CONFIDENTIEL

Lay person study Biosynex Autotest antigénique COVID-19 Ag

Table of Contents

1. Introduction

Coronaviruses are a large family of viruses that can be pathogenic to humans and animals. Several coronaviruses are known to cause respiratory infections in humans, ranging from the common cold to more serious illnesses such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The most recently discovered coronavirus is responsible for Coronavirus 2019 disease (COVID-19).

The most common symptoms of COVID-19 are fever, fatigue and a dry cough. Some patients experience pain, nasal congestion, runny nose, sore throat or diarrhea. These symptoms are usually mild and appear progressively. Some people, although infected, have no symptoms and feel fine. Most people (about 80%) recover without needing any special treatment. About one in six people who get the disease have more severe symptoms, including shortness of breath. The elderly and those with other health problems (such as high blood pressure, heart problems or diabetes) are more likely to have severe symptoms. COVID-19 is transmitted by people who are carriers of the virus.

The disease can be spread from person to person through respiratory droplets expelled through the nose or mouth when a person coughs or sneezes. These droplets can be found on objects or surfaces around the person. You can get COVID-19 if you touch these objects or surfaces and then touch your eyes, nose or mouth. COVID-19 can also be contracted by inhaling droplets from a sick person who has just coughed or sneezed.

The incubation period of the virus is 3 to 5 days but can extend up to 14 days.

We assessed the practicability of a self-test version of Biosynex Autotest antigénique COVID-19 Ag and the ability of participants to interpret the test results. The participants had not been trained to perform the test; therefore, the testing conditions were similar to those met during usual self-testing process.

The study was divided in two sub-studies:

1 / **Handling evaluation study** to ensure that laymen handle the test correctly,

2 / **Result interpretation study** to ensure the laymen are able to read and understand a result of Biosynex Autotest antigénique COVID-19 Ag

2. Materials and methods

2.1. Selection of participants

This cross-sectional study was performed on February 2021.

The participants were selected by persons who lead the study. The inclusion criteria were an age ≥ 18 years, willingness to be tested for the COVID-19 (by rapid test), capacity to speak and understand French and willingness to give consent to participate in the study. All participants gave their informed oral consent to participate in this study.

The Biosynex autotest antigénique COVID-19 Ag test is a qualitative membrane based immunoassay that uses highly sensitive monoclonal antibodies to detect the nucleocapsid protein of SARS-CoV-2 in nasopharyngeal (NP) swab. The test strip contains colloidal-gold conjugated particles with monoclonal antibodies against the nucleocapsid protein of SARS-CoV-2. The secondary antibodies for nucleocapsid

protein of SARS-CoV-2 are coated on the membrane. When the sample is added to the sample well, the conjugates dried in the reagent pad are dissolved and migrate along with the sample. If SARS-CoV-2 antigen is present in the sample, a complex formed between the anti-SARS-CoV-2 conjugate and the virus will be captured by the specific anti-SARS-CoV-2 monoclonal antibodies coated on the test line region (T). Absence of the T line suggests a negative result.

2.2. The study was divided into 2.sub-studies

Sub-study 1: Handling evaluation study

Handling the test + evaluation of the assay performance

Laymen were invited to operate Biosynex Autotest antigénique COVID-19 Ag self-test in standalone condition. For this study the laymen got a full kit of the COVID-19 rapid test including its instructions for use. The layman performed the test up to the addition of the drops. The observer noted the actions of the laymen and also noted the result of the Biosynex Autotest antigénique COVID-19 Ag (figure 2): positive, negative or invalid.

After the first 28 participants, we have improved the record for the following participants. Sub-study 1 was divided into 2 parts: sub-study 1a and sub-study 1b.

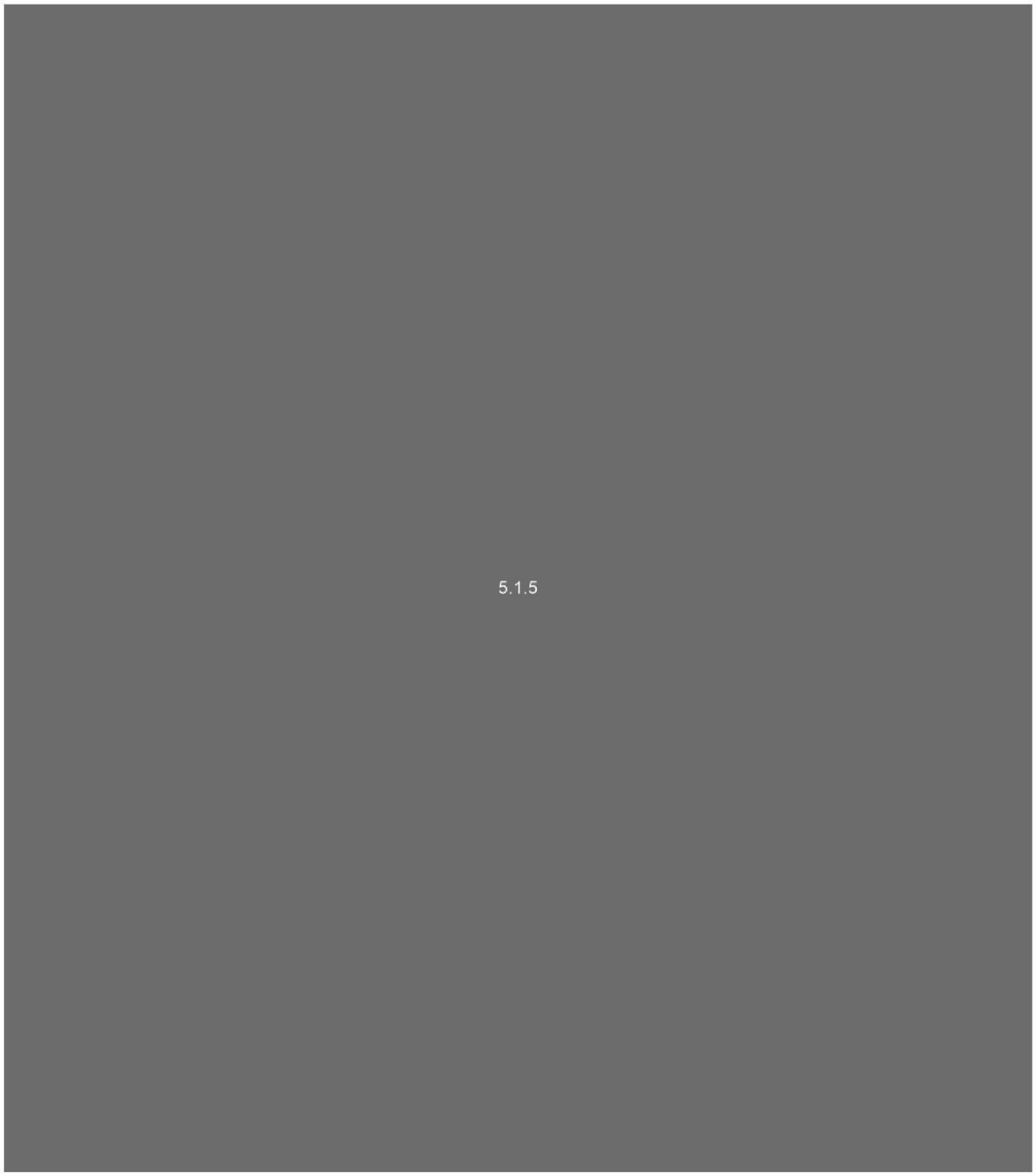
Following the first results of sub-study 1a, the first instructions for use (figure 1a) has been improved to make it easier to handle. Sub-study 1b was done using the new instructions for use (figure 1b).

