Test ID: PDS290-UT117-2013

Focused Usability Test of colour-blind individuals' ability to differentiate between Tresiba® 100 units/mL FlexTouch®, Tresiba® 200 units/mL FlexTouch®, and NovoRapid® FlexPen® pen-injectors and cartons

Redacted protocol
Includes redaction of personal identifiable information only.

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Table 1. Abbreviations and Terms

Abbreviation / Term	Definition
A-level	General Certificate of Education Advanced Level
AAMI	Association for the Advancement of Medical Instrumentation
CRO	Contract Research Organisation
DE	Germany
DK	Denmark
EMA	European Medicines Agency
GCSE	General Certificate of Secondary Education
HCP	Healthcare professional (e.g., doctor, nurse, pharmacist)
IEC	International Electrotechnical Commission
n	Number of participants within a test sub-group / sub-sample
NN	Novo Nordisk
PDS290 prefilled pen-injector	Novo Nordisk PDS290 prefilled pen-injector
O-level	General Certificate of Education Ordinary Level
OAD	Oral antidiabetic drug
PIP	Pseudo-Isochromatic plates
UK	United Kingdom

1 Introduction

Novo Nordisk will conduct a post-approval usability test (code name: PDS290-UT117-2013) requiring red-green colour-blind individuals to differentiate the two Tresiba® FlexTouch® variants (i.e., Tresiba® FlexTouch® 100 units/mL and Tresiba® FlexTouch® 200 units/mL) and the marketed NovoRapid® FlexPen®. The Tresiba® product packaging is in a green colour scheme and the NovoRapid packaging is in a red colour scheme. Novo Nordisk will contract with a Contract Research Organisation (CRO) to perform the usability test.

The usability test methodology is based on applicable portions of the human factors process, usability testing, and risk management guidance provided in the following documents:

- IEC 62366:2007, titled *Medical devices -- Application of usability engineering to medical devices*, published by the International Electrotechnical Commission (IEC). This document addresses the need to implement a human factors engineering program in conjunction with medical device development efforts. It focuses on device safety, effectiveness, and usability. This document replaces ANSI/AAMI HE74, titled *Human factors Design Process for Medical Devices*, published by the Association for the Advancement of Medical Instrumentation (AAMI)

- ANSI/AAMI HE75:2009, titled *Human factors engineering – Design of medical devices*. This document presents a large set of human factors guidelines pertaining to a medical device's user interface design. However, it also provides detailed guidance on the conduct of usability tests in Section 9

- *Applying Human Factors and Usability Engineering to Optimize Medical Device Design*. FDA draft guidance published June 22, 2011 regarding conducting appropriate usability testing and applying human factors engineering throughout device development

- Novo Nordisk's *Risk Management Analysis Input to Focused Usability Test* (UT117), final version 2.0, Doc. no. 001497415 dated 12 December 2013

2 Test Objectives

To fulfil Novo Nordisk's commitment to the European Medicines Agency (EMA) the test objective is to investigate whether people suffering from red-green colour-blindness can differentiate between different coloured prefilled pen-injectors and their respective packages (i.e., cartons).

Test personnel will document any use errors, close calls, and operational difficulties that occur when red-green colour-blind individuals select and interact with the Tresiba® 100 units/mL FlexTouch®, Tresiba® 200 units/mL FlexTouch®, and/or NovoRapid® FlexPen® and the respective

cartons. In the event of any use errors, close calls, or operational difficulties, test personnel will identify the root cause(s) associated with each event.

3 Test Data

3.1 Use Errors

The usability test will focus on identifying all the relevant safety-related use errors identified in the use error risk analysis as listed in Section 16 Attachment A: Usability extract of safety-related hazards from the Use Error Risk Analysis.

A use error is a case in which a participant performs a task in an incorrect manner that will not lead to the intended outcome.

In this usability test, a use error is a case in which the participant selects the incorrect prefilled pen-injector or carton (e.g., selects the Tresiba® 200 units/mL FlexTouch® instead of the NovoRapid® FlexPen® if the intention was to select NovoRapid® FlexPen®).

The root cause(s) of each identified use error will be evaluated in the context of potential clinical consequence and the severity of the potential, associated harm. Novo Nordisk will document the results of these follow-up evaluations as part of its risk management process.

The CRO will identify and document use errors based on its observations of participants' task performance. The CRO will also consider use errors that participants report during the post-test interview.

If usability testing reveals new hazards not already accounted for in Novo Nordisk's risk management document, Novo Nordisk will analyse the occurrence and associated potential hazard to determine if further mitigations are needed.

3.2 Close Calls

A close call is a case in which a participant almost commits a use error, but "catches" himself or herself and avoids committing the use error. The term also describes a case in which a user commits a use error but detects it in short order and recovers before the error becomes consequential.

The CRO will identify close calls based on its observations of participants' task performance. The CRO will also consider close calls that participants report during the post-test interview.

3.3 Operational Difficulties

An operational difficulty is a case in which a participant appears to struggle to perform a task or part thereof.

Such a struggle might be indicated by multiple attempts to perform the task; anecdotal comments about the task's difficulty; facial expressions and vocalizations suggesting frustration or confusion, for example, higher than usual task performance times. In this usability test, an operational difficulty is a case in which a participant struggles to differentiate between two products' prefilled pen-injectors or cartons.

