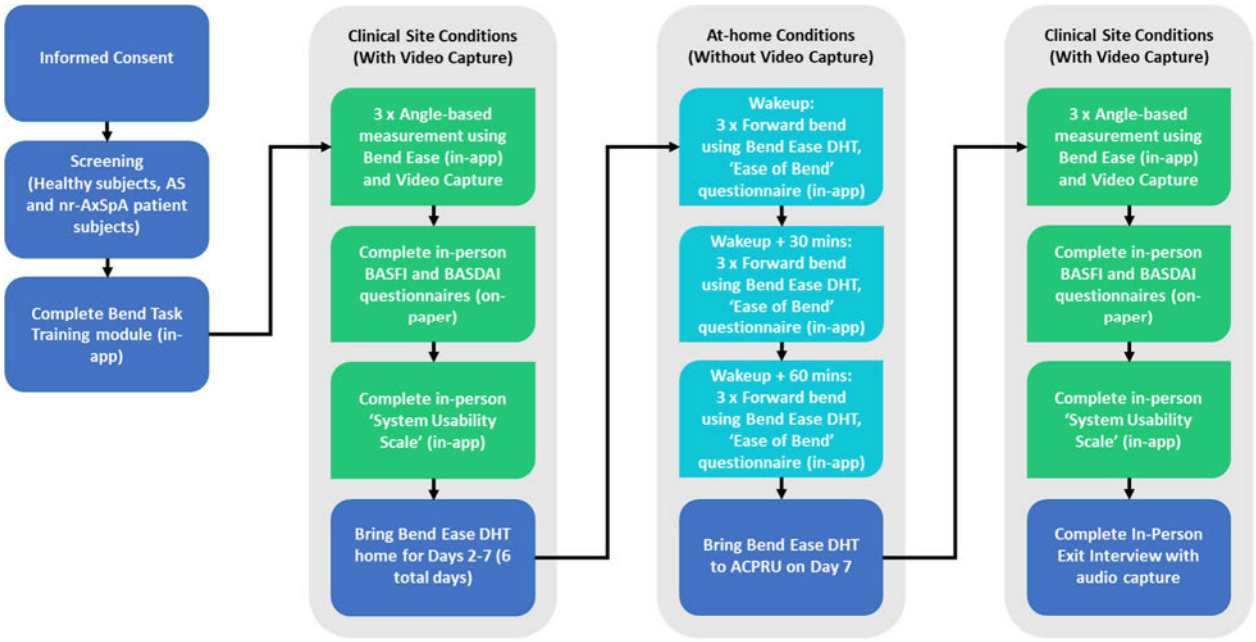
Subjects will take Bend Ease home on a provisioned device, an iPhone, for Days 2 - 6. At home, subjects will complete forward flexion bends using Bend Ease at 3 different time points: upon wakeup, 30 minutes after wakeup, and 60 minutes after wakeup. Measurements will be taken in triplicate at each time point. At each time point, subjects will also complete a Functional Bend severity questionnaire (Functional Bend PGI-S) built into Bend Ease that captures the perceived difficulty with which subjects complete each bend task. These measurements are designed to investigate the peak severity and alleviation of morning stiffness that is prevalent in the axSpA patient population, or the natural variation in forward flexion in the healthy control population.

On Day 7, subjects will return to the clinic and repeat the in-clinic activities listed above. After completing triplicate bends using Bend Ease which will be captured on video, subjects will complete BASFI, BASDAI, and App Usability Survey Questionnaire. Subjects will also complete an exit interview with standard questions meant to understand their individual experience using Bend Ease and participating in the study.

The schematic of the study is shown in Figure 1. Further details regarding study procedures are included in the Operations Manual (Appendix F).

See Section 5.1 for information regarding eligibility criteria. An interim analysis will not be conducted. The study site and subjects will not be blinded.

Figure 1. Study Schematic



4.2 Discussion of Study Design

Discussion of Study Design and Choice of Control Groups

The above study design follows an analytical validation study design, intended to assess the accuracy, reliability and usability of the novel digital measurement tool, Bend Ease. This design is distinguishable from a *clinical* validation design intended to investigate the clinical utility and generalizability of the measurements in a diverse patient population. Such a study is anticipated for future Bend Ease development in a larger remote cohort if analytical validity within tolerances can be established.