The results of this screenings are recorded in the laymen study record.

We asked the volunteers to provide demographic information (gender, age, origin, education level) and their impression regarding the handling of the Biosynex Autotest antigénique COVID-19 Ag (figure 3).

CONFIDENTIEL

Figure 1a: instruction for use, used by participants during substudy 1a.



CONFIDENTIEL

Figure 1b: instruction for use, used by participants during substudy 1b.

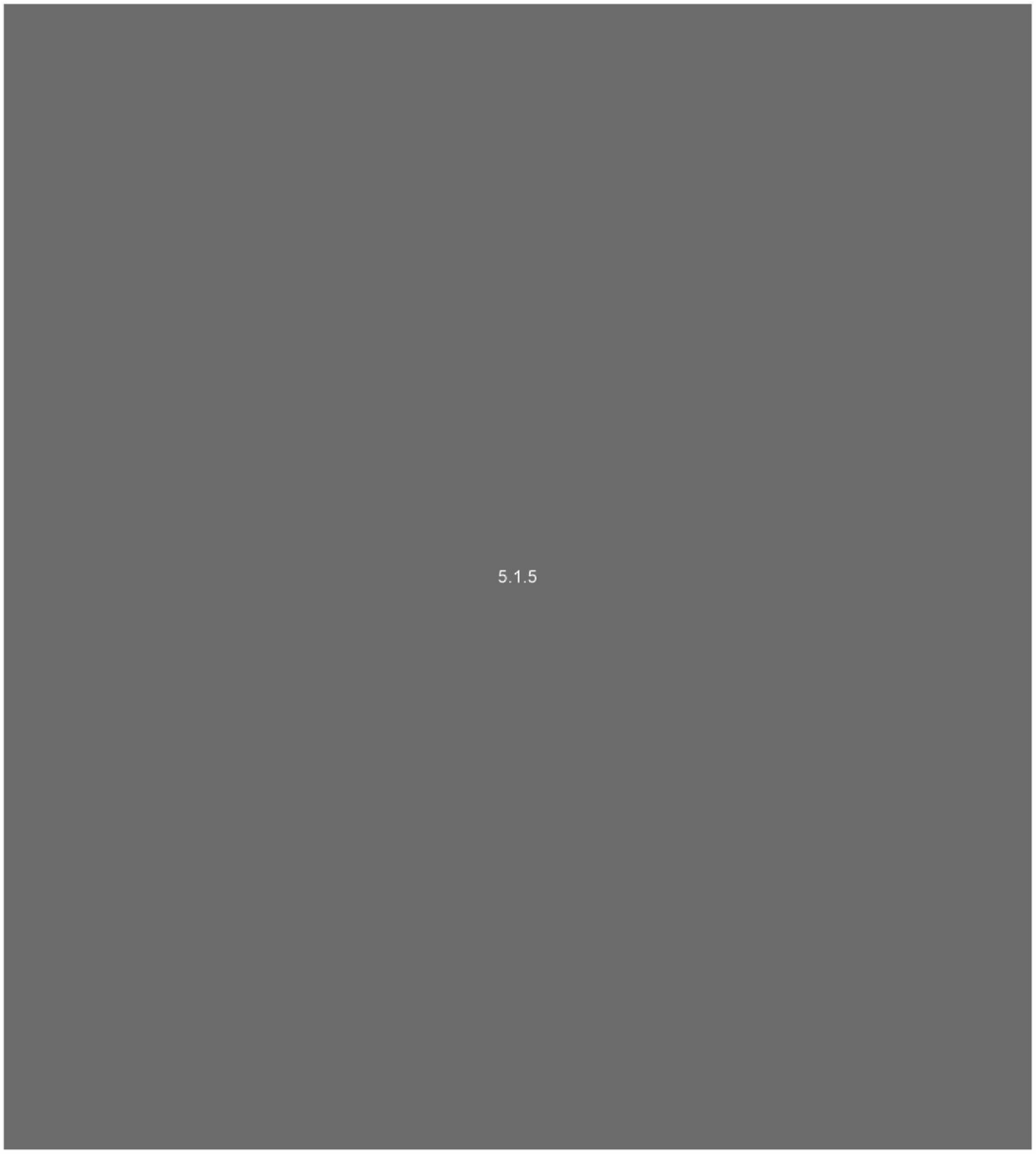


Figure 2: observer's evaluation grid for substudy 1a and 1b

OBSERVER'S ANALYSIS GRID

Site:

Date:

Symptoms of COVID-19 infection? ☐ Yes ☐ No

Heure de début de l'observation : .....

Heure de fin de l'observation : .....

OBSERVATION – TEST PRATICABILITY & PROCEDURE	Did the layperson ask for help?	Question(s) asked by the layperson	Did the answer allow the layperson to go to the next step?	Comments
Opening the box				
Reading of the instructions for use				
Hands washing				
Discovering the elements included in the box				
Opening the aluminium pouch				
Remove the cover from the diluent and place it on the rack				
Insert the swab into both nostrils				
Insert the swab into the tube and twist it 6 times				
Wait 1 minute				
Extract the liquid				
Put the dropper on the tube				
Depositing the sample diluent on the well				
Observation of the transfer time				
Start of the migration				

