IRB Approved at the Protocol Level Apr 14, 2023

DEVICE:

APPLICABLE FOR INTERFACE VERSIONS:

NMOSDCOPILOT MOBILE APPLICATION

v1.0.X

CLINICAL TRIAL ENTITLED:

"PERFORMANCE AND SAFETY OF A DIGITAL TOOL FOR THE UNSUPERVISED SELF-ASSESSMENT OF NEUROMYELITIS
OPTICA SPECTRUM DISORDER"

ACRONYM:

OPTIS

NCT: 05566769 / ADS-OPTIS-2023

SPONSOR:

AD SCIENTIAM SAS
21-23 RUE ALBERT BAYET
75013 PARIS
FRANCE



INSTRUCTIONS FOR USE For Patients

CAUTION - Investigational device. Limited by United States law to investigational use.

This document is strictly for the use of the users of NMOSDCopilot. It cannot be used or distributed for any other purpose, and/or otherwise disclosed, communicated or reproduced without the prior written consent of its manufacturer, Ad Scientiam.

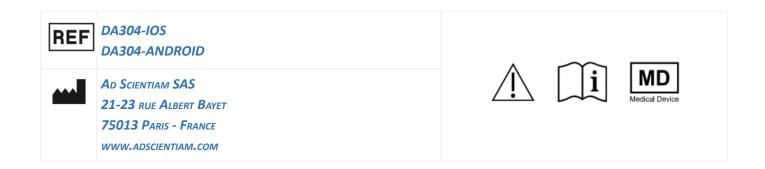




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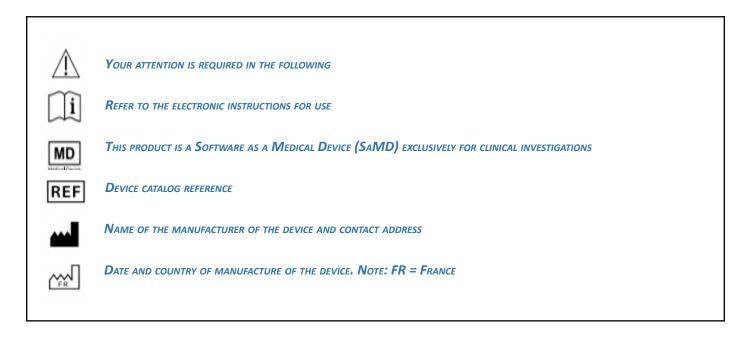
About this document

These instructions for use are intended for patients.

Before using NMOSDCopilot for the first time, you must read this document entirely.

Useful information

The product and its instruction manual use symbols and icons whose meaning is described below:





What is NMOSDCopilot?

NMOSDCopilot is a smartphone application which includes five tests that have been developed based on the clinical tests performed by NeuroMyelitis Optica Spectrum Disorder (NMOSD) specialists



Perimeter test ≅... 0.62 miles (1km) max

This test allows you to track your walking abilities.



Dexterity test
② 2 minutes

This test allows you to track your dexterity.



© 2 minutes

This two-part test allows you to track your cognitive abilities by measuring information processing time.



Vision test

© 10 minutes

This test allows you to track your visual abilities.



Endurance test

© 6 minutes

This test allows you to track your walking abilities.



NMOSDCopilot also includes six questionnaires



My Pain Questionnaire **© 1 minute**

Digital version of Pain VAS



My Fatigue Questionnaire

© 5 minutes

Digital version of Modified Fatigue Impact Scale



My Bladder Function Questionnaire

(§ 1 minute

Digital version of Bladder **Control Scale**



My Bowel Function Questionnaire

© 1 minute

Digital version of Bowel Control Scale



My Mental Health Questionnaire

© 2 minutes

Digital version of Patient Health Questionnaire - 8



My Quality of Life Questionnaire

() 10 minutes

Digital version of Short Form Survey





Start

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Intended use of the device

NMOSDCopilot is a software as a medical device consisting of a mobile application running on smartphones and a web portal.

The NMOSDCopilot smartphone application will be used as an investigational version of the Software as a medical device during the OPTIS study. This means that the version of the app was specifically developed by Ad Scientiam for this clinical investigation.

The mobile application is intended to be used by patients living with Neuromyelitis Optica Spectrum Disorder (NMOSD), in their home environment, as an unsupervised self-assessment digital tool of various functional parameters. These parameters include walking perimeter, walking speed, hand function, low contrast visual acuity and cognitive processing time. It also includes digital questionnaires.

