Virusee®

Clinical Study Report
For

SARS-CoV-2 Antigen Rapid Test (Colloidal Gold)

(Saliva/Swab)

Researched by: Yuehui Zhou

Approved by: Qinghua Yuan

Report Date: 2021.05.19

Summary

The Virusee® SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) produced by Genobio Pharmaceutical Co., Ltd. was clinically validated according to the requirements of the "Management Measures for Registration of In Vitro Diagnostic Reagents (Trial Implementation)".

The purpose of this clinical study is to investigate the conformity and consistency of assessment reagents and clinical diagnosis, understand the performance of the product, and provide a basis for evaluating the clinical utility of the product.

The following is a study of interference reaction, cross-reaction, clinical diagnostic sensitivity and specificity of this product.

1. Product Description

1.1 Principle

SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) adopts a colloidal gold method based on the principle of the double antibody-sandwich technique. It is designed to detect nucleocapsid protein antigen from the SARS-CoV-2 in saliva, nasopharyngeal swab, and oropharyngeal swab, from patients who are suspected of SARS-CoV-2 infection.

During testing, the specimen migrates upward under capillary action. The SARS-CoV-2 antigens, if present in the specimen, will bind to the anti- SARS-CoV-2 nucleocapsid protein monoclonal antibody-colloidal gold complex formed immune complex, the immune complex is then captured on the membrane by the pre-coated SARS-CoV-2 nucleocapsid protein monoclonal antibody coated on the T-line, and a visible colored line will show up in the test line region indicating a positive result. In the absence of SARS-CoV-2 antigens, no colored line will form in the test line region, which indicating a negative result. To serve as a procedural control, a colored line will always appear at the control line region, indicating that proper volume of specimen has been added and membrane wicking has occurred.

1.2 Intended Use

The SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) is a colloidal gold method intended for the qualitative detection of SARS-CoV-2 nucleocapsid protein antigens in saliva, nasopharyngeal swab and oropharyngeal swab from individuals who are suspected of SARS-CoV-2 infection by their healthcare provider.

Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease.

Negative results do not rule out of SARS-CoV-2 infection and should not be used as the sole basis for treatment patient management decisions, including infection control decisions. Negative results should be considered in the context of a patient’s recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19, and confirmed with a molecular assay, if necessary, for patient management.

The SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) is intended for use by trained clinical laboratory personnel specifically instructed and trained in vitro diagnostic procedures.

The test kit only detects the N protein, and cannot detect the S protein and its mutation structure.

For in vitro diagnostic use only. For professional use only.

2. Sensitivity and Specificity

Comparing the result of test reagent SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) produced by Genobio Pharmaceutical Co., Ltd., and reference reagent on the same clinical sample, verify whether the test reagent and the reference reagent are equivalent, to verify the applicability and effectiveness of the product in clinical testing. To show that the SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) kit can be safely and effectively applied to clinical practice

2.1 Study Design

2.1.1 Requirements for reference reagents

Choose products that have been approved for marketing and are generally considered to be of good quality in clinical practice as reference reagents. At the same time, the name of the manufacturer of the reference reagent, product specification and model, registration number and other information should be indicated.

2.1.2 Selection of test samples

2.1.2.1 Basis for sample selection

According to the Technical Guidelines for Clinical Trials of In-Vitro Diagnostic Reagents, the total number of samples for clinical research of the second category of products is at least 200, and the number of clinical trial institutions is two or more. Therefore, this plan requires that the number of samples participating in this clinical trial should not be less than 100 per hospital.

2.1.2.2 Selection criteria

Choose fresh samples; gender is not limited; samples should meet the test range requirements of the kit. The sample concentration should cover the linear range of the kit and be as evenly distributed as possible. As far as possible, the measured value of 30% of the sample is outside the reference interval, but within the measurement range.

2.1.2.3 Exclusion criteria

Unclear sample collection time or information; samples with too much sample volume due to errors in the test operation; persons found to be contaminated in the specimen storage process before the test operation.

2.1.2.4 Elimination criteria

Before the statistics, it was found that any information required for the original record of a clinical study was missing; redundant samples with duplicate ID numbers.