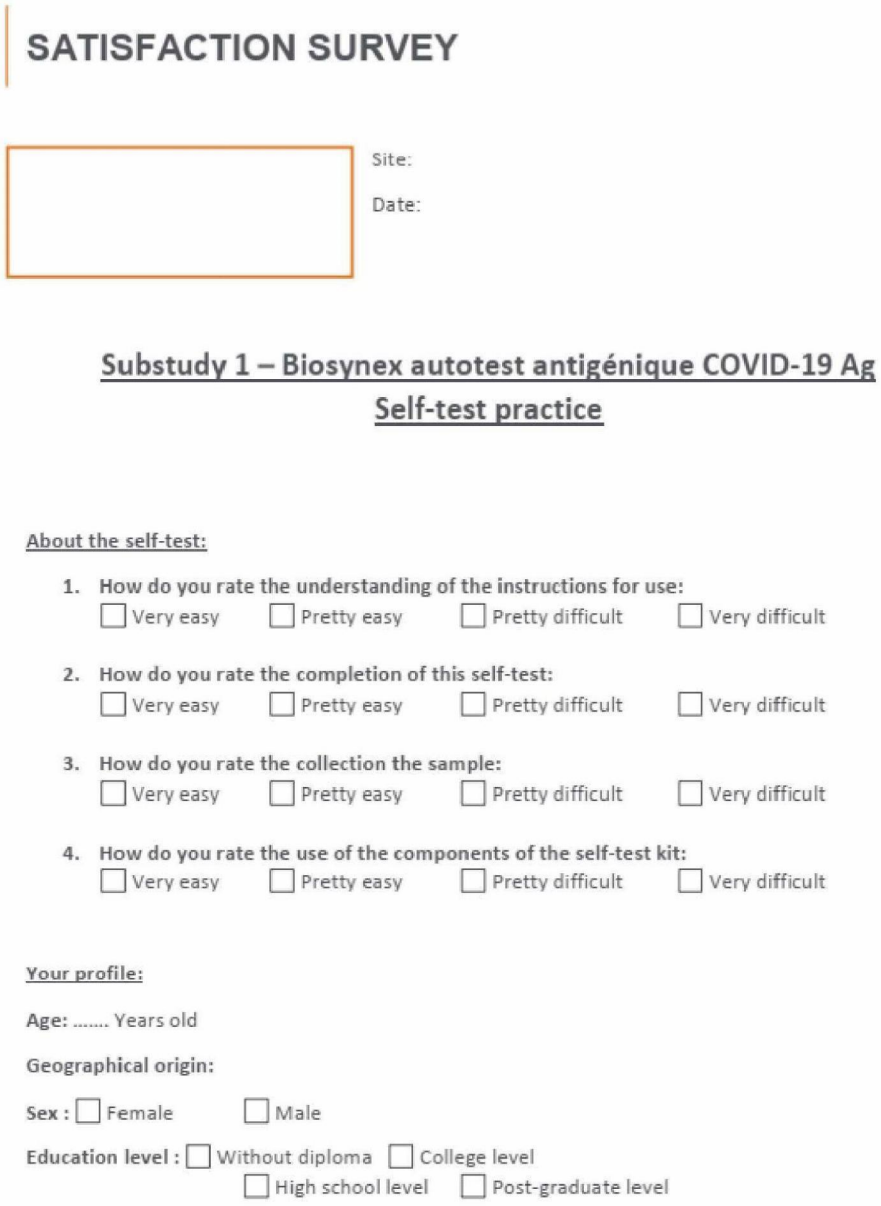
Observer's analysis	-	Result		Remarks
Is the test interpretable ?	Y/N	☐ T	☐ C	

BIOSYNEX

CONFIDENTIEL

Figure 3:

Satisfaction survey for substudy 1a and 1b



SATISFACTION SURVEY

Site:

Date:

Substudy 1 – Biosynex autotest antigénique COVID-19 Ag
Self-test practice

About the self-test:

1. How do you rate the understanding of the instructions for use:
   ☐ Very easy ☐ Pretty easy ☐ Pretty difficult ☐ Very difficult
2. How do you rate the completion of this self-test:
   ☐ Very easy ☐ Pretty easy ☐ Pretty difficult ☐ Very difficult
3. How do you rate the collection the sample:
   ☐ Very easy ☐ Pretty easy ☐ Pretty difficult ☐ Very difficult
4. How do you rate the use of the components of the self-test kit:
   ☐ Very easy ☐ Pretty easy ☐ Pretty difficult ☐ Very difficult

Your profile:

Age: ..... Years old

Geographical origin:

Sex : ☐ Female ☐ Male

Education level : ☐ Without diploma ☐ College level
☐ High school level ☐ Post-graduate level

Sub-study 2: Result interpretation study

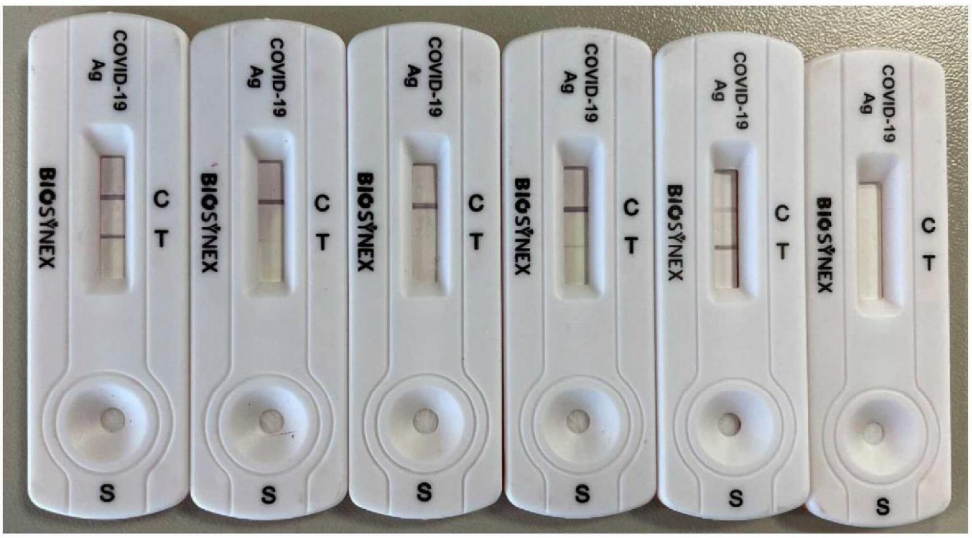
The participants were invited to test the grid test reading and interpretation of Biosynex autotest antigénique COVID-19 Ag . Each volunteer successively drew 4 tests among a panel of 6 (figure 5) and interpreted them with the help of the reading and interpretation scale (figure 6a and 6b). This panel was composed of: 4 positive test, 1 negative tests and 1 invalid tests. The observer noted the number of the drawn test and the result given by the participant (figure 7).

After the first 28 participants, we have improved the record for the following participants. Sub-study 2 was divided into 2 parts: sub-study 2a and sub-study 2b.

At the end of the study we asked the volunteer to provide demographic information (gender, age, origin, education level) and his or her impression on the interpretative reading scale and we questioned him or her on the understanding of the results through 3 questions (figure 8).