The patient should not take action on the device output without consultation with a qualified Healthcare Professional (HCP).

The assessment results are intended to be visualized on the web portal by healthcare professionals qualified to interpret the functional assessment results over time, for remote patient monitoring. NMOSDCopilot is an adjunctive tool and is not intended to be used as a standalone diagnostic device nor to identify the presence or absence of clinical diagnoses.

Intended users of the device

NMOSDCopilot (mobile application) is intended to be used by the patients themselves if they meet the criteria of the intended patient population.

Indications for use and intended population

The NMOSDCopilot mobile application is intended to be used by the patients who have given their consent to participate in the OPTIS study.

NMOSDCopilot (mobile application) is intended for the follow-up of adult patients diagnosed with NMOSD who meet the criteria of inclusion of the OPTIS study:

- 18 years or older
- Aquaporin 4+ NMOSD as defined by the 2015 international consensus diagnostic criteria
- With NMOSD treatment (treatment must be unchanged since 6 months before enrollment, and 1 month for analgesics, antidepressants, neuroleptics)
- With an EDSS (Expanded Disability Scale Status) score ranging from 0 to 7
- Able to use a smartphone and to read and interpret texts and pictograms on this support



Recommendation for use

During your participation in the OPTIS study, you will have to use NMOSDCopilot as described in the Informed Consent Form:

- Perform the NMOSDCopilot Digital Checkup in clinic under the supervision of your study doctor during the three scheduled in-clinic visits at D0, after 6 months and after 12 months;
- Perform the **NMOSDCopilot Digital Checkup at home** at D0+7 days, M6-7 days and once a month between D0 and the end of the study (after 12 months).
- Answer online questionnaires that you will receive via email or text message.

You will receive push notifications, emails and/or text messages to remind you to do the Digital Checkups at home.



Risks and Benefits

General warnings and precautions for use



THE TEST RESULTS PROVIDED BY THE **NMOSDC**OPILOT MOBILE APPLICATION ARE FOR INFORMATION PURPOSES ONLY AND SHOULD ONLY BE INTERPRETED IN THE PRESENCE OF A HEALTHCARE PROFESSIONAL.

Contra-indications



THE USE OF NMOSDCOPILOT IS NOT RECOMMENDED FOR PEOPLE WITH A NEUROLOGICAL DISEASE OTHER THAN NMOSD AND FOR PATIENTS WITH A PHYSICAL OR MENTAL INCAPACITY TO USE A SMARTPHONE.

Benefits and residual risks

You will not personally benefit from using this device. However, information obtained from this app may benefit people in the future and may contribute to the creation of new tests, new medicines, or other items that may further expand the knowledge about NMOSD and its management through the use of innovative digital tools.

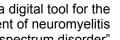
The risks of performing NMOSDCopilot tests may involve some discomfort to you:

- You may feel temporarily tired.
- You may feel anxiety triggered by misinterpretation of tests results
- You may hurt yourself if you perform the tests in an unsafe environment (for instance, performing a walking test when there is ice on the ground could lead to you slipping and falling).

To reduce these risks, you should follow the instructions presented in this leaflet. You should also pay attention to the instructions given to you by the study personnel during in-clinic visits, and to the instructions given to you in the NMOSDCopilot app.

Adverse Events

An adverse event is defined as an undesirable experience associated with the use of a device. In case of any adverse event observed during the use of NMOSDCopilot, refer to your study doctor.



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<u>Setup</u>

Minimum requirements for smartphone compatibility



DO NOT USE NMOSDCOPILOT ON A DAMAGED SMARTPHONE (CRACKED OR BROKEN GLASS FOR INSTANCE) AS THIS COULD COMPROMISE THE MEASUREMENT PERFORMANCE OF THE DEVICE.

To function properly, the application must be used on a smartphone whose language of use is supported by the application.