2.2 Test sample requirements

2.2.1 Requirements for clinical sample types

The samples are collected according to the conventional method, and must be stored in a clean, dry, waterproof container that does not contain detergents and preservatives after collection. Sampling at multiple locations in order to get a representative sample.

Process the samples in accordance with the instructions. The processed samples are recommended to be tested immediately; if they cannot be tested within 6 hours, they should be sent to the laboratory for storage and transportation at 2-8°C; if they are not tested within 72 hours, they should be placed Frozen storage below -20℃, but not repeated freezing and thawing.

2.2.2 Number of clinical samples

According to the "Technical Guidelines for In Vitro Diagnostic Reagents Clinical Trials" formulated by the State Food and Drug Administration and statistical requirements, the number of positive cases for each sample type is not less than 100.

2.3 Reagent

2.3.1 Test reagents

SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab), perform the test in accordance with the product instructions.

2.3.2 Reference reagents

RT-PCR manufactured by BGI Genomics, perform the test in accordance with the product instructions.

2.3.3 Third-party reagents

RT-PCR manufactured by Vazyme Biotech Co., Ltd.

2.3.5 Test procedure

2.3.5.1 Comparison Test

After the person in charge of statistics collects the samples and encodes the order of the selected samples, the test operator uses the test reagents and reference reagents to provide samples from the same subject under the condition that the information of the subjects who provided the samples is kept in a blind state. Perform simultaneous testing in accordance with the requirements of their

respective manuals.

Interpret the test results of the test reagent and the reference reagent according to the requirements of the instruction manual. When the results are consistent, record the test results; when the two test results are inconsistent, the test operator shall use the test reagent and the reference reagent to retest, at least Repeat the test twice to comprehensively evaluate the test results; if there are still large differences in the retest results, use third-party reagents to verify the samples and analyze them. After clarifying the results, unblind and evaluate the clinical application performance of the SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) kit, and investigate the equivalence of this kit with the kit of the same variety that has been approved for marketing.

2.3.5.2 Third-party reagent testing

When the test results are inconsistent, the test reagent and the reference reagent need to be retested, at least twice, to comprehensively evaluate the test results; if the retest results still have large differences, use a third-party reagent to verify the sample and analyze it.

2.4 Evaluation method

2.4.1 Diagnostic Sensitivity and Specificity

		Clinical result		Total
		Positive	Negative	
Virusee®	Positive	A	B	A+B
	Negative	C	D	C+D
Total		A+C	B+D	A+B+C+D

（1）Sensitivity: A/(A+C) *100%

（2）Specificity: D /(B+D) *100%

Where:

A—The result of clinical is positive and the result of Virusee® is also positive;

B—The result of clinical results is negative while the result of Virusee® is positive;

C—The result of clinical results is positive while the result of Virusee® is negative;

D—The result of clinical results is negative and the result of Virusee® is also negative.

2.4.2 Consistency coefficient Kappa value（K)

Kappa=(PA－Pe)/ (1－Pe)

PA=(A＋D)/ (A＋B＋C＋D)

Pe=[(A＋B) (A＋C)＋(C＋D) (B＋D)] /$(A＋B＋C＋D)^2$

Kappa (K>0.75)，it can be considered that the strength of agreement between the assessment reagent result and the nucleic acid test result is extremely high. (K=? >0.75)

2.5 Study Results

2.5.1 Saliva sample

2.5.1.1 Sensitivity, specificity

		RT-PCR		Total
		Positive	Negative	
SARS-CoV-2 Antigen	Positive	100	2	102
	Negative	5	268	273
Total		105	270	375

Sensitivity =95.23% (100/105); (95%CI: 88.71-98.23%)

Specificity =99.26% (268/270); (95%CI: 97.06-99.87%)

2.5.1.2 Kappa value

K=(PA − Pe)/ (1 − Pe)=0.95>0.75

2.5.2 Swab sample (Nasopharyngeal swab and oropharyngeal swab)

2.5.2.1 Sensitivity, specificity

		RT-PCR		Total
		Positive	Negative	
SARS-CoV-2 Antigen	Positive	104	4	108
	Negative	3	534	537
Total		107	538	645