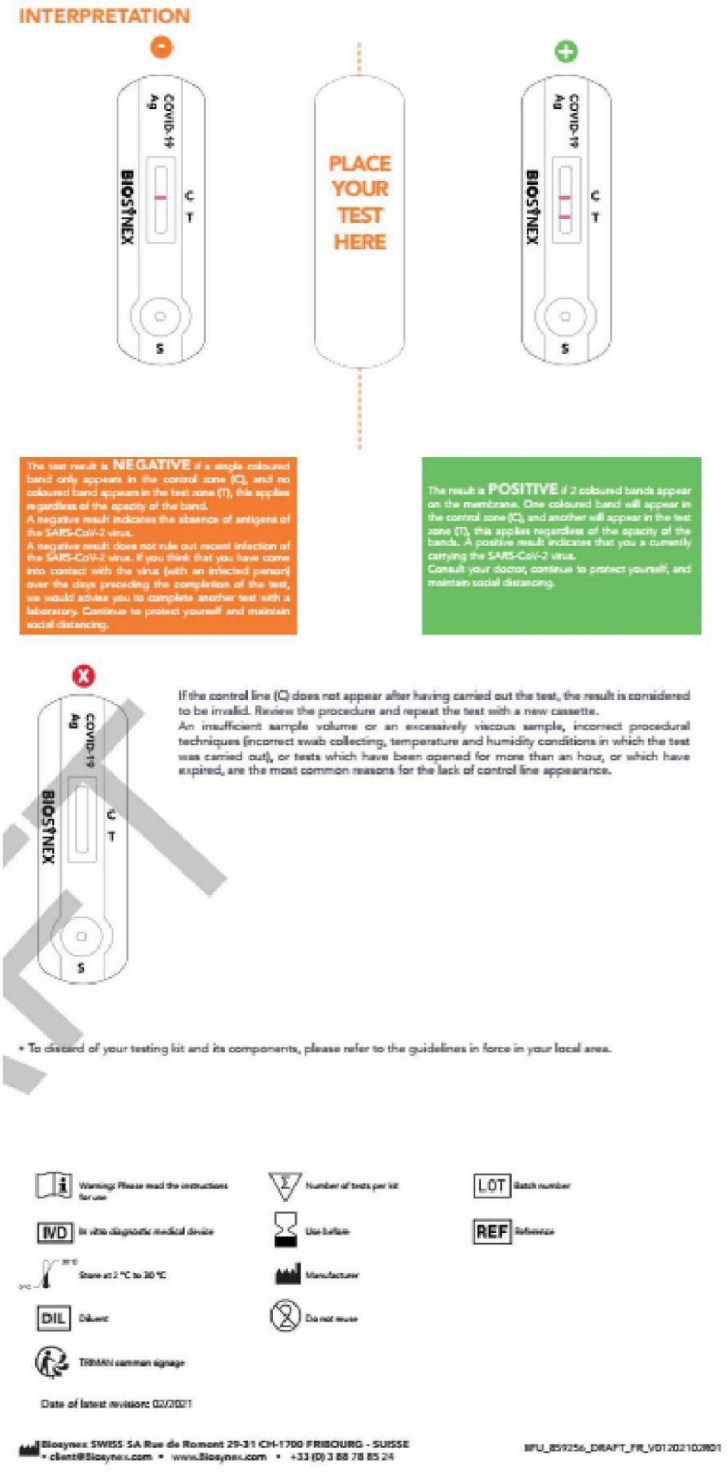
Figure 5a: Panel of 6 Biosynex Autotest antigénique COVID-19 Ag cassettes, self-test n°1, n°2, n°4 and n°5 are positive, self-test n°3 are negative, and n°6 are invalid. The n°2 is very weakly positive.

Figure 5



CONFIDENTIEL

Figure 6a: Reading Sheet used during sub-study 2a.



CONFIDENTIEL

Figure 6b: Reading Sheet used during sub-study 2b.

OBSERVERS'S ANALYSIS GRID

Site:

Date:

Study workflow :

1. You have read the reading grid of the Biosynex autotest antigénique COVID-19 Ag self-test, at any time you can consult it again.
2. Choose randomly one out of the 6 proposed tests.
3. Circle the test number on this grid.
4. Write down the meaning (result) of this test.
5. Repeat step 3 and 4 for 3 other tests picked up randomly among the remaining tests.
6. Fill in the questionnaire when the test is complete.
7. Your participation is over. Thank you for your help.

Casette N°	To be completed by the participant (layperson) - result read			To be completed by the observer - expected results			Remarks
	Negative (-)	Positive (+)	Invalid		Negative (-)	Positive (+)	Invalid

In case of discrepancy between the result read by the layman and the expected result, please identify the cause:

☐ bad reading of the bands

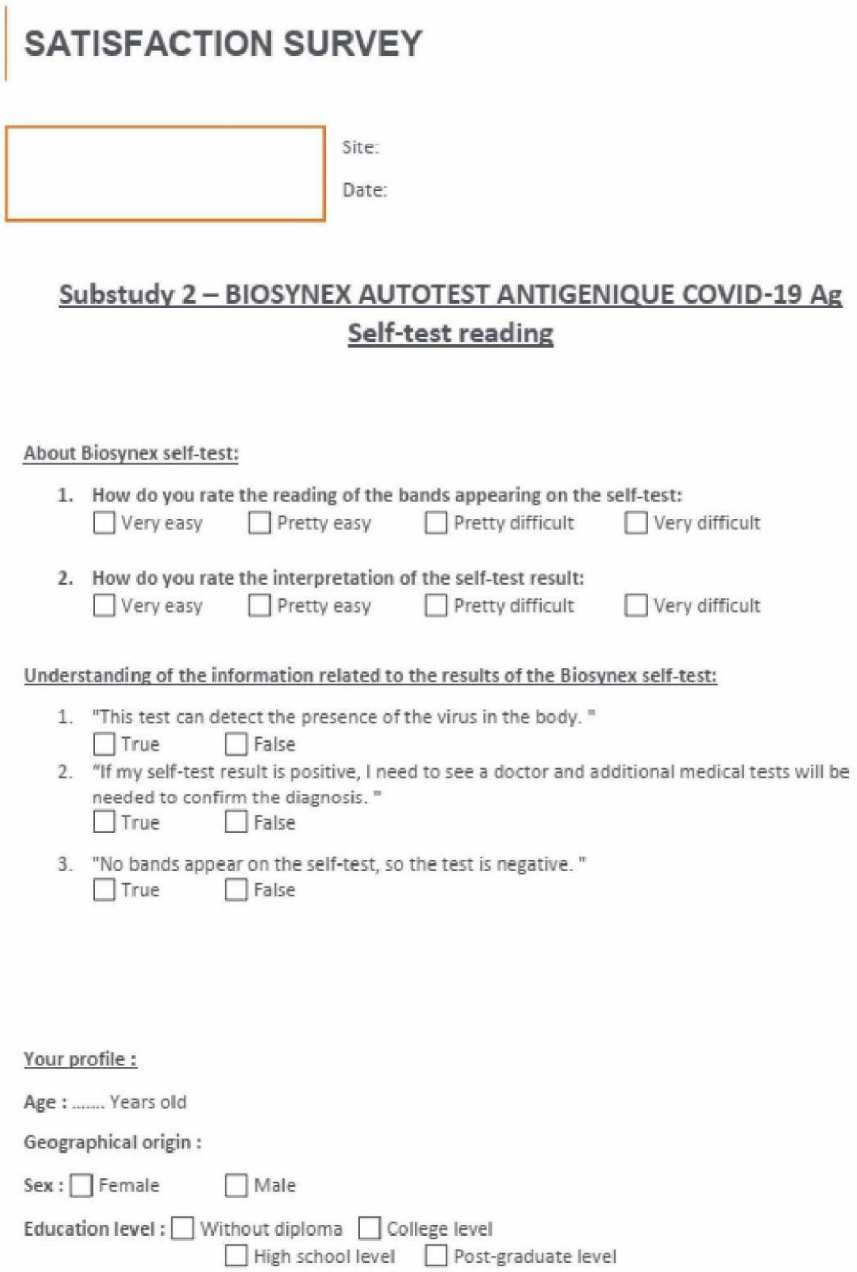
☐ bad interpretation

BIOSYNEX

Figure 7: Evaluation grid on a panel of 6 self-tests for substudy 2

CONFIDENTIEL

Figure 8: Satisfaction survey for substudy 2a and 2b



SATISFACTION SURVEY

Site:

Date:

Substudy 2 – BIOSYNEX AUTOTEST ANTIGENIQUE COVID-19 Ag
Self-test reading

About Biosynex self-test:

1. How do you rate the reading of the bands appearing on the self-test:
   ☐ Very easy ☐ Pretty easy ☐ Pretty difficult ☐ Very difficult
2. How do you rate the interpretation of the self-test result:
   ☐ Very easy ☐ Pretty easy ☐ Pretty difficult ☐ Very difficult

Understanding of the information related to the results of the Biosynex self-test:

1. "This test can detect the presence of the virus in the body. "
   ☐ True ☐ False
2. "If my self-test result is positive, I need to see a doctor and additional medical tests will be needed to confirm the diagnosis. "
   ☐ True ☐ False
3. "No bands appear on the self-test, so the test is negative. "
   ☐ True ☐ False

Your profile :

Age : ..... Years old

Geographical origin :

Sex : ☐ Female ☐ Male

Education level : ☐ Without diploma ☐ College level
☐ High school level ☐ Post-graduate level

3. RESULTS

3.1. Participation rate

Overall, 81 participants were included in the study (table 1)

Table 1: number of participants

	No
Substudy 1	80
Substudy 1a	25
Substudy 1b	55
Substudy 2	80
Substudy 2a	25
Substudy 2b	55

3.2. Demographic characteristics of the study population

The demographic characteristics of the study population in each substudy are presented in Table 2

Table 2: demographic data by substudy

	Male		*Male <= 40 years old*		**Female**		*Female <= 40 years old*	
	No	%	No	%	No	%	No	%
Substudy 1 N = 80	**40**	50	26	65	**40**	50	31	77.5
Substudy 1a N = 25	**11**	44	8	72.7	**14**	56	10	71.4
Substudy 1b N = 55	**29**	52.7	18	62.1	**26**	47.3	21	80.8

Substudy 2 N = 80	**40**	50	26	65	**40**	50	31	77.5
Substudy 2a N = 25	**11**	44	8	72.7	**14**	56	10	71.4
Substudy 2b N = 55	**29**	52.7	18	62.1	**26**	47.3	21	80.8

Table 3: Presentation of educational level in each sub study

	Substudy 1 N = 80	*Substudy 1a N = 25*	*Substudy 1b N = 55*	**Substudy 2 N = 80**	*Substudy 2a N = 25*	*Substudy 2b N = 55*
Without diploma	**2.5%**	0%	3.6%	**2.5%**	0%	3.6%
College level	**13.8%**	0%	20%	**13.8%**	0%	20%
High school level	**16.3%**	0%	23.6%	**16.3%**	0%	23.6%
Post-graduate level	**67.5%**	100%	52.7%	**67.5%**	100%	52.7%

We designed the readability substudy 2 in order to interpret positive and negative results regardless of the status of the reader. For this purpose, we included cassettes with positive, negative and invalid results patterns to be read and interpreted by laymen with educational background as exhibited in Table 3.

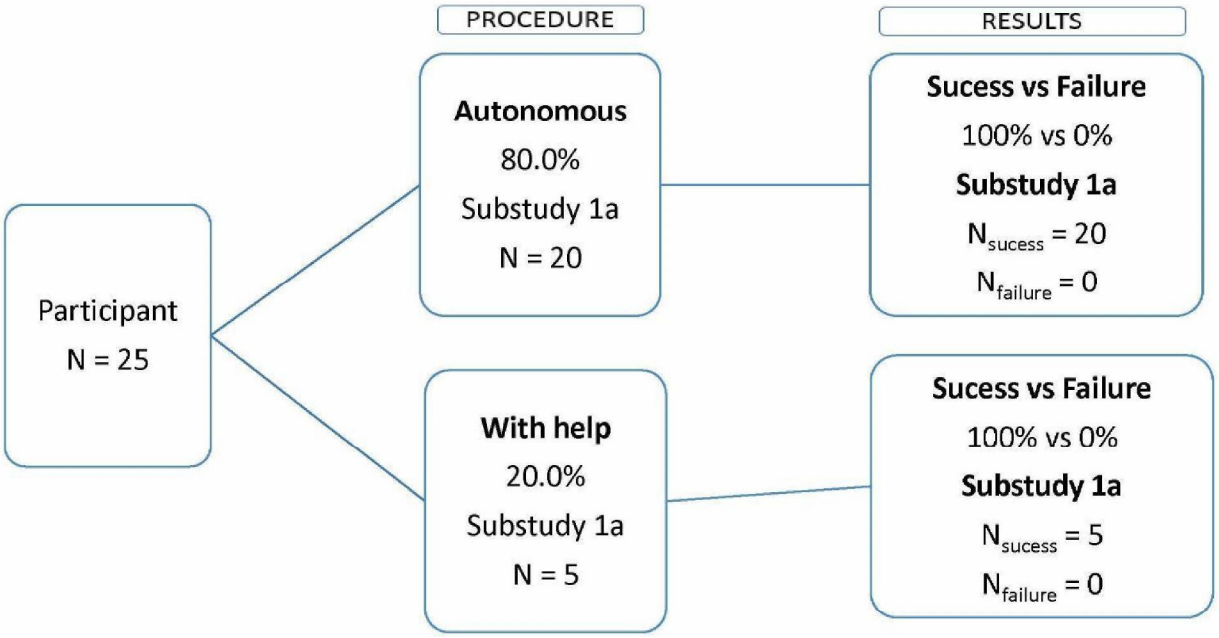
3.3. Handling evaluation study

Data analysis on the handling and interpretation of the Biosynex autotest antigénique COVID-19 Ag.

3.3.1 Substudy 1a

CONFIDENTIEL

Figure 9: report on the study on the handling of Biosynex autotest antigénique COVID-19 Ag and obtaining an interpretable test



25 participants from substudy 1a were included. In total 80.0% of participants used the test by themselves without help and 120.0% of participants needed help (figure 9).

If we analyse the 20.0% of people who asked for help (N=5), we observe that:
- 100 % (N=5) of problems relate to the part " Extract the liquid " see below table of analysis (9) : the layman doesn't understand how to extract the liquid.