The CRO will identify operational difficulties based on its observations of participants' task performance, as well as feedback participants provide when performing the tasks and responding to post-test interview questions.

3.4 Potential Root Causes

The potential root causes of use errors, close calls, and operational difficulties will be identified by analysing:

- Impromptu comments that participants make while performing tasks
- Participant responses post-test interview questions regarding what participants consider to be the root causes of observed and/or reported use errors, close calls, and operational difficulties

In the usability test report, the CRO will supplement the participant-reported root causes with root cause analysis based upon observations, experience conducting previous packaging differentiation usability tests, and professional judgment based on accepted human factors principles and practices.

4 Test Items

4.1 Product Packaging

The test will include the cartons and prefilled pen-injectors (i.e., packaging) for three products: Tresiba® 100 units/mL FlexTouch®, Tresiba® 200 units/mL FlexTouch® and NovoRapid® FlexPen® (see Figure 1, Figure 2 and Figure 3). The cartons and prefilled pen-injectors will be the currently marketed ones, with the exception that the prefilled pen-injectors will be filled with an inactive placebo (i.e., test medium) rather than active medication.

Figure 1. From left to right: cartons for Tresiba® 100 units/mL FlexTouch®, Tresiba® 200 units/mL FlexTouch® and NovoRapid® FlexPen®

Figure 2. From top to bottom: prefilled pen-injectors (without pen caps) for Tresiba® 100 units/mL FlexTouch®, Tresiba® 200 units/mL FlexTouch® and NovoRapid® FlexPen®

Figure 3 From top to bottom: prefilled pen-injectors for Tresiba® 100 units/mL FlexTouch®, Tresiba® 200 units/mL FlexTouch® and NovoRapid® FlexPen®

4.2 Participant Screening Materials

All test participants should be red-green colour-blind. To confirm prospective test participants' are in fact red-green colour-blind, each individual will be shown various Pseudo-Isochromatic plates (PIP, a.k.a. Ishihara plates, see Figure 4 and Figure 5) and asked to describe what they see. The CRO will collaborate with Novo Nordisk to determine exactly how the Ishihara test will be administered. The CRO tentatively plans to have a test team member and/or research facility representative administer the test once the participant arrives to the research facility for his/her scheduled introduction session appointment.

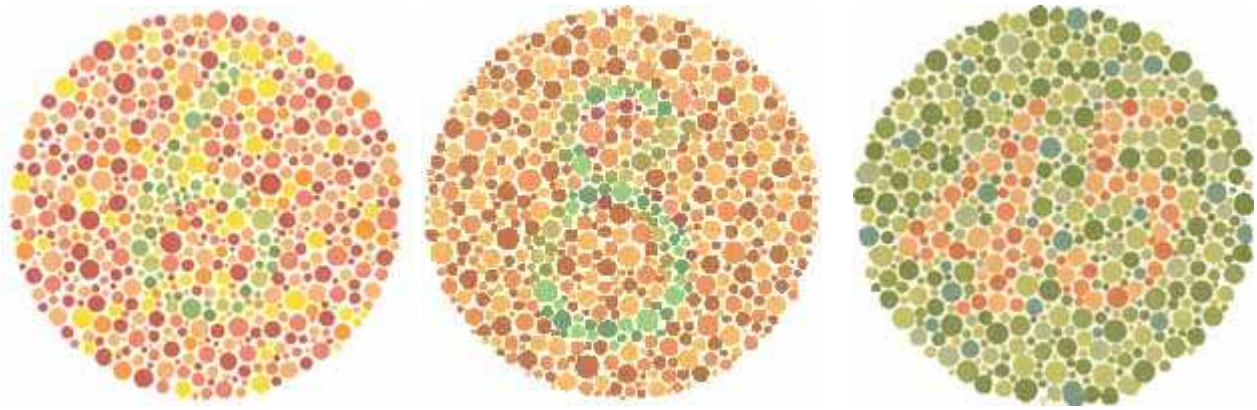

Figure 4. Sample Ishihara plates used to diagnose red-green colour deficiencies

4.3 Testing Materials

The CRO will use the following materials to conduct the usability test:

- Mini refrigerator or like-sized container in which to present the prefilled pen-injector cartons
- Open-top bin (i.e., cup) in which to present the prefilled pen-injectors
- Digital video camera (to record the introduction and test sessions)
- Tripod (to stabilize the video camera)
- Digital still camera (to photograph pertinent user interactions with the prefilled pen-injectors and cartons)
- Laptop computer running Microsoft Excel for data collection
- Snacks suitable for consumption by people with diabetes
- Water and other beverages suitable for consumption by people with diabetes
- Stopwatch (to measure time for completing tasks)
- Working telephone (landline or mobile) to summon help in the event of a health emergency

5 Test Participants

The usability test will involve approximately 30 people with diabetes who are red-green colour-blind. The test will be carried out until 20 participants have completed the test without committing any errors.

The test will include people with diabetes who are red-green colour-blind as it is not considered to be reflecting real life to include random people being red-green colour-blind for the test.