Sensitivity =97.19% (104/107); (95%CI: 91.42-99.27%)

Specificity =99.26% (534/538); (95%CI: 97.97-99.76%)

2.5.2.2 Kappa value

K=(PA − Pe)/ (1 − Pe)=0.96>0.75

2.5.3 Total Result

2.5.3.1 Sensitivity, specificity

	RT-PCR		Total
	Positive	Negative	

SARS-CoV-2 Antigen	Positive	204	6	210
	Negative	8	802	810
Total		212	808	1020

Sensitivity=96.23% (204/212); (95%CI: 92.43-98.23%)

Specificity=99.26% (802/808); (95%CI: 98.31-99.70%)

2.5.3.2 Kappa value

K=(PA − Pe)/ (1 − Pe)=0.96>0.75

2.5.4 Analysis of inconsistent results

No	Assessment	Reference	Third-part	No	Assessment	Reference	Third-part
1	-	+	+	8	-	+	+
2	-	+	+	9	+	-	-
3	-	+	+	10	+	-	-
4	-	+	+	11	+	-	-
5	-	+	+	12	+	-	-
6	-	+	+	13	+	-	-
7	-	+	+	14	+	-	-

Note:

Assessment- SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab)

Reference- RT-PCR manufactured by BGI Genomics

Third-part- RT-PCR manufactured by Vazyme Biotech Co., Ltd.

2.6 Study Results

The sensitivity and specificity of saliva samples were calculated, which are 95.23% and 99.26% respectively. The kappa analysis value is 0.95>0.75, it can be considered that the strength of agreement between the ARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) result and the nucleic acid test result is extremely high. And the sensitivity and specificity of swab samples were calculated, which are 97.19% and 99.26% respectively. The kappa analysis value is 0.96>0.75, it can be considered that the strength of agreement between the ARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) result and the nucleic acid test result is extremely high.

The total of the test result of the sensitivity and specificity of SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) are 96.23% and 99.26% respectively. The kappa analysis value is 0.96>0.75, it can be considered that the strength of agreement between the ARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) result and the nucleic acid test result is extremely high.

The results show that the "SARS-CoV-2 Antigen Rapid Test (Colloidal Gold)

(Saliva/Swab)" developed by Genobio Pharmaceutical Co., Ltd. has good clinical application value.

2.7 Clinical Record

See appendix I.

3. Analytical Specificity

3.1 Cross-Reactivity

Cross-reactivity studies are performed to demonstrate that the test does not react with related pathogens, high prevalence disease agents, and normal or pathogenic flora that are reasonably likely to be encountered in the clinical specimen.

3.1.1 Product

Name: SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab)
Company: Genobio Pharmaceutical Co., Ltd.
Specification: VSLFA-01, VSLFA-20
Method: Colloidal Gold
Lot No.: VS210210, VS210215, VS210220

3.1.2 Method

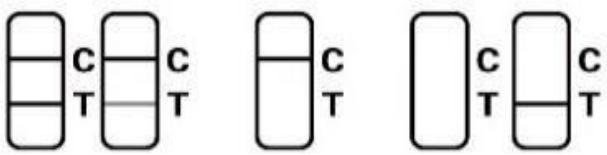
Samples from healthy donors (negative clinical matrix) were collected and eluted in extraction buffer to be used as a negative standard material. For each test, the diluted sample was added to the Extraction Tube with Extraction Reagent before conducting the test according to the instruction for use.

The Limit of Detection (LoD) of the SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) is $5\times10^{2.50}TCID_{50}$/mL (cultured SARS-CoV-2 virus).

Positive standard materials (*$1\times10^{7.50}$ $TCID_{50}$/mL, approx. 2,000xLoD*) were spiked into negative sample and were diluted to make low concentration level (*$1\times10^{3.50}$ $TCID_{50}$/mL, approx. 2xLoD*) for testing.

Potential cross-reactant organisms were prepared at the concentration of 10^5 PFU/mL or higher for viruses and 10^6 CFU/mL or higher for bacteria. They were spiked into the negative and low positive samples and were tested in 3 replicates.