This study follows a 'hybrid' study design that includes in-clinic measurements and at-home (or remote) measurements to assess the reliability of the app in both its intended contexts of use. Objective reference measurements will not be performed during the at-home phase of the study; however, at-home measures will be 'anchored' to the self-reported bend difficulty questionnaire performed in both settings. The healthy control population is not expected to demonstrate significant differences in bend angle throughout the week, providing an assessment of test-retest reliability between settings.

The study is planned to enroll approximately 40 subjects, 20 healthy control participants and 20 patients with a confirmed diagnosis of axSpA (a disease classification that includes nr-axSpA and the more severe AS). These groups are intended to capture a wide dynamic range of bend angles, and the healthy control population will serve as a comparator during the exploratory morning measurements.

Appropriateness of Measurements

The app-based Bend Ease measurement DHT is designed to provide frequent and accurate self-measurement of SRoM with ubiquitous and familiar technology. While recognizing that a 'digital divide'

exists between those who have access and familiarity with technology and those who do not, smartphone technology is relatively pervasive[1] and provides a significant increase in access when compared to clinical measurements for SRoM. While the accuracy and precision of the measurements compared to reference remain to be characterized, the angle calculations from accelerometry data are granular, to the level of a single degree, which compared favorably to a clinical instrument such as an inclinometer with a minimum metrically detectable change of 9 degrees.[2]

Video capture of bend angle is planned as a reference measure due to its ability to capture reviewable evidence of the bend dynamics by investigators or independent raters, and the ability to analyze the data with objective pose estimation models using hip and shoulder landmarks. While other reference measures were considered such as the Modified Schober's test (a tape measure-based method) or a goniometer, these tools isolate specific mechanisms of bend such as lower lumbar flexion and may not reflect compensatory bend mechanisms such as increased thoracic spine bend that axSpA patients employ to achieve a functional bend in their everyday lives. In summary, video capture provides a reviewable assessment of overall functional bend and was chosen to be the most appropriate measure of overall functional bend for activities such as putting on shoes or picking up an item from the floor that are achieved in real-world settings, which is the intended context of use of this measurement tool.

The BASFI and BASDAI questionnaires are widely used and validated instruments for clinical trials. BASFI assess patient abilities, an example being "Please indicate your level of ability with each of the following activities during the past week: Putting on your socks or tights without help or aids (e.g., sock aid; bending from the waist to pick up a pen from the floor without aid)." This instrument was selected as an appropriate anchor with well-established validity and interpretation for our experimental measures for functional bend. The BASDAI instrument offers a patient-reported outcome of disease severity and contains two questions (question 5 and question 6) that relate the magnitude and duration of morning stiffness that will be used to anchor our exploratory measurements of morning functional bend and its change during the first hour after awakening.

The Ease of Bend Questionnaire has been chosen as a subjective assessment to provide interpretation and anchoring for the at-home Bend Ease measurements. The questionnaire follows a 7- item choice rubric that uses answers that have been described in the Patient Global Impression of Severity questionnaire that has an established minimum clinically important difference of 2 items between administrations.[3] However, our customized question asks that patients provide a free-text description of a meaningful task that requires a functional bend (e.g., pick up my children, gardening) by which to evaluate their level of difficulty in forward bending. This question is designed to provide subjects with the ability to interpret their difficulty in the context of a task that they routinely perform and is meaningful. The collection of this information provides a survey of meaningful tasks that may be used for future 'multiple-choice' implementations of this question and potentially addresses a frequent regulatory critique of new measurements that do not assess meaningful aspects of health to patient populations.

Suitability of Subject Population

The selection of subjects in general good health as controls is standard for a DHT validation study and provides a baseline for variability of bend angle. Patients with diagnosed AS or nr-axSpA (collectively, axSpA subjects) are included as subjects with relevant disease symptoms of impaired spinal mobility, greater variance in spinal mobility upon waking (morning stiffness), and to establish a wide dynamic range for the accuracy of the measurement of bend angle.

Selection of Doses in the Study

There is no study drug in this study.

Blinding

There will be no blinding of healthy control and patient subjects as there is no study drug in this study.

Meals and Dietary Requirements

There are no subject dietary requirements.

5 STUDY ACTIVITIES

5.1 Eligibility Criteria

Subjects must meet all the following criteria in order to be included in the study. Anything other than a positive response to the questions below will result in exclusion from study participation. A subject who has failed screening may be re-screened at an investigator's discretion.

Consent

- 1. Subjects must voluntarily **sign and date an informed consent**, approved by an IEC/IRB, prior to the initiation of any screening or study-specific procedures.

Demographics

- 2. Males and females at least 18 years of age inclusive at the time of screening.

Subject History/Physical Exam and Vital Signs

Healthy Volunteers

- 3. A condition of overall health that enables subjects to safely and independently stand and perform forward bending motions as determined by the investigator.
- 4. Healthy subjects: No prior history of diagnosed AS or AxSpA.
- 5. In the opinion of the investigator, this subject is a suitable candidate for enrollment in the study.

AS or AxSpA Patients

- 6. Must have the following as determined by medical history or the discretion of the investigator:
  - A prior diagnosis of nr-axSpA or AS
  - Chronic back pain of ≥3 months

- 7. No history of the following as determined by medical history or the discretion of the investigator:
  - Severe lumbar stenosis
  - Prior lower back surgery
  - Any acute or chronic syndrome that puts a subject at risk of falling when bending forward independently (i.e., Potts Syndrome, Vertigo, Labrynthitis)
  - In the opinion of the investigator, this subject is a suitable candidate for enrollment in the study.

5.2 Prior and Concomitant Therapy

Prior or concomitant therapies will not be collected.

5.3 Withdrawal of Subjects and Discontinuation of Study

A subject may voluntarily withdraw or be withdrawn from the study at any time for reasons including, but not limited to, the following:

- AEs, which rule out continuation of the study, as determined by the investigator or the AbbVie Therapeutic Area Medical Director.
- The investigator believes it is in the best interest of the subject.
- The subject requests withdrawal from the study.
- The investigator determines the subject is significantly noncompliant with study procedures.

AbbVie may terminate this study prematurely, either in its entirety or at any site. The investigator may also stop the study at their site if they have safety concerns. If AbbVie terminates the study for safety reasons, AbbVie will promptly notify the investigator.

5.4 Follow-Up After Subject Discontinuation from the Use of the DHT or Study

In the event that a subject withdraws or is discontinued from the study, the primary reason for discontinuation and any other reason(s) for the discontinuation from the study will be recorded and an assessment of AEs will be performed as soon as possible after discontinuation from the study.

If a subject is discontinued from the study with an ongoing AE, the investigator will attempt to provide follow-up until a satisfactory clinical resolution of the AE is achieved.

Subjects who withdraw from the study will be replaced in order to meet cohort size calculations that have been estimated to adequately power the study.

5.5 Study Digital Health Technology

Bend Ease is the study DHT.

Digital Health Technology Accountability

The investigator or their representative will verify that the DHTs – specifically, study-provisioned iPhones with the Bend Ease app – are received intact and in the correct amounts. A proof-of-receipt or similar document will be kept in the site files as a record of what was received.

In addition, sites will maintain records of traceability, accountability, and return including, but not limited to, date received/dispensed/returned, subject number, and the identification of the person dispensing/returning the DHTs.

5.6 Randomization

As they are enrolled in the study, subjects will be assigned unique consecutive numbers beginning with 101 for healthy control subjects and 201 for subjects with axSpA. There will be no randomization schedule for this study.

5.7 Protocol Deviations

AbbVie does not allow intentional/prospective deviations from the protocol except when necessary to eliminate an immediate hazard to study subjects. The investigator is responsible for complying with all protocol requirements, written instructions, and applicable laws regarding protocol deviations. If a protocol deviation occurs (or is identified), the investigator is responsible for notifying an IRB, regulatory authorities (as applicable), and AbbVie.

6 SAFETY CONSIDERATIONS

6.1 Complaints and Adverse Events

Complaints

A complaint is any written, electronic, or oral communication that alleges deficiencies related to the physical characteristics, identity, quality, purity, potency, durability, reliability, safety, effectiveness, or performance of a product/device. Complaints associated with any component of this investigational product must be reported to AbbVie.

Product Complaint

A product complaint is any complaint related to the biologic or drug component of the product or to the medical device component(s).

For a product this may include, but is not limited to, damaged/broken product or packaging, product appearance whose color/markings do not match the labeling, labeling discrepancies/inadequacies in the

labeling/instructions (e.g., printing illegible), missing components/product, device damage or not working properly, or packaging issues.

Product complaints concerning the investigational product and/or device must be reported to AbbVie within 24 hours of the study site's knowledge of the event. Product complaints occurring during the study will be followed up to a satisfactory conclusion.

Digital Health Tool Adverse Events

An AE is defined as any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the DHT.

If an AE meets any of the following criteria, it is to be reported to AbbVie Clinical Pharmacovigilance as a SAE within 24 hours after the site is made aware of the SAE (refer to Section 4.3 of the Operations Manual for reporting details and contact information):

- Led to death, injury, or permanent impairment to a body structure or a body function
- Led to a serious deterioration in the health of a subject that either resulted in:
  - a life-threatening illness or injury, or
  - a permanent impairment of a body structure or a body function, or
  - inpatient hospitalization or prolongation of existing hospitalization, or
  - medical or surgical intervention to prevent life threatening illness
- Led to fetal distress, fetal death, or a congenital abnormality or birth defect.

A planned hospitalization for a preexisting condition, or a procedure required by the protocol, without a serious deterioration in health, is not considered an SAE.

Adverse DHT Effects

Adverse DHT effects are AEs related to the use of the DHT. This includes any AE resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the installation, the operation, or any malfunction of the DHT. This includes any event that is a result of a use error or intentional abnormal use of the investigational DHT.

Serious Adverse DHT Effects

Serious adverse device effects are adverse DHT effects that have resulted in any of the consequences characteristic of an SAE.

DHT Deficiency

A DHT deficiency is an inadequacy of an investigational DHT related to its identity, quality, durability, reliability, safety, or performance. This may include malfunctions, use error, or inadequacy in the information supplied by the manufacturer.

If a DHT deficiency meets any of the following criteria, it is to be reported to AbbVie Clinical Pharmacovigilance within 24 hours after the site is made aware:

- Any SAE
- Any DHT deficiency that may have led to an SAE if:
  - suitable action had not been taken or
  - intervention had not been made or
  - circumstances had been less fortunate
- New findings/updates in relation to already reported events

DHT Causality Assessment

The investigator will use the following definitions to assess the relationship of the reportable DHT event.

Not Related – Relationship to the DHT can be excluded when:

- the event is not a known side effect of the product category the DHT belongs to or of similar devices and procedures;
- the event has no temporal relationship with the use of the investigational DHT or the procedures;
- the serious event does not follow a known response pattern to the medical DHT (if the response pattern is previously known) and is biologically implausible;
- the discontinuation of application or the reduction of the level of activation/exposure – when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure) do not impact on the serious event;
- the event involves a body site or an organ not expected to be affected by the DHT or procedure;
- the serious event can be attributed to another cause (e.g., an underlying or concurrent illness/clinical condition, an effect of another device, drug, treatment, or other risk factors);
- the event does not depend on a false result given by the investigational device use for diagnosis when applicable;
- harms to the subject are not clearly due to use error.

For non-relatedness to be established, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

Unlikely – the relationship with the use of the DHT seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.

Possible – the relationship with the use of the investigational DHT 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 – the relationship with the use of the investigational DHT seems relevant and/or the event cannot be reasonably explained by another cause, but additional information may be obtained.

Causal relationship – the serious event is associated with the investigational DHT or with procedures beyond reasonable doubt when:

- the event is a known side effect of the product category the DHT belongs to or of similar devices and procedures;
- the event has a temporal relationship with investigational DHT use/application or procedures;
- the event involves a body site or organ that
  - the investigational DHT or procedures are applied to;
  - the investigational DHT or procedures have an effect on;
- the serious event follows a known response pattern to the medical DHT (if the response pattern is previously known);
- the discontinuation of application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of level of activation/exposure) has impact on the serious event (when clinically feasible);
- other possible causes (e.g., an underlying or concurrent illness/clinical condition and/or an effect of another device, drug or treatment) have been adequately ruled out;
- harm to the subject is due to error in use;
- the event depends on a false result given by the investigational device used for diagnosis, when applicable.

For relatedness to be established, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

7 STATISTICAL METHODS & DETERMINATION OF SAMPLE SIZE

7.1 Statistical and Analytical Plans

The following sections provide a brief overview of the statistical methods used to evaluate the study endpoints. Completed and specific details of the statistical analysis will be described and fully documented in the DDAP.

7.2 Statistical Analyses

The primary endpoint will be assessed and reported using Lin's concordance correlation coefficient with 95% Confidence Interval to evaluate the level of agreement between angles measured by Bend Ease and by video capture, for each cohort and then pooled data.

For secondary endpoints, test-retest reliability of Bend Ease measurements using in-clinic measurements over the course of 7 days will be evaluated by intraclass correlation. Pearson/Spearman correlation coefficient will be calculated to assess the relationship between angular measurement of forward flexion derived from the Bend Ease app and results from the BASFI patient-reported outcome questionnaire, as well as the relationship between average daily change in digital bend angle from wake-up to 'wake-up + 1 hour' with the BASDAI question 5 and question 6 administered at the end of study clinical visit. Analysis of one hour change from wake-up will be conducted using MMRM for both Bend Ease angle measures and BASFI questionnaire results. Analyses for secondary endpoints will be performed separately on each cohort.

For descriptive analysis, categorical variables will be summarized with the number and percentage of subjects; percentages will be calculated based on the number of non-missing observations. Continuous variables will be summarized with descriptive statistics (number of non-missing observations, mean and standard deviation, median, minimum, and maximum).

7.3 Statistical Analyses for Safety

The statistical methods provided in this protocol will be focused on primary and exploratory analyses. Safety data aside from collection of AEs is not being collected nor analyzed in this protocol.

7.4 Sample Size Estimation

The sample size has been calculated for the primary endpoint of concordance correlation coefficient between angles measured by Bend Ease app and by video capture. With the initial sample size of 6 people in each cohort, a one sided 95% confidence interval for Lin's concordance coefficient will have lower limit 0.9, assuming a concordance coefficient of 0.98 with a variance term of 0.96 in each cohort. The estimates of the concordance coefficient and variance term were obtained from a preliminary dataset generated by 7 healthy volunteers internally. The final sample size of 20 subjects per cohort is to account for any unobserved variations not captured in this preliminary dataset.

8 ETHICS

8.1 Independent Ethics Committee/Institutional Review Board

The protocol, ICF(s), recruitment materials, and all subject materials will be submitted to the IEC/IRB for review and approval. Approval of both the protocol and the ICF(s) must be obtained before any subject is enrolled. Any amendment to the protocol will require review and approval by the IEC/IRB before the changes are implemented to the study. In addition, all changes to the consent form(s) will be IEC/IRB approved.

8.2 Ethical Conduct of the Study

The study will be conducted in accordance with the protocol, Operations Manual, ICH guidelines, applicable regulations, and guidelines governing clinical study conduct and the ethical principles that

have their origin in the Declaration of Helsinki. Responsibilities of the investigator are specified in Appendix B.

8.3 Subject Confidentiality

To protect subjects' confidentiality, all subjects and their associated samples will be assigned numerical study identifiers or "codes." The sponsor will only receive coded data, with the exception of the videos taken of the study participants in which they are identifiable.

9 SOURCE DOCUMENTS AND CASE REPORT FORM COMPLETION

The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be attributable, legible, contemporaneous, original, accurate, and complete to ensure accurate interpretation of data. Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol, ICH GCP, and applicable local regulatory requirement(s).

10 DATA QUALITY ASSURANCE

AbbVie will ensure that the clinical trial is conducted with a quality management system that will define quality tolerance limits in order to ensure human subject protection and reliability of study results. Data will be generated, documented, and reported in compliance with the protocol, ICH GCP, and applicable regulatory requirements.

11 START AND COMPLETION OF THE STUDY

The start-of-study is defined as the date of the first site activated.

The end-of-study is defined as the date of end of study participation by the last subject in the last country where the study was conducted.

12 REFERENCES

1. Smartphone penetration per capita. Available from: www.statista.com/statistics/203734/global-smartphone-penetration-per-capita-since-2005/.
2. Kolber MJ, Pizzini M, Robinson A, et al. The reliability and concurrent validity of measurements used to quantify lumbar spine mobility: an analysis of an iphone® application and gravity based inclinometry. Int J Sports Phys Ther. 2013;8(2):129-37.

3. Eremenco S, Chen WH, Blum SI, et al; PRO Consortium's Communication Subcommittee. Comparing patient global impression of severity and patient global impression of change to evaluate test-retest reliability of depression, non-small cell lung cancer, and asthma measures. Qual Life Res. 2022;31(12):3501-12.

APPENDIX A. STUDY-SPECIFIC ABBREVIATIONS AND TERMS

Abbreviation	Definition
[redacted]	[redacted]
AE	Adverse event
AS	Ankylosing Spondylitis
axSpA	Axial Spondylarthritis
BASFI	Bath Ankylosing Spondylitis Functional Index
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BMI	Body mass index
DDAP	Digital data analysis plan
DHT	Digital health technology
GCP	Good Clinical Practice
HCP	Health care provider
ICF	Informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent ethics committee
IRB	Institutional review board
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed effect model repeat measurement
Nr-axSpA	Non-radiographic axial spondylarthritis
NRS	Numerical pain rating scale
PE	Physical examination
PT	Preferred term
SAE	Serious adverse event
SAP	Statistical analysis plan
SOC	System organ class/standard of care
SRoM	Spinal range of motion
TEAE	Treatment-emergent adverse event

APPENDIX B. RESPONSIBILITIES OF THE INVESTIGATOR

Protocol H24-501: A Non-Drug, Exploratory Study to Demonstrate Changes in Spinal Range of Motion in Healthy Controls and Axial Spondylarthritis Patients

Protocol Date: 05 September 2023

Clinical research studies sponsored by AbbVie are subject to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practices (GCP), as well as applicable laws, regulations, and guidelines. Certain laws, regulations, or guidelines may apply to conduct of the study at investigator's site even if such laws, regulations, or guidelines originate in a foreign jurisdiction. The investigator agrees and acknowledges that applicable laws or regulations may require AbbVie to submit inspection reports, instances of significant non-compliance with the study protocol, or other documents regarding conduct of the study at the investigator's site to regulatory authorities, and such documents may be publicly disclosed by such authorities. In signing the Investigator Agreement, the investigator is agreeing to the following:

1. Conducting the study in accordance with ICH GCP, the applicable regulatory requirements, current protocol and operations manual, and making changes to a protocol only after notifying AbbVie and the appropriate Institutional Review Board (IRB)/Independent Ethics Committee (IEC), except when necessary to protect the subject from immediate harm.
2. Personally conducting or supervising the described investigation(s).
3. Informing all subjects, or persons used as controls, that the drugs are being used for investigational purposes and complying with the requirements relating to informed consent and ethics committees (e.g., IEC or IRB) review and approval of the protocol and its amendments.
4. Reporting complaints that occur in the course of the investigation(s) to AbbVie.
5. Reading the information in the Investigator's Brochure/safety material provided, including the instructions for use and the potential risks and side effects of the investigational product(s).
6. Informing all associates, colleagues, and employees assisting in the conduct of the study about their obligations in meeting the above commitments.
7. Maintaining adequate and accurate records of the conduct of the study, making those records available for inspection by representatives of AbbVie and/or the appropriate regulatory agency, and retaining all study-related documents until notification from AbbVie.
8. Maintaining records demonstrating that an ethics committee reviewed and approved the initial clinical protocol and all of its amendments.
9. Reporting the following to AbbVie within 1 calendar day of becoming aware:
   - Any unanticipated problems involving risks to human subjects
   - Any departure from relevant clinical trial regulation, GCP, or the trial protocol that has affected or is likely to affect to a **significant** degree the following:
     - Rights, safety, physical or mental integrity of the subjects in the clinical trial
     - Scientific value of the clinical trial, reliability or robustness of data generated

   Where required by local regulation, inform relevant Ethics Committees / Institutional Review Boards and other appropriate individuals (e.g., Co-ordinating Investigator, Institution Director).
10. Providing direct access to source data documents for study-related monitoring, audits, IEC/IRB review, and regulatory inspection(s).

Signature of Principal Investigator	Date
Name of Principal Investigator (printed or typed)	

APPENDIX C. LIST OF PROTOCOL SIGNATORIES

Name	Title	Functional Area
[redacted]		Digital Health Strategy
		Digital Health Strategy
		Statistics
		Clinical Pharmacology

APPENDIX D. ACTIVITY SCHEDULE

The following table shows the required activities. The individual activities are described in detail in the **Operations Manual** (Appendix F).

Study Activities Table

Activity	Screening	Day 1 (Clinical Visit)	Days 2-6 (At Home)	Day 7 Final Visit (Clinical Visit)
INTERVIEWS & QUESTIONNAIRES				
Informed Consent	✓			
Eligibility criteria	✓	✓		
Medical/surgical history (update only on Day 1)	✓	✓		
Adverse event assessment	✓	✓		✓
System usability scale (at end of visit)		✓		✓
Exit interview				✓
LOCAL LABS & EXAMS				
Height and Weight	✓	✓		
Vital signs	✓	✓		
Physical exam	✓	✓		
DIGITAL HEALTH TECHNOLOGY MEASUREMENTS				
Provide provisioned iPhone with Bend Ease app installed		✓		
Bend Ease Training module (in App)		✓		
Bend Ease measurements (triplicate), video capture of bend		✓		✓
(triplicate), ease of bend questionnaire		✓		✓
BASFI and BASDAI Questionnaire		✓		✓
Bend Ease measurements (in triplicate), ease of bend questionnaire @ Wake-up			✓	
Bend Ease measurements (in triplicate), ease of bend questionnaire @ Wake-up + 30 minutes			✓	
Bend Ease measurements (in triplicate), ease of bend questionnaire @ Wake-up + 1 hour			✓	
Return Provisioned Device				✓

APPENDIX E. PROTOCOL SUMMARY OF CHANGES

Protocol	Date
Version 1.0	03 August 2023

The purpose of this version is to correct minor clerical errors for consistency throughout the protocol in addition to the following:

Revision Made	Rationale
Updated language in Section 8.3, removed last sentence and replaced with applicable language for subject confidentiality.	Statement is needed to clarify details of subject confidentiality as it applies to this study.
Updated Section 4.2 of the Ops Manual regarding recording data and analyses of safety findings	Removed sentences 2 and 3, language is not applicable to this study.
Added language to Section 3.9 of the Ops Manual regarding BASFI and BASDAI questionnaires.	Statement added for clarification regarding bend ease measurements.
Updated language in Section 3.3 of the Ops Manual regarding height and weight	Removed language to align with eligibility criteria.
Updated language in Section 4.3 of the Ops Manual regarding reporting adverse events	Updated language for consistency throughout document. Removed language as it does not apply to this study and there will not be a monitor.
Updated activities table in Appendix D regarding adverse event assessment.	Removed checkmark because it is not a clinical visit for subjects.
Added language to Section 4.1 regarding overall study design and plan.	Language added for clarification.
Added language to Section 4.2 regarding discussion of study design.	Language added for clarification.
Updated language in Section 5.4 title	Language replaced for consistency throughout document.
Updated signatory in Appendix C.	Original assigned signatory does not have access to COSMOS due to nature of role. Signatory replacement is the manager.

APPENDIX F. OPERATIONS MANUAL