5.1 Inclusion Criteria

- **Diabetes type.** Individuals with Type 1 or Type 2 diabetes who currently self-administer insulin daily using a prefilled pen-injector, vial and syringe, or insulin pump, or who have self-administered insulin in the past
- **Gender.** Recognizing that colour-blindness predominantly affects men, the test will likely include mainly males but females may also be included. We do not expect sex to affect participants' interactions with the test materials

- **Vision.** All participants will be red-green colour-blind. Participants with other mild and moderate visual impairments (e.g., near-sightedness, glaucoma) will be included to the extent that they are identified during participant recruitment. The CRO will not specifically aim to include or exclude individuals with visual impairments other than colour-blindness

- **Ability to read dose counter.** All participants must be able to read the numerals displayed in the prefilled pen-injector's dose window (e.g., 16), consistent with the IFU which states the following: "If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help"

- **Education.** The test will include participants with various levels of education. However, the CRO will not specifically aim to include or exclude individuals with any certain distribution of educations

5.2 Exclusion Criteria

- **Cognitive or Physical Impairments.** Mental or extreme physical incapacity, such as self-reported dementia and paralysis, respectively

- **Hearing.** Hearing impairment to an extent that the subject cannot hear the test administrator speaking at a normal volume

- **Literacy.** Illiteracy

- **Prior participation.** Prior participation in any prefilled pen-injector usability test / research study involving hands-on use of prefilled pen-injector packaging within the past year

5.3 Colour-blindness screening

As mentioned in Section 4.2: Participant Screening Materials, to confirm prospective test participants' are in fact red-green colour-blind, each individual will be shown various Pseudo-Isochromatic plates (PIP, a.k.a. Ishihara plates, see Figure 4 and Figure 5) and asked to describe what they see.

Specifically, prospective test participants will be shown plates #1-14. Individuals will only be eligible to serve as test participants if they cannot read the correct number in at least 12 of the 14 plates. Note that eligible individuals might be able to see a number, but not necessarily the correct number. For example, on plate #5, a participant who reports seeing the number 21 will be eligible because the actual number visible by individuals with normal colour vision is 74.

To the extent that it is feasible in the different research facilities, the plates will be presented in a room that is well-lit by daylight, as opposed to only overhead, flourescent lighting.

The plates are held 75 centimeters (29.5 inches) from the participant and oriented such that the page is at a right angle to the line of the vision (i.e., the page is held straight up such that participant has a "head-on" view). Individuals should verbally identify the numeral presented on the page within less than 3 seconds. Hesitation of 3 or more seconds suggests a colour vision deficiency, and will be considered a failure to read the plate. Participants using glasses or contact lenses should be wearing these during the colour-blindness screening.

Pseudo-Isochromatic Plates (PIP) Score Sheet

Plate	Normal	Color Vision Defect	Color Vision Defect
Demo	16	16	16
1	2	Nothing	Nothing
2	42	Nothing	Nothing
3	28	Nothing	Nothing
4	8	Nothing	Nothing
5	74	21	Nothing
6	15	17	Nothing
7	5	2	Nothing
8	29	70	Nothing
9	57	35	Nothing
10	5	Nothing	Nothing
11	45	Nothing	Nothing
12	10	Nothing	Nothing
13	6	Nothing	Nothing
14	7	Nothing	Nothing
15	35	3 (5) Mild Green Defect (3) 5 Mild Red Defect	3 Strong Green Defect 5 Strong Red Defect
16	2	Nothing	Nothing
17	9	Nothing	Nothing

Figure 5. PIP score sheet used to determine whether a person is red-green colour-blind

The third column of Figure 5 shows results from a person with some red-green colour vision deficiencies, whereas the fourth column shows results for a person with total red-green colour-blindness and weakness. Test Participants who fail according to column 3 and column 4 qualify for the test.

Plates #15-17 are intended for advanced colour vision testing and are not relevant for this usability test.

5.4 Test Participant Withdrawal

The test administrator will inform the test participant that she/he may withdraw from the usability test at any time without cause or explanation, or without forfeiting the compensation. Participants might opt to withdraw from the usability test for the reasons listed below (or for other, unanticipated reasons):

- Participants feeling ill during the test

- Participants who want to withdraw their previously provided consent
- Participants who exhibit cognitive impairment and/or are reportedly or apparently unable to perform the duties required by study participation (e.g., read task instructions)

5.5 Recruitment

[redacted] in Denmark, [redacted] in the UK, and/or [redacted] in Germany, all external market research and recruiting firms,[1] will be contracted to recruit, screen, and schedule all participants according to the above criteria and Novo Nordisk-approved recruiting screeners. The CRO and Novo Nordisk will collaboratively determine which country/countries to conduct testing in based on the results of a pre-screening activity intended to identify potential participants.

5.6 Compensation

The market research and recruiting firms will compensate participants approximately 1300 DKK in Denmark, £150 in the UK, and 175 € in Germany for participating in the usability test's introduction and test sessions. If a test participant attends the introduction session but cannot attend the usability test session, she/he will receive half of the total compensation.

These compensation levels are set to maximize recruiting efficiency and help ensure that the scheduled participants attend their scheduled introduction and usability test sessions.

5.7 Identity Protection / Data Confidentiality

The CRO will record participants' names as evidence that the usability test involved identifiable individuals with the proper qualifications. The CRO will not provide participants' names to Novo Nordisk.

Data will be collected in a confidential manner and will not be linked to participants' full names, but rather to an alphanumeric code (e.g., [redacted] for the twelfth participant). Participants' full names will not appear in the test report or raw data sheet. All data will be stored in a secure location, and computer-based files will be available only to authorized staff.