3.1.3 Interpretation of results



Positive Negative Invalid

Positive: Two lines appear. One colored line should be in the control region (C),

and another apparent colored line adjacent should be in the test line (T). Positive for presence of SARS-CoV-2 nucleocapsid protein antigen with patient history and other diagnostic information is necessary to determine infection status Positive results do not rule bacterial infection or co -infection with other viruses. The agent detected may not be the definite cause of disease.

Negative: One colored line appears in the control region (C). No line appears in the test line (T). Negative test results do not preclude infection and should not be used as the sole basis for treatment or other patient management decisions, including symptoms consistent with COVID-19, or in those who have been in contact with virus. It is recommended that these results be confirmed by a molecular testing method, if necessary, for patient management.

Invalid: Control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test using a new test cassette.

3.1.4 Acceptance criteria

Potential cross-reactant organisms listed in the table were spiked into the negative and low positive samples (*1 ×$10^{3.50}$ $TCID_{50}$/mL, approx. 2xLoD)* and were tested in 3 replicates, the result is not affected by adding cross-reactant organisms.

3.1.5 Results

List of organisms	Test concentration	Test result	
		Negative *(No.of negative/No.of replicates)*	Positive *(No.of positive/No.of replicates)*
Human coronavirus 229E	1×10^6 PFU/mL	3/3	3/3
Human coronavirus OC43	1×10^6 PFU/mL	3/3	3/3
Human coronavirus NL63	1×10^6 PFU/mL	3/3	3/3
MERS-coronavirus	1×10^6 PFU/mL	3/3	3/3
Human coronavirus HKU1	1×10^6 PFU/mL	3/3	3/3
Human adenovirus 1	1×10^6 PFU/mL	3/3	3/3
Human adenovirus 3	1×10^6 PFU/mL	3/3	3/3
Human adenovirus 5	1×10^6 PFU/mL	3/3	3/3
Human adenovirus 7	1×10^6 PFU/mL	3/3	3/3
Respiratory syncytial virus A	1×10^6 PFU/mL	3/3	3/3
Respiratory syncytial virus B	1×10^6 PFU/mL	3/3	3/3
Parainfluenza virus 1	1×10^6 PFU/mL	3/3	3/3
Parainfluenza virus 2	1×10^6 PFU/mL	3/3	3/3
Parainfluenza virus 3	1×10^6 PFU/mL	3/3	3/3
Parainfluenza virus 4	1×10^6 PFU/mL	3/3	3/3

Rhinovirus	1×10^6 PFU/mL	3/3	3/3
Influenza A	1×10^6 PFU/mL	3/3	3/3
Influenza B	1×10^6 PFU/mL	3/3	3/3
Pooled human nasal wash	1×10^6 CFU/mL	3/3	3/3
Haemophilus influenzae	1×10^6 CFU/mL	3/3	3/3
Streptococcus pneumoniae	1×10^6 CFU/mL	3/3	3/3
Streptococcus pyogenes	1×10^6 CFU/mL	3/3	3/3
Candida albicans	1×10^6 CFU/mL	3/3	3/3
Bordetella pertussis	1×10^6 CFU/mL	3/3	3/3
Mycoplasma pneumoniae	1×10^6 CFU/mL	3/3	3/3
Chlamydia pneumoniae	1×10^6 CFU/mL	3/3	3/3
Legionella pneumophila	1×10^6 CFU/mL	3/3	3/3
Staphylococcus aureus	1×10^6 CFU/mL	3/3	3/3
Staphylococcus epidermidis	1×10^6 CFU/mL	3/3	3/3
Mycobacterium tuberculosis	1×10^6 CFU/mL	3/3	3/3

3.1.6 Conclusion

Cross reactivity with following potential cross-reactant culture with certain concentration has been studied. The results were found there is no effect by adding cross substances when tested with the SARS-CoV- 2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab).

3.2 Interference Study

Interfering reactivity studies are performed to demonstrate that the test does not react with endogenous interfering substances.