Your smartphone must run on an Android or iOS operating system, according to one of the following configurations:

| A NDROID [®] SMARTPHONES |
|--|
| Operating systems: Android 8 or higher version |
| Models: Any model (with the compatible OS) |
| INTERNAL STORAGE: 150 MB MINIMUM |
| RAM: 150 MB MINIMUM |
| |

You can find this information on your phone settings the following way:

IF YOU ARE AN IPHONE USER:

- 1. Press the Menu button until the main menu appears.
- 2. OPEN YOUR PHONE'S SETTINGS APP AND SELECT GENERAL. TAP
- 3. THE SOFTWARE VERSION OF YOUR DEVICE SHOULD APPEAR ON THIS SCREEN

IF YOU ARE AN ANDROID USER:

- 1. OPEN YOUR PHONE'S SETTINGS APP.
- 2. NEAR THE BOTTOM, TAP ABOUT PHONE.
- 3. TAP SOFTWARE INFORMATION, THEN ANDROID VERSION.

Downloading the application

An internet connection (WiFi/3G/4G/5G) is required to download and install NMOSDCopilot. Your doctor will assist you in downloading the application on your smartphone and login. Open the application store: (App Store for Apple® smartphones; Google Play for Android® smartphones)



Open the search function, enter manually the name of the application: "NMOSDCopilot" and validate the search. To start the download and installation of this application, click on the "get" or "install" button. The application will download and install automatically. The installation is successful when the NMOSDCopilot application is present in the application directory. It can be identified by its logo and name:



Login

Welcome

The email will be composed as follows: Countrycode-sitecode-000X@optis.study

No identifying information will be collected in NMOSDCopilot.

The study doctor will maintain the login information in their medical record to assist with the access to the application. If you forget your email or password, please contact them using the contact provided at the end of this document.

You must not share the password with anyone.



Use of the NMOSDCopilot application

IMPORTANT NOTE:

YOUR PHONE MUST BE SUFFICIENTLY CHARGED TO PERFORM THE TESTS (AT LEAST 30% OF THE BATTERY).

Walking tests (perimeter and endurance)



TO MINIMIZE THE RISK OF FALL, DO NOT ATTEMPT TO PERFORM THE PERIMETER AND ENDURANCE TESTS IF YOU ARE NOT IN A SAFE OUTDOOR ENVIRONMENT, OR IF YOU FEEL UNSAFE TO KEEP YOUR BALANCE WHEN WALKING.

THE AREA CHOSEN FOR THE WALKING TEST SHOULD BE EASILY ACCESSIBLE, FLAT, FREE OF OBSTACLES (CROSSINGS, STEPS, SIDEWALKS, ETC.)

Wear comfortable clothes and footwear and make sure to rest well before starting the test. If needed, take a break before starting or before the return trip.

ALWAYS USE YOUR WALKING AIDS IF YOU NEED THEM.

IF POSSIBLE, WALK ON A CIRCULAR ROUTE, WITH PLACES WHERE IT IS POSSIBLE TO REST (BENCHES, SEATS, ETC.)

Both the perimeter and endurance tests begin with a mandatory tutorial at first launch. GPS access authorization must be granted in order to perform the test.

A checklist will appear on the screen, you must check all the items before starting the tests. You must turn on the volume on your phone before starting the tests.



- The Perimeter Test requires you to walk at your own pace for as long as you can, without stopping.
- The Endurance Test requires you to walk as fast as possible for up to 6 minutes.

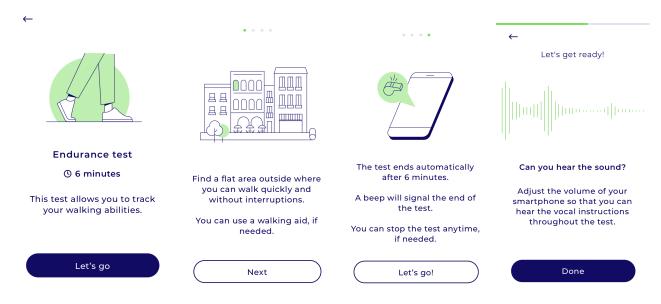
During both tests, you must place your smartphone in your pocket so that the distance and the duration of the walk can be recorded.



The Perimeter test can only take place if the investigator declares that you are able to walk safely when you are at the clinic. At home, please follow all the recommendations written above.