The test report will include photos of participants performing certain tasks. Such photos will not include participants' names. The informed consent form will seek each participant's approval to video record and take still photographs during the test session. Each participant will have the option to limit the use of video recordings and photographs for internal project purposes, or to extend the

[1] [redacted] and [redacted]

use of video recordings and photographs to broader purposes, such as for inclusion in technical papers and presentations. All participants must allow us to video record the session and take still photographs for internal project purposes to participate in the usability test.

5.8 Potential Risks to Human Subjects

This usability test poses minimal risks to participants. The participants will not deliver any drug product, interact with needles, nor receive medical treatment during the test.

The potential, arguably minimal, risks include:

- The participant might become fatigued during the test session
- The participant might experience negative emotions, such as frustration and annoyance; emotions that mentally healthy individuals should be able to handle without consequence

5.9 Human Subjects Protection

The following human subjects' protections will be exercised during each usability test session:

- The participant will not participate in the usability test without first providing his or her informed consent
- The test administrator will notify the participant that she/he may withdraw from the test at any time without cause or explanation and without forfeiting the compensation
- The test administrator will advise the participant that the study's focus is on the test item's performance, and not on their performance per se
- Test prefilled pen-injectors will be filled with test medium rather than drug product
- There will be a first aid kit and a telephone (available to call emergency services [e.g., 112]) in the test room

6 Test Environment

6.1 Locations

The CRO might conduct the usability test in one or more cities in Denmark, the UK; and/or Germany. The CRO expects these locations to provide sufficient access to a representative sample of people with diabetes who are red-green colour-blind.

6.2 Testing Space

This test will require a space equivalent to a living room or small conference room. The test administrator will sit at a table with the participant. The CRO will use a simultaneous interpreter in Denmark and/or Germany; the interpreter will sit at the table with the test administrator and participant.

Introduction to test products shall take place in a small conference space (or equivalent) near the test room in the test locations. The person giving the introduction will sit at a table with the participant. In the event that we use a simultaneous interpreter in Denmark and/or Germany, the interpreter will sit at the table or a few meters from the person giving the introduction and participant.

6.3 Observation Space

Novo Nordisk representatives and other approved observers will sit in a room adjacent to the test room where they can view the test proceedings through a one-way mirror. Alternatively, observers may view the test proceedings remotely via live video that can be streamed over the Web.

6.4 Lighting Level

The test room will be illuminated by overhead fluorescent lights. The average lighting level at table level is likely to be in the range of 400 to 1500 Lux, noting that the time of day and local facility conditions (e.g., windows, presence or absence of window shades, natural light level) might result in some variability in the final lighting levels.

6.5 Sound Level

The test room will be relatively quiet (about 50 dBA), comparable to a physician's office or home in which there is no major source of unwelcome noise. However, there may be occasional, unplanned acoustic distractions, such as telephones ringing, doors opening and closing, footsteps, and cars driving by as in an actual use environment.

7 Test Personnel

7.1 Test Administrator

The test administrator's responsibilities will include:

- Conducting a pre-test interview to review the participant's responses to the background questionnaire (see Section 18: Attachment C: Background Questionnaire)

- Guiding the participant through the test session's administrative and technical activities
- Using a Microsoft Excel spread sheet to document use errors, close calls, and operational difficulties that the participant encounters while performing tasks, as well as to document participants' comments regarding the associated root causes and other data listed in Section 12: Data Collection
- Conducting a post-test interview regarding the ease of performing the differentiation tasks and asking in-depth questions regarding the potential root causes for use errors, close calls, and operational difficulties not previously discussed
- Observing for any participant distress that would suggest the need to take a break or end the test session prematurely, consistent with human subjects protection
- Asking follow-up questions during the interviews
- Adjusting the video camera to capture informative views of the test activities
- Taking digital photographs of pertinent test events
- Reviewing the video-recordings as needed between and/or after the test sessions to supplement the data collected in real-time

A CRO staff member will introduce test participants to the test materials, one at a time, for approximately 10 to 15 minutes similar to what is expected in real life. The session will involve an introduction and orientation to the three products involved in the test: Tresiba® 100 units/mL FlexTouch®, Tresiba® 200 units/mL FlexTouch® and NovoRapid® FlexPen®. The session will take place at least 30 minutes and up to 36 hours before the scheduled usability test session.

A Novo Nordisk representative will train the CRO staff member to ensure she/he knows how to deliver an appropriate introduction regarding how to identify each prefilled pen-injector and carton in terms of product name, strength, and insulin type.

7.2 Simultaneous Interpreter

To facilitate testing in Denmark and/or Germany, the CRO will engage a simultaneous interpreter experienced at supporting usability tests to enable the English-speaking test administrator to communicate clearly with the Danish- or German-speaking participant. The interpreter will sit in the test room and, in real-time, translate the test administrator's comments and questions from English to Danish/German, and translate the participant's comments and responses from Danish/German to English.

8 Test Limitations

The ability to simulate device use is limited by the fact that participants will not be asked to perform actual drug injections after they have selected the product, hence they might be less focused on selecting the correct product as there is no risk for the test subjects if they choose a wrong product. Hence, a participant may be much more careful about choosing the right product in real life than about a choice he/she is pretending to make for the sake of the usability test.