3.2.1 Product

Name: SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab)
Company: Genobio Pharmaceutical Co., Ltd.
Specification: VSLFA-01, VSLFA-20
Method: Colloidal Gold
Lot No.: VS210210, VS210215, VS210220

3.2.2 Method

Extraction buffer was used as negative sample.

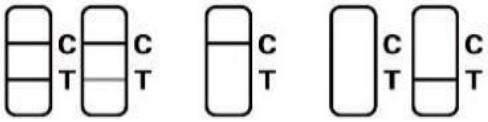
The Limit of Detection (LoD) of the SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) (Saliva/Swab) is $5\times10^{2.50}TCID_{50}$/mL (cultured SARS-CoV-2 virus).

Positive standard materials (*$1\times10^{7.50}$ $TCID_{50}$/mL, approx. 2,000xLoD*) were spiked into negative sample and were diluted to make low concentration level (*$1\times10^{3.50}$ $TCID_{50}$/mL, approx. 2xLoD*) for testing.

Potential interfering substances were added to the negative and positive samples and were tested using the SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) in 3

replicates.

3.2.3 Interpretation of results



Positive Negative Invalid

Positive: Two lines appear. One colored line should be in the control region (C), and another apparent colored line adjacent should be in the test line (T). Positive for presence of SARS-CoV-2 nucleocapsid protein antigen with patient history and other diagnostic information is necessary to determine infection status Positive results do not rule bacterial infection or co -infection with other viruses. The agent detected may not be the definite cause of disease.

Negative: One colored line appears in the control region (C). No line appears in the test line (T). Negative test results do not preclude infection and should not be used as the sole basis for treatment or other patient management decisions, including symptoms consistent with COVID-19, or in those who have been in contact with virus. It is recommended that these results be confirmed by a molecular testing method, if necessary, for patient management.

Invalid: Control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test using a new test cassette.

3.2.4 Acceptance criteria

Potential interfering substances listed in the table were spiked into the negative and low positive samples (*1 ×$10^{3.50}$ $TCID_{50}$/mL, approx. 2xLoD)* and were tested in 3 replicates, the result is not affected by adding interfering substances.

3.2.5 Results

Interfering samples	Concentration	Results					
		LOT 1		LOT 2		LOT 3	
		Negative sample	Positive sample	Negative sample	Positive sample	Negative sample	Positive sample
Whole Blood	*4%*	3/3	3/3	3/3	3/3	3/3	3/3
Mucin	*0.5%*	3/3	3/3	3/3	3/3	3/3	3/3
Chloraseptic (Menthol/Benzocaine)	*1.5 mg/mL*	3/3	3/3	3/3	3/3	3/3	3/3
Naso GEL (NeilMed)	*5% v/v*	3/3	3/3	3/3	3/3	3/3	3/3
CVS Nasal Drops (Phenylephrine)	*15% v/v*	3/3	3/3	3/3	3/3	3/3	3/3

Afrin (Oxymetazoline)	*15% v/v*	3/3	3/3	3/3	3/3	3/3	3/3
CVS Nasal Spray (Cromolyn)	*15% v/v*	3/3	3/3	3/3	3/3	3/3	3/3
Zicam	*5% v/v*	3/3	3/3	3/3	3/3	3/3	3/3
Homeopathic (Alkalol)	*1:10 dilution*	3/3	3/3	3/3	3/3	3/3	3/3
Sore Throat Phenol Spray	*15% v/v*	3/3	3/3	3/3	3/3	3/3	3/3
Tobramycin	*4 µg/mL*	3/3	3/3	3/3	3/3	3/3	3/3
Mupirocin	*10 mg/mL*	3/3	3/3	3/3	3/3	3/3	3/3
Fluticasone Propionate	*5% v/v*	3/3	3/3	3/3	3/3	3/3	3/3
Tamiflu (Oseltamivir Phosphate)	*5 mg/mL*	3/3	3/3	3/3	3/3	3/3	3/3

3.2.6 Conclusion

Interfering reactivity with following potentially interfering substances with certain concentration has been studied. The results were found the result is not affected by adding interfering substances