Step		Percentage of questions asked to observer
1	Washing hands	0%
2	Discovering the elements included in the box	0%
3	Opening the aluminium pouch	0%
4	Remove the cover from the diluent and place it on the rack	0%
5	Take the swab out of its packaging	0%
6	Insert the swab into the first nostril	0%
7	Twist the swab into the nostril	
8	Repeat this processus in the other nostril	0%
9	Insert the swab into the tube and twist it 6 times	0%
10	Wait 1 minute	0%
11	Extract the liquid	100%
12	put the dropper on the tube	0%
13	Depositing the sample diluent on the well	0%
14	Start of the migration	0%
15	Put the cap in the tube	0%

In total, 80 laymen operated the Biosynex Autotest antigénique COVID-19 Ag and all tests were run successfully.

Practicability experienced by the participants, it is noted that:

- 92,0% of participants found it easy or very easy to understand the instruction for use
- 100% of participants found the test procedure easy or very easy
- 88% of participants found it easy or very easy to collect the sample
- 92% of participants found it easy or very easy to the handling of the kit components

After this first study, we made the following changes to the instructions:

- reformulation of step 11

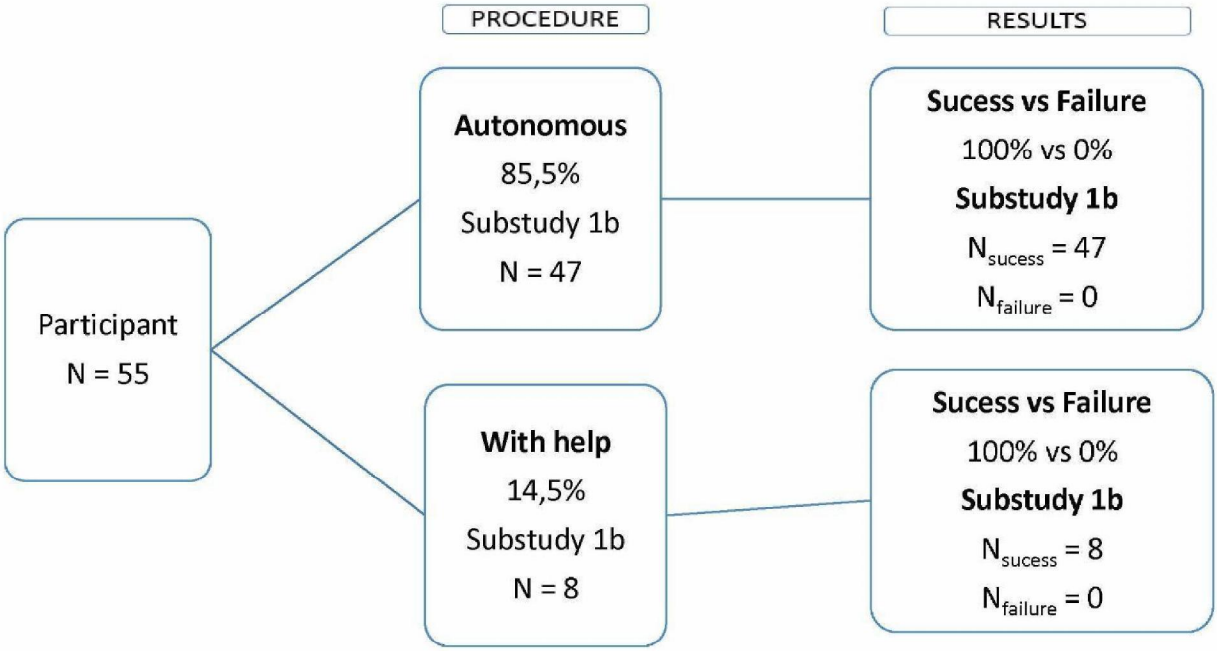
- bold and color the wait of 1 minute

- assemble the 3 stages of sampling

- highlighted certain sentences

3.3.1 Substudy 1b

Figure 9: report on the study on the handling of Biosynex autotest antigénique COVID-19 Ag and obtaining an interpretable test



55 participants from substudy 1b were included. In total 85.5% of participants used the test by themselves without help and 14,5% of participants needed help (figure 9).

If we analyse the 14.5% of people who asked for help (N=8), we observe that:
- 100 % (N=8) of problems relate to the part " Extract the liquid " see below table of analysis (11) : the layman doesn't understand how to extract the liquid.
- 12,5 % (N=1) of problems relate to the part " Insert the swab into the tube and twist it 6 times " see below table of analysis (9) : the layman doesn't understand the instructions ; he doesn't speak French very well
- 12,5 % (N=1) of problems relate to the part " Wait 1 minute" see below table of analysis (10) : the layman doesn't understand the instructions ; he doesn't speak French very well
- 12,5 % (N=1) of problems relate to the part " put the dropper on the tube " see below table of analysis (12) : the layman doesn't understand the instructions ; he doesn't speak French very well
- 25 % (N=2)) of problems relate to the part " Depositing the sample diluent on the well " see below table of analysis (13)

Step		Percentage of questions asked to observer
1	Washing hands	0%
2	Discovering the elements included in the box	0%
3	Opening the aluminium pouch	0%
4	Remove the cover from the diluent and place it on the rack	0%
5	Take the swab out of its packaging	0%
6	Insert the swab into the first nostril	0%
7	Twist the swab into the nostril	
8	Repeat this processus in the other nostril	0%
9	Insert the swab into the tube and twist it 6 times	12,5%
10	Wait 1 minute	12,5%
11	Extract the liquid	100%
12	put the dropper on the tube	12,5%
13	Depositing the sample diluent on the well	25%
14	Start of the migration	0%
15	Put the cap in the tube	0%