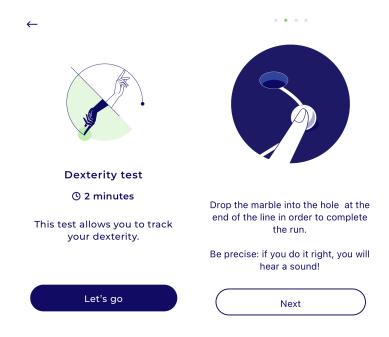
The test ends in one of the following cases:

- For the perimeter test: when you have walked 3,300 feet or during 30 minutes without having encountered any difficulty, your smartphone emits a sound signal to indicate that the test is over (no action is required from you).
- For the endurance test: when you have walked for 6 minutes, the smartphone will emit a sound signal to indicate that the test is over (no action is required from you).
- For the perimeter and endurance tests: when you decide to stop the test for any reason, press the "hold to stop stop" button for 3 seconds to end the test. A questionnaire will pop up asking you why you stopped the test.





Dexterity test



- The test starts with a mandatory tutorial at the first launch. You should sit in a quiet room, place the smartphone flat on a table and move a sphere along a defined shape using your index fingertip. Before starting the exercise, choose which hand to start with.
- The goal is to complete all the shapes as quickly and accurately as possible. After 6 shapes, you must start again with the other hand if possible, or indicate that you are not able to perform the test with the other hand. The test stops after the 12th shape is completed.

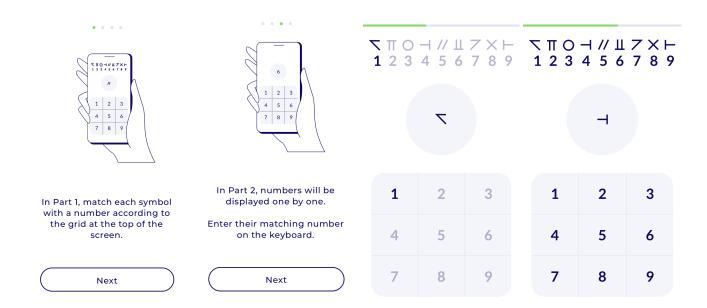






Cognition test

The test begins with a mandatory tutorial at the first launch. You should sit in a quiet room, and you can hold your phone in your hand or place it on a table. You must grant permission to access the microphone in order to perform the test.



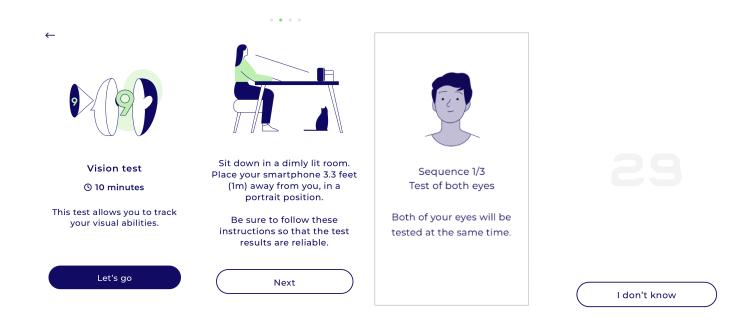
You will be asked to associate digits with symbols according to a correspondence table. The goal of the test is to make as many associations as possible.

- symbol-digit test: In this first sequence, symbols are presented on the screen and you must, according to the correspondence table, press the number corresponding to the symbol using the keyboard at the bottom of the screen. This sequence ends after 90 seconds.
- digit-to-digit test: In the second part of the test, digits are presented on the screen and you must press the corresponding digit using the keyboard at the bottom of the screen. This sequence stops after 30 seconds and marks the end of the test.



Vision test

The test begins with a mandatory tutorial at first launch. You should sit in a quiet room. You must grant permission to access the microphone and voice recognition in order to perform the test. You need to answer the questionnaire asking if you can test both of your eyes, only the left eye, or only the right eye.



You will be asked to sit 1 meter away from your smartphone, in ambient light (with no direct light from a lamp or the sun on the screen or in the eyes) and in a quiet room.

You will see a succession of numbers of decreasing size. You must read aloud the number displayed on the screen (for example: "thirty-two").

The goal of the test is to recognize as many numbers as possible. If you fail to read a number, you can say "I don't know" aloud in order to move on to the next number.

The test stops when you have read 55 numbers, given 3 successive wrong answers or said "I don't know" three times.



Performances of the digital tests

The performances of the five NMOSDcopilot digital tests are expressed as the expected analytical mean error in absolute or percentage (%) of the outcomes values (covering both iOS and Android operating systems). The numbers in brackets [...] indicate either the percentage (%) of outcomes values that have an expected error below X%, or the standard deviation of the value.

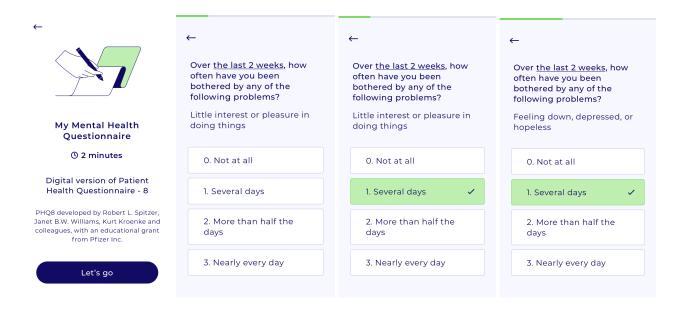
| DIGITAL TEST | Оитсоме | MEAN ERROR [% OF OUTCOMES WITH ERROR ≤ 10%] |
|--------------|--|---|
| MWPT | PERIMETER VALUE (MAX. 1 KM) MEAN WALKING SPEED | ≤ 10% [≥ 90%] ≤ 10% [≥ 90%] |
| MWET | WALKED DISTANCE VALUE (AT 6 MIN) MEAN WALKING SPEED | ≤ 10% [≥ 90%] ≤ 10% [≥ 90%] |
| MVT | NUMBER OF CORRECT RESPONSES | ≤ 2.5% [100%] |
| МСТ | RESPONSE TIME NUMBER OF CORRECT RESPONSES | ≤ 5% [100%] ≤ 1% [100%] |
| MDT | AVERAGE DEVIATION FROM SHAPES | ≤ 1.5 мм [± 0.5 мм] |



Questionnaires

The questionnaires are intended to assess the following:

- My Pain Questionnaire: digital version of the Pain Visual Analogue Scale (Pain VAS)
 0-100 to assess the intensity of your pain
- **My Fatigue Questionnaire:** digital version of the Modified Fatigue Impact Scale (MFIS-5) to assess the fatigue that you feel
- **My Bladder Function Questionnaire**: digital version of the Bladder Control Scale (BLCS) to assess your bladder symptoms
- **My Bowel Function Questionnaire**: digital version of the Bowel Control Scale (BWCS) to assess your bowel symptoms
- **My Mental Health Questionnaire**: digital version of the Patient Health Questionnaire-8 (PHQ-8) to assess your mental health
- **My Quality of Life Questionnaire:** digital version of the 36-Item Short Form Survey (SF-36 v1) to assess your quality of life in general.



To answer the questionnaires, you must validate each of your answers. The questionnaires will be validated if you answer all of the items only.



Digital Checkups

You can access the NMOSDCopilot tests and questionnaires in the Digital Checkups:

<u>Digital Checkup - in clinic</u>

| WHAT'S IN IT ? | When should I do it ? |
|--|--|
| TESTS: PERIMETER, DEXTERITY, COGNITION, VISION | |
| | IN-CLINIC WITH YOUR STUDY DOCTOR AT DO, AFTER 6 MONTHS AND AFTER |
| QUESTIONNAIRE: MY QUALITY OF LIFE | 12 MONTHS. |

<u>Digital Checkup - at home</u>

| WHAT'S IN IT ? | WHEN SHOULD I DO IT ? |
|--|--|
| <u>Tests:</u> Perimeter, dexterity, cognition, vision, and endurance | |
| Questionnaires: My Pain, My Fatigue, My Bladder | At home in autonomy once a month until the end of the study, as well as 7 days after your inclusion visit and 7 days before your |
| FUNCTION, MY BOWEL FUNCTION, MY MENTAL HEALTH, MY QUALITY OF LIFE | Month 6 visit. |



When you start the first test, it will trigger a countdown: you will have <u>four days to</u> <u>complete all the tests and questionnaires.</u>

If you do not complete all the tests and questionnaires in time, the Digital Checkup will be locked and you will not be able to perform them again until the next one.



To help you remember, you will receive push notifications, email and/or text messages to remind you to do your Digital Checkups at home, and to complete them if you have started them but not finished the totality of the tests and questionnaires.

If you feel too tired to complete all of the tests and questionnaires in one go, please wait until you feel capable to resume the digital check-up.

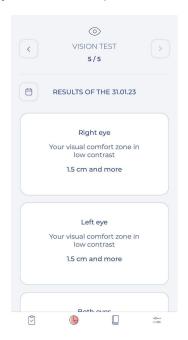
Results



THE TEST RESULTS PROVIDED BY THE **NMOSDC**OPILOT MOBILE APPLICATION ARE FOR INFORMATION PURPOSES ONLY AND SHOULD ONLY BE INTERPRETED IN THE PRESENCE OF A HEALTHCARE PROFESSIONAL.



NMOSDCopilot allows you to see your test and questionnaire results





Log out

To log out of the app, go to the Settings page from the navigation menu at the bottom of the screen (the "Settings" button is at the far right of the menu).

Then, click on the "Logout" button at the bottom of the settings page and confirm the action by selecting "Confirm".

Saving, modifying and deleting personal data



ALWAYS ENSURE THAT YOUR SMARTPHONE IS PROTECTED BY A PASSCODE OR OTHER SECURE MEANS OF IDENTIFICATION

The privacy policy and terms of use of NMOSDCopilot are available via the "Settings" section of the mobile application.

Synchronization of data

The data entered in the application and the acquisitions of the NMOSDCopilot tests are temporarily stored on the smartphone. Once synchronized, these data and acquisitions are sent and stored in a certified health data host.

Modifying and deleting data

NMOSDCopilot is compliant with the Health Insurance Portability and Accountability Act (HIPAA) and the General Data Protection Regulation (GDPR) regarding the processing of personal data. In accordance with the provisions of the GDPR, NMOSDCopilot users have the right to object at any time to the processing of their personal data and to withdraw their consent to such processing without justification and without consequences (Art 21 EU GDPR). They have a right of access to their data, a right to rectify inaccurate data, a right to limit the processing of their data and a right to be forgotten, allowing them to request the erasure of their personal data (Art 15 to 18 EU GDPR). Users also have the right to know the technical and organizational security measures concerning the processing of their personal data (Art 46 EU GDPR)

You have the right to access your data, through your study doctor, and request that they be rectified or completed.

optica spectrum disorder"



You can also request the limitation of the processing of your data (for instance, you can ask the Sponsor to temporarily stop the use of your data).

Even if you agree to participate in the study, you can change your mind at any time. If you change your mind, you must let the study team know and no additional information about you will be collected. The information collected up to this point may still be used.

The deletion of the user's data (meaning all data related to the account, including test results) can be done by writing to Ad Scientiam at : privacy@adscientiam.com

All the information regarding the processing of your personal data and your rights can be found in the NMOSDCopilot privacy policy, available via the "Settings" section of the mobile application.

| IMPORTANT NOTE: | ONCE VALIDATED, THE DELETION OF THE ACCOUNT DATA IS IRREVERSIBLE. |
|-----------------|---|
|-----------------|---|

Maintenance of the application

The application may require regular updates which are necessary to maintain the performances of NMOSDCopilot. When a new application version is available on the stores, users are invited to perform the upgrade. The process to upgrade is the same as for any other mobile application.

Deletion of the application

| IMPORTANT NOTE | LOG OUT OF THE APPLICATION FIRST BEFORE ANY APPLICATION DELETION TO TRIGGER THE UPLOAD OF ANY REMAINING |
|----------------|---|
| | DATA OF TESTS |

To delete the NMOSDCopilot application, perform the logout operation and then the standard operation to delete a mobile application on your smartphone:

- On an iPhone, make a long press on the application icon from the home view of the smartphone, then click on "Delete" (These instructions may differ depending on your smartphone's operating system).
- On an Android smartphone, go to the applications library and make a long press on the application icon, then click on "Uninstall". Alternatively, make a long press on the application icon from the home view of the smartphone, then click on "Information", then on "Uninstall" (These instructions may differ depending on your smartphone's operating system)

| IMPORTANT NOTE | DELETING THE APPLICATION DOES NOT DELETE THE ACCOUNT DATA. |
|----------------|--|
|----------------|--|

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Contact

| -or more information, contact your study doctor |
|---|
| Or/Pr: |
| Email: |
| Phone: |

Legal notice

Manufacturer of NMOSDCopilot

AD SCIENTIAM, Simplified Joint Stock Company with a capital of 13 405,00 euros registered at the RCS of Paris under the number B 795 083 336, whose head office is located 38 rue Dunois 75647 Paris CEDEX 13.