In real life although patients might be exposed to different products at home, they would not be introduced to three new products at once and repeating the same type of task multiple times may cause confusion and lead to errors. In general people might behave differently when they know they are being observed in the simulated test setting; i.e. be more careful or less careful or be stressed.

Novo Nordisk does not expect the limitations cited above to unduly compromise the ability to conduct an effective usability test due to the simplicity of the test.

9 Introduction to Products

As such participants will not be trained but a CRO staff member, interpreter, or other individual trained by Novo Nordisk will introduce the test participants to the three products[2] prefilled pen-injectors and cartons and explain how to identify each prefilled pen-injector and carton based on the insulin type, product name and strength. This approach is expected to mimic a real life introduction with the limitation that there will be no introduction to how to actually use the product. Each session will be video recorded.

Introduction will take place 30 minutes to 36 hours prior to participating in the usability test. This approach recognises that some users might need to differentiate products independently within hours of receiving introduction to the product, whereas others might need to do so a day later.

The delay period is intended to shift the test's focus from the participant's immediate recall of how to identify each product and its associated packaging to his/her ability to identify the product(s) based on retained knowledge, pre-existing knowledge, and skill.

10 Test Execution

Novo Nordisk expects each test session to last upwards of one hour, which should provide sufficient time to administer the colour vision test and 6 differentiation tasks, ask interview

[2] Tresiba® 100 units/mL FlexTouch®, Tresiba® 200 units/mL FlexTouch®, and NovoRapid® FlexPen®

questions, and debrief about any use errors, close calls, or operational difficulties that the participant encounters.

10.1 Execute Informed Consent

Prior to beginning the introduction session, the participant will review and sign the informed consent form. Test personnel will answer any questions participants have and ensure that the participant is comfortable participating in the usability test. A participant who is not comfortable signing the informed consent form will be excluded and dismissed from the study without compensation.

10.2 Welcome and Orient Participant

The test administrator will begin each test session by welcoming the participant into the test room and initiating "small talk" to create a friendly working atmosphere and reduce any tension that the participant might be experiencing. The CRO considers this to be an effective way to get participants to interact naturally with the test items, noting that any interactive difficulties encountered might introduce performance-shaping stress.

10.3 Administer Colour Vision Test

One of the test team members or a research facility staff member will administer a colour vision test using Pseudo-Isochromatic plates (PIP), the Ishihara plates (see Figure 4), to confirm the participant is red-green colour-blind. The result page (see Figure 5) will serve as guidance.

10.3.1 Dose reading exercise

Prior to performing the tasks, the test administrator will set a prefilled pen-injector dose to 16 units and ask each participant to read the dose counter. To be eligible, the participants should be able to read and understand a dose on the prefilled pen-injector with and without visual impairment, consistent with the IFU which states the following: *"If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help."*.

10.4 Review Completed Background Questionnaire

After arriving at the research facility and signing the informed consent form, each participant will complete a questionnaire (see Section 18: Attachment C: Background Questionnaire) focused on the participant's demographic characteristics and insulin administration experience. The test administrator will review the participant's responses to the questionnaire and ask additional follow-up questions as needed to clarify the participant's responses.

10.5 Read Session Introduction

Next, the test administrator will read the test session introduction presented in Section 19: Attachment D: Test Session Introduction. This introduction will serve to describe the test session in general as well as:

- Encourage the participant to perform tasks at a comfortable pace, rather than rushing or taking more time than they might normally take if performing the task at home or in another casual setting
- Direct the participant to work independently, explaining that test personnel will observe quietly and without intervening or interrupting the participant
- Remind the participant that the research goal is to evaluate the prefilled pen-injectors' packaging rather than judge the participant
- Encourage the participant to exercise the normal level of care that he or she would if selecting a prefilled pen-injector or carton of essential medication (i.e., behave as if use errors could be hazardous to his or her health)

10.6 Administer Tasks

The hands-on portion of the test will require all participants to perform a total of 3 carton differentiation tasks and 3 pen-injector differentiation tasks (see Section 11: Tasks). Each participant will perform 1 carton differentiation task and 1 prefilled pen-injector differentiation task with each of the three products: Tresiba® 100 units/mL, Tresiba® 200 units/mL, and NovoRapid®. Approximately half of the participants will be assigned to "Group A" and the remaining half will be assigned to "Group B." Each group will perform a different set of 6 differentiation tasks, presented in a random order.

We will counterbalance the order in which participants retrieve the two products to control for ordering effects. During carton differentiation tasks, participants will select a specified prefilled pen-injector carton from a refrigerator or comparable container that includes 2 of the 3 different prefilled pen-injector cartons pictured in Figure 1. The prefilled pen-injector differentiation tasks will require participants to select a specified prefilled pen-injector from a cup containing 2 of the 3 different prefilled pen-injectors pictured in Figure 2 and Figure 3. The time each participant used for completion of each differentiation task will be recorded.

Each task instruction will be printed in large text on an individual card and placed in front of the participant. Refer to Section 11: Tasks for the full task list and detailed task instructions. Prior to beginning each task, the participant will read the task instructions aloud, which will designate the task starting point.

10.7 Conduct Post-Test Interview

After the participant performs all tasks and other aforementioned activities, the CRO will conduct a post-test (i.e., exit) interview. The interview will focus on collecting feedback regarding the tasks' usability and identifying root causes for any use errors, close calls, and operational difficulties.

The test administrator will ask the following questions:

1. On a 1-7 scale (1 = difficult, 7 = easy), please rate the ease of selecting the requested cartons from the refrigerator. *[Ask "why" as a follow-up to any ratings of 1-4.]*

2. On a 1-7 scale (1 = difficult, 7 = easy), please rate the ease of selecting the requested prefilled pen-injectors from the bin. *[Ask "why" as a follow-up to any ratings of 1-4.]*

3. *[To collect feedback regarding operational difficulties]* Was there anything difficult or confusing about the tasks?

4. *[To collect feedback regarding use errors]* Do you believe you made any mistakes while performing the tasks?

5. *[To collect feedback regarding close calls]* Were there any "close calls," or cases in which you almost made a mistake but you avoided it or quickly recovered from it?

The CRO will ask follow-up questions as needed to gain a full understanding of the root cause(s) associated with any reported use errors, close calls, and operational difficulties. The CRO will also seek to collect information regarding what the participant might have done differently (if anything) if performing the task at home.

These usability-related ratings collected in response to Questions #1 and #2 above will serve as gross indicators of the ease of identifying particular prefilled pen-injectors and cartons. As noted above, the test administrator will probe more deeply to understand the cause of medium-to-low ratings (i.e., ratings in the 1-4 range).

10.8 Compensate and Dismiss Participant

At each test session's conclusion, each participant will be compensated according to the compensation amounts listed in Section 5.5: Recruitment. Note that these amounts also account for travel time, and travel expenses, though participants might be reimbursed for parking fees.

Participants will be compensated after the test session (rather than the introduction session) to help ensure that participants attend their second session. However, if a participant cannot attend the second session, she/he will be mailed the appropriate compensation amount.

11 Tasks

The tasks will be administered as described in Section 10.6: Administer Tasks. In addition Table 2 and Table 3 list the task instructions and products presented for each Group A and Group B tasks, respectively.

Table 2. Group A Differentiation tasks

#	Task card instructions	Products presented
Carton differentiation tasks		
C1	Retrieve a Tresiba® 100 units/mL FlexTouch® carton from the refrigerator. Take out one prefilled pen-injector, remove the pen cap and confirm that right product has been chosen.	Tresiba® 100 units/mL / NovoRapid®
C2	Retrieve a Tresiba® 200 units/mL FlexTouch® carton from the refrigerator. Take out one prefilled pen-injector, remove the pen cap and confirm that right product has been chosen.	Tresiba® 200 units/mL / Tresiba® 100 units/mL
C3	Retrieve a NovoRapid® FlexPen® carton from the refrigerator. Take out one prefilled pen-injector, remove the pen cap and confirm that right product has been chosen.	NovoRapid® / Tresiba® 200 units/mL
Prefilled pen-injector differentiation tasks		
P1	Retrieve a Tresiba® U100 units/mL FlexTouch® from the cup. Remove the pen cap and confirm that right product has been chosen.	Tresiba® 100 units/mL / NovoRapid®
P2	Retrieve a Tresiba® U200 units/mL FlexTouch® from the cup. Remove the pen cap and confirm that right product has been chosen.	Tresiba® 200 units/mL / Tresiba® 100 units/mL
P3	Retrieve a NovoRapid® FlexPen® from the cup. Remove the pen cap and confirm that right product has been chosen.	NovoRapid® / Tresiba® 200 units/mL

Table 3. Group B Differentiation tasks

#	Task card instructions	Products presented
Carton differentiation tasks		
C4	Retrieve a Tresiba® 100 units/mL FlexTouch® carton from the refrigerator. Take out one prefilled pen-injector, remove the pen cap and confirm that right product has been chosen.	Tresiba® 100 units/mL / Tresiba® 200 units/mL
C5	Retrieve a NovoRapid® FlexPen® carton from the refrigerator. Take out one prefilled pen-injector, remove the pen cap and confirm that right product has been chosen.	NovoRapid® / Tresiba® 100 units/mL
C6	Retrieve a Tresiba® 200 units/mL FlexTouch® carton from the refrigerator. Take out one prefilled pen-injector, remove the pen cap and confirm that right product has been chosen.	Tresiba® 200 units/mL / NovoRapid®
Pen-injector differentiation tasks		
P4	Retrieve a Tresiba® U100 units/mL FlexTouch® from the cup. Remove the pen cap and confirm that right product has been chosen.	Tresiba® 100 units/mL / Tresiba® 200 units/mL
P5	Retrieve a NovoRapid® FlexPen® from the cup. Remove the pen cap and confirm that right product has been chosen.	NovoRapid® / Tresiba® 100 units/mL
P6	Retrieve a Tresiba® 200 units/mL FlexTouch® from the cup. Remove the pen cap and confirm that right product has been chosen.	Tresiba® 200 units/mL / NovoRapid®

12 Data Collection

12.1 General Approach

A single CRO human factors specialist will serve as both the test administrator and data analyst. In other words, one person will administer (i.e., moderate) the test session and record test data in real-time. The test administrator will document key findings – use errors, close calls, operational difficulties – within a test-specific Microsoft Excel spread sheet. The CRO will video record all test sessions, and will provide video recordings to Novo Nordisk upon request.

The test administrator and person introducing the participant to the products will review excerpts of the introduction and/or test session video recordings as needed to resolve any uncertainties about the recorded data or review a particular participant action or comment in more detail. However, the

CRO does not plan to review all introductions and/or test session videos during the course of collecting or analysing test data.

There will be no collection and reporting of Adverse Events since the participants will not be administering any drug and will not interact with needles during the test.

12.2 Introduction Session Data

The following data will be collected on the product introduction record (see Section 17: Attachment B: Product Introduction Record) during the introduction session:

- Session start and end time
- Session length (in number of minutes)
- Whether the participant is a current prefilled pen-injector user
- Free-hand notes regarding participant behaviour and competency

12.3 Test Session Data

The following data will be collected by the CRO during the test session:

- Use errors, close calls, and operational difficulties observed during the tasks
- Time used for completion of each task
- Participants' comments (paraphrased)[3] before, during, and after task performance
- Participants' comments (paraphrased) regarding how they might respond to certain scenarios and perform certain tasks if they were at home
- Participants' responses (paraphrased) to pre-test and post-test interview questions, as well as to questions related to the root cause(s) of use errors, close calls, and operational difficulties
- Participants' subjective task ratings
- Test administrator comments and observations regarding pertinent events

[3] All participant comments documented in real-time will be paraphrased as opposed to verbatim. The CRO will review test session video recordings as needed to document verbatim comments associated with specific use errors and discussions of interest to Novo Nordisk

- Timestamps (i.e., notes regarding the time into the video-recording) associated with pertinent events such as use errors and root cause-related interviews

13 Data Analysis

After completing the test, the CRO will consolidate and analyse the test data as follows:

- Review test data and apply professional judgment to describe and determine the root cause(s) for use errors, close calls, and operational difficulties
- Count the total number of each type of use error, close call, and operational difficulty
- Calculate the means and ranges of the ratings and visualize the data as a bar graph
- Calculate the means and ranges of time used for completion of task and visualize the data as a bar graph
- Summarize participant demographic / background information

14 Test Report

The CRO will document the test findings in a Microsoft Word-based narrative report using the Novo Nordisk style template. Pending further discussion with Novo Nordisk, the CRO anticipates that the report might include the following sections:

- Executive Summary
- Summary Methodology
- Participants
- Use Errors
- Close Calls
- Operational Difficulties
- Subjective Task and Post-Test Ratings
- Attachments
    - Detailed Participant Background Information

- Task List

Novo Nordisk will review and comment on a draft report before the CRO finalises it. Importantly, the CRO will not render a decision regarding whether the usability test findings are satisfactory (i.e., whether the test "passed" or "failed").

14.1 Timelines

The test will start immediately after approval of the protocol by EMA and the outcome of the test will be reported to EMA within six months from approval of the protocol.

15 Risk Management

Novo Nordisk will perform a follow-up analysis of every use error, close call, and operational difficulty described in the usability test report. This analysis will determine if any of the aforementioned events pose a residual risk to device users.

Novo Nordisk will assess the consequence of use errors and to determine whether any additional risk mitigations are required to reduce the risk of use errors/hazards to be As Low As Reasonably Practicable (ALARP).

16 Attachment A: Usability extract of safety-related hazards from the Use Error Risk Analysis

Step to be tested	Risk identifier	HAZOP ID	Non-serious use error criterion	Potentially serious use error criterion	Close call criterion	Comments
Step 1 Pick the correct carton box / prefilled pen-injector	See "**Step 3**"	See "**Step 3**"	See "**Step 3**"	See "**Step 3**"	See "**Step 3**"	See "**Step 3**"
Step 3 Verification via label and cartridge holder that it is the correct carton box / prefilled pen-injector	Picks Tresiba® 100 units/mL FlexTouch® Basal insulin – should have been Tresiba® 200 units/mL FlexTouch® Basal insulin	1.B.20 1.B.38	N/A	N/A	(see comments column)	Only a use error if participant has retrieved the wrong prefilled pen-injector/carton and confirmed that this (wrong product) is the correct product. Close call if initial selection of prefilled pen-injector/carton box is wrong, but corrected before confirming that the correct product has been chosen. **Please note:** If the participant omits step 3 (Verification via label and cartridge holder that it is the correct carton box / prefilled pen-injector) but has successfully completed step 1 (Pick the correct carton box / prefilled pen-injector), this shall not be registered as a use error.
	Picks NovoRapid® FlexPen® Bolus insulin – should have been Tresiba® 200 units/mL FlexTouch® Basal insulin	1.B.7 1.B.8 1.B.23 1.B.41	N/A	(see comments column)	(see comments column)	
	Picks Tresiba® 200 units/mL FlexTouch® Basal insulin – should have been Tresiba® 100 units/mL FlexTouch® Basal insulin	1.B.15 1.B.30	N/A	N/A	(see comments column)	

Step to be tested	Risk identifier	HAZOP ID	Non-serious use error criterion	Potentially serious use error criterion	Close call criterion	Comments
	Picks NovoRapid® FlexPen® Bolus insulin – should have been Tresiba® 100 units/mL FlexTouch® Basal insulin	1.B.1 1.B.2 1.B.18 1.B.33 1.B.36	N/A	(see comments column)	(see comments column)	For a mix-up between Tresiba® 100 units/mL and Tresiba® 200 units/mL it is classified to be without any medical consequence as the dose counter shows the amount of insulin units which will be injected If a user selects a NovoRapid® FlexPen® instead of a Tresiba® 100 units/mL FlexTouch® it is classified as a potential serious use error. If a user selects a NovoRapid® FlexPen® instead of a Tresiba® 200 units/mL FlexTouch® it is classified as a potential serious use error. If a user selects a Tresiba® 100 units/mL FlexTouch® instead of a NovoRapid® FlexPen® it is classified as a non-serious use error. If a user selects a Tresiba® 200 units/mL FlexTouch® instead of a NovoRapid® FlexPen® it is classified as a non-serious use error.
	Picks Tresiba® 100 units/mL FlexTouch® Basal insulin – should have been NovoRapid® FlexPen® Bolus insulin	1.A.11 1.A.17	(see comments column)	N/A	(see comments column)	
	Picks Tresiba® 200 units/mL FlexTouch® Basal insulin – should have been NovoRapid® FlexPen® Bolus insulin	1.A.11 1.A.17	(see comments column)	N/A	(see comments column)	

17 Attachment B: Product Introduction Record

Participant first name / last initial_____ **Participant #**_____

Date_____ **Start time**_____ **End time**_____ **# mins**_____

Circle "Yes" or "No" for each row below.

Current durable (re-fillable) pen-injector user?	Yes	No
Current pre-filled pen-injector user?	Yes	No
Current vial & syringe user?	Yes	No
Current pump user?	Yes	No

Notes:

_____

_____

_____

_____

_____

_____

Participant competency indication (please initial):

_____ The participant understands the differences between the prefilled pen-injector products' packaging in terms of insulin type, product name and strength. He/she is appropriate to participate in the usability test

_____ The participant does **NOT** understand the differences between the prefilled pen-injector products' packaging in terms of insulin type, product name and strength. He/she is **NOT** appropriate to participate in the usability test

Signature _____ **Date:**_____

18 Attachment C: Background Questionnaire

Note: The CRO will write the participant number at the top of the completed questionnaire at the start of the test session. The questionnaire will be translated into Danish and/or German as needed to enable Danish and German test participants, respectively, to complete the questionnaire in their native language. Moreover, the multiple choice options for education level will be revised as needed to reflect the typical education levels in Denmark and/or Germany.

Background Questionnaire	
What is your age?	_____Years
How is your eyesight?	_____Normal _____Reading glasses _____Glasses _____Contacts _____Impairment: _____ How does the impairment affect your ability to inject insulin, if at all? _____
Have you been diagnosed with any vision impairments?	_____No _____Yes (check items below) _____Retinopathy _____Cataract _____Glaucoma _____Age-related maculopathy Colour-blindness, type _____ _____Other: _____ How does your visual impairment affect your ability to inject insulin, if at all? _____

Background Questionnaire	
What is your current or most recent occupation? (If you are retired / unemployed / disabled / etc., please list your previous occupation.)	_____
What is the highest level of education you have completed?	_____GCSE / O-level _____A-level _____Foundation degree _____Undergraduate Degree _____Postgraduate degree _____Doctorate
Is [English/Danish/German] your first language?	_____Yes _____No, First language:_____
What medication do you take to treat your diabetes?	Name of injectable: _____ Name of tablets: _____ Name of other medications: _____ (if more than one) Name of device (if any): _____
How many injections do you normally perform per day and how much medication do you normally inject at those times?	Number of injections per day: _____ or use pump (circle) If you inject using pen-injector or vial and syringe, record information about each injection you provide during an average day: Medication: _____Time of day:_____ Dose: _____ Medication: _____Time of day:_____ Dose: _____ Medication: _____Time of day:_____ Dose: _____ Medication: _____Time of day:_____ Dose: _____ Medication: _____Time of day:_____ Dose: _____ Medication: _____Time of day:_____ Dose: _____ Medication: _____Time of day:_____ Dose: _____

Background Questionnaire	
How do you currently administer your medication?	_____Syringe _____Durable (re-fillable) pen-injector _____Insulin Pump ____Pre-filled pen-injector Other: _____

19 Attachment D: Test Session Introduction

19.1 General Introduction

Today we will have you interact with a few different insulin prefilled pen-injectors and their associated packaging. The goal of our research is to have you perform some tasks and to collect your feedback regarding the ease of identifying the products.

It is important to remember that we are not evaluating you – we are evaluating the products. So, please do not feel nervous or under pressure.

You can take a break at any time, and you can end the session at any time you wish if you are feeling unwell or uncomfortable.

19.2 Task Administration and Performance

We will ask you to read task instructions from a card aloud and then perform specific tasks with the product. You do not need to think aloud or tell us what you are doing while you perform the task. Rather, you can work silently. However, please let us know if something is difficult or confusing, or if you think you made a mistake at any point.

We would like you to work at a comfortable pace, rather than rushing or taking more time than you might normally take if working at home.

Do you have any questions?

19.3 Test material presentation (performed before administering each product's task set)

[Show the first product the participant will retrieve from the refrigerator and open-top bin; put open-top bin on the table.] Imagine that you just returned home from the pharmacy with your new prefilled pen-injector and you will be using it later today for the first time. Take a moment to look at the carton and prefilled pen-injector, and then place the carton in the refrigerator and the pen-injector in this bin. Note that I might move the products around later on during the session.

Note: The two products' presentation order will be counterbalanced to control for ordering effects.