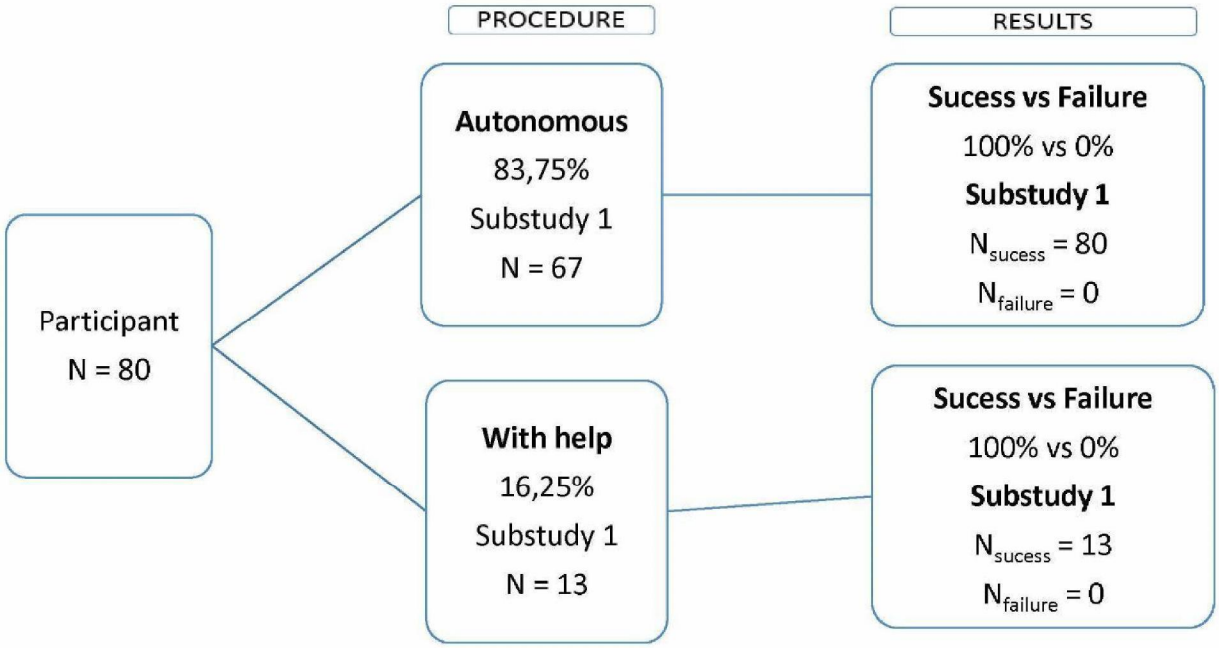
In total, 55 laymen operated the Biosynex Autotest antigénique COVID-19 Ag and all tests were run successfully.

Practicability experienced by the participants, it is noted that:

- 98,0% of participants found it easy or very easy to understand the instruction for use
- 98% of participants found the test procedure easy or very easy
- 98% of participants found it easy or very easy to collect the sample
- 100% of participants found it easy or very easy to the handling of the kit components

3.3.1 Substudy 1

Figure 9: report on the study on the handling of Biosynex autotest antigénique COVID-19 Ag and obtaining an interpretable test



80 participants from substudy 1 were included. In total 83,75% of participants used the test by themselves without help and 16,25% of participants needed help (figure 9).

If we analyse the 16,25% of people who asked for help (N=13), we observe that:
- 100 % (N=13) of problems relate to the part "Extract the liquid " see below table of analysis (11) : the layman doesn't understand how to extract the liquid.
- 7,7 % (N=1) of problems relate to the part " Insert the swab into the tube and twist it 6 times " see below table of analysis (9) : the layman doesn't understand the instructions ; he doesn't speak French very well
- 7,7 % (N=1) of problems relate to the part " Wait 1 minute" see below table of analysis (10) : the layman doesn't understand the instructions ; he doesn't speak French very well
- 7,7 % (N=1) of problems relate to the part " put the dropper on the tube " see below table of analysis (12) the layman doesn't understand the instructions ; he doesn't speak French very well
- 15,4 % (N=2) of problems relate to the part " Depositing the sample diluent on the well " see below table of analysis (13)

Step		Percentage of questions asked to observer
1	Washing hands	0%
2	Discovering the elements included in the box	0%
3	Opening the aluminium pouch	0%
4	Remove the cover from the diluent and place it on the rack	0%
5	Take the swab out of its packaging	0%
6	Insert the swab into the first nostril	0%
7	Twist the swab into the nostril	0%
8	Repeat this processus in the other nostril	0%
9	Insert the swab into the tube and twist it 6 times	7,7%
10	Wait 1 minute	7,7%
11	Extract the liquid	100%
12	put the dropper on the tube	7,7%
13	Depositing the sample diluent on the well	15,4%
14	Start of the migration	0%
15	Put the cap in the tube	

A total of 13 people needed help performing the test. Among these, 30.8% are foreigners and do not speak or understand the French language poorly.

All 13 people who needed help had a problem on step 11. The potential impact is not harvesting enough volume and not having enough drops to perform the test. But, we noticed that those who did this step badly still had enough drops to perform the test.

In total, 80 laymen operated the Biosynex Autotest antigénique COVID-19 Ag and all tests were run successfully.

Practicability experienced by the participants, it is noted that:

- 96,0% of participants found it easy or very easy to understand the instruction for use
- 99% of participants found the test procedure easy or very easy
- 95% of participants found it easy or very easy to collect the sample
- 98% of participants found it easy or very easy to the handling of the kit components

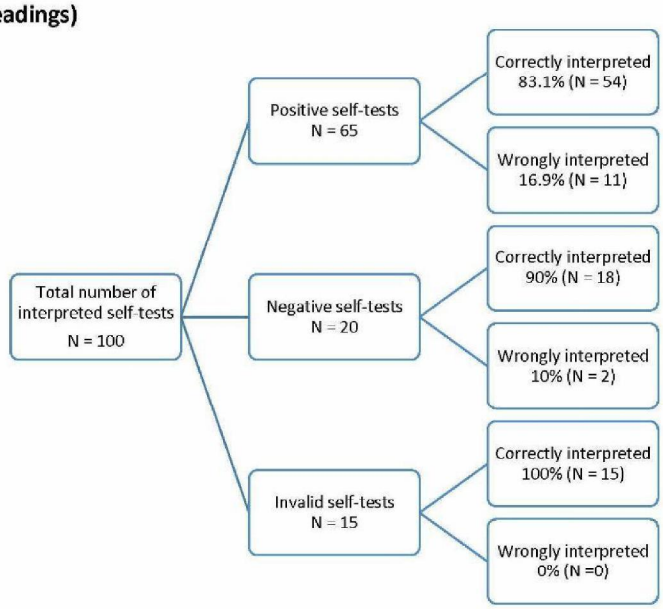
3.4. Result interpretation study

3.4.1 Substudy 2a

Evaluation of the ability to read and understand the Biosynex Autotest antigénique COVID-19 Ag result.

Figure 10: ability of participants to read and interpret the Biosynex Autotest antigénique COVID-19 Ag results using a chart from panel of 6 standardized tests.

Participants
N = 25
(4 successive readings)



Finally, 87.0% of Biosynex Autotest antigénique COVID-19 Ag were interpreted correctly in the substudy 2a. Indeed 11 Biosynex Autotest antigénique COVID-19 Ag with positive results and 2 Biosynex Autotest antigénique COVID-19 Ag with negative result were misinterpreted. 6 positive tests were interpreted as negative because the test band was very weak. In 100% of cases, it is the test number 2 that has not been interpreted correctly. 4 positive tests were interpreted as an invalid test because the control band was very weak. In 100% of cases, it is the test number 5 that has not been interpreted correctly. 2 negative tests were interpreted as a positive test. In 100% of cases, it is the test number 3 that has not been interpreted correctly.

Participants were also evaluated on their understanding of the results of the Biosynex autotest antigénique COVID-19 Ag :

- 92,0% of participants understood that this test detects the presence of the virus.

- 96,0% of the participants understood that if the test is positive you need to go see a doctor to confirm the result.

- 100% of participants understood that there is no band on the test, it is invalid.

88,0% of participants declared easy or very easy reading bands on self-test Biosynex and 92,0% declared the interpretation of the Biosynex Autotest antigénique COVID-19 Ag is easy or very easy.

After this first study, we made the following changes to the package insert:

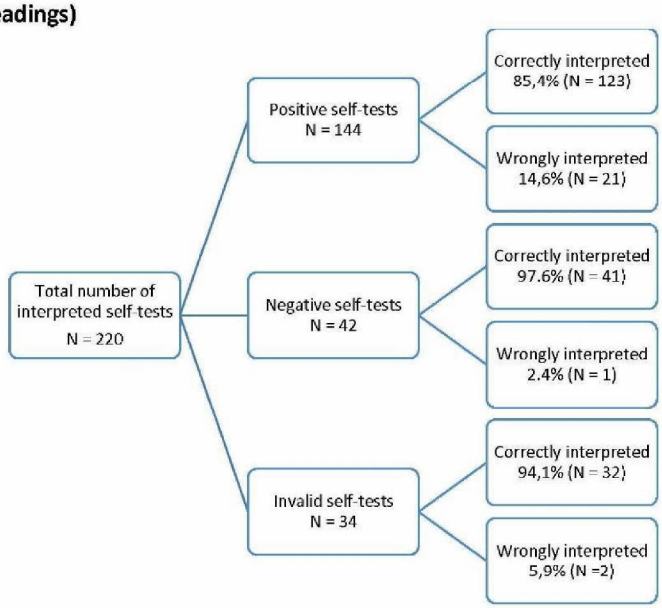
- highlighting of the "invalid" part

- bolding "whatever the intensity of the band"

3.4.2 Substudy 2b

Evaluation of the ability to read and understand the Biosynex Autotest antigénique COVID-19 Ag result.

Figure 10: ability of participants to read and interpret the Biosynex Autotest antigénique COVID-19 Ag results using a chart from panel of 6 standardized tests.



Finally 89.1% of Biosynex Autotest antigénique COVID-19 Ag were interpreted correctly in the substudy 2a. Indeed 21 Biosynex Autotest antigénique COVID-19 Ag with positive results, 1 Biosynex Autotest antigénique COVID-19 Ag with negative result and 2 Biosynex Autotest antigénique COVID-19 Ag with invalid result were misinterpreted. 19 positive tests were interpreted as negative. In 84.2% of cases, it is the test number 2 that has not been interpreted correctly, because the test band was very weak. 2 positive tests were interpreted as an invalid. 1 negative test was interpreted as an invalid test and 2 invalid tests were interpreted as a negative test.

Participants were also evaluated on their understanding of the results of the Biosynex autotest antigénique COVID-19 Ag :

- 98,2% of participants understood that this test detects the presence of the virus.
- 96,4% of the participants understood that if the test is positive you need to go see a doctor to confirm the result.
- 92,7% of participants understood that there is no band on the test, it is invalid.

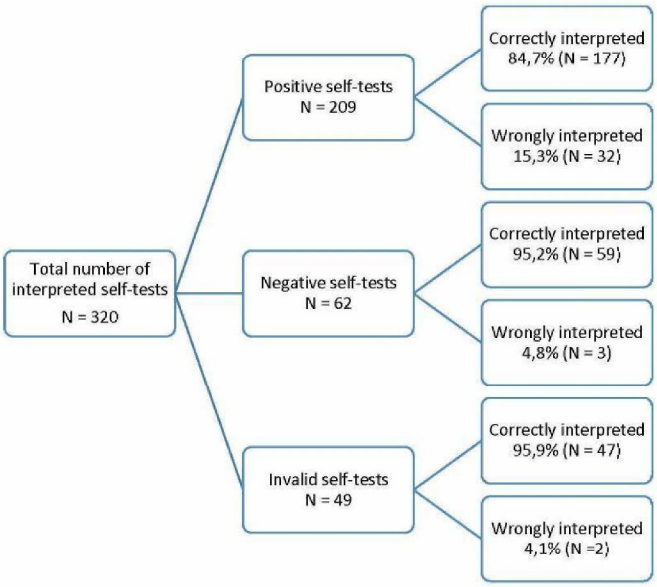
98,2% of participants declared easy or very easy reading bands on self-test Biosynex and 98,2% declared the interpretation of the Biosynex Autotest antigénique COVID-19 Ag is easy or very easy.

3.4.3 Substudy 2

Evaluation of the ability to read and understand the Biosynex Autotest antigénique COVID-19 Ag result.

Figure 10: ability of participants to read and interpret the Biosynex Autotest antigénique COVID-19 Ag results using a chart from panel of 6 standardized tests.

Participants
N = 80
(4 successive readings)



Finally 88,4% of Biosynex Autotest antigénique COVID-19 Ag were interpreted correctly in the substudy 2a. Indeed 32 Biosynex Autotest antigénique COVID-19 Ag with positive results, 3 Biosynex Autotest antigénique COVID-19 Ag with negative result and 2 Biosynex Autotest antigénique COVID-19 Ag with invalid result were misinterpreted. 26 positive tests were interpreted as negative. In 84.6% of cases, it is the test number 2 that has not been interpreted correctly, because the test band was very weak. 6 positive tests were interpreted as an invalid. 1 negative test were interpreted as an invalid test, 2 negative tests were interpreted as a positive test and 2 invalid tests were interpreted as a negative test.

In total, 29 people made at least 1 error in the interpretation. Among those there, 27.6% are foreigners and do not speak or understand the French language badly.

Participants were also evaluated on their understanding of the results of the Biosynex autotest antigénique COVID-19 Ag :

- 96,3% of participants understood that this test detects the presence of the virus.

- 96,3% of the participants understood that if the test is positive you need to go see a doctor to confirm the result.

- 95% of participants understood that there is no band on the test, it is invalid.

95% of participants declared easy or very easy reading bands on self-test Biosynex and 96% declared the interpretation of the Biosynex Autotest antigénique COVID-19 Ag is easy or very easy.

4. CONCLUSION

In this study, we show that Biosynex Autotest antigénique COVID-19 Ag is easy to handle and to interpret by laymen.

	N	Success	Without assistance	With assistance
Substudy 1	80	100%	83,75%	16,25%

Substudy 1: 83.75% (N=67) of lay users could perform the test on their own without seeking for any assistance.

To conclude, we can say that Biosynex Autotest antigénique COVID-19 Ag shows a good practicability with the information in the instruction for use. As part of the launching of the test, support materials for the realization (videos) will be available to help users in the manipulation / interpretation of the test.

Substudy 2: This study shows some sporadic cases of wrongly interpreting a positive test as negative and an invalid test as negative test. Given the weak proportion of misinterpretation cases and the preventive measures taken (packaging & IFU instructions,...), this risk can be considered as a low risk, especially when we consider the good performances of the test.

5. REFERENCES

1. Organisation Mondiale de la Santé - Maladie à coronavirus 2019 (COVID-19) : questions-réponses (2020)

2. Ministère des Solidarités et de la Santé - Réponses à vos questions sur le COVID-19 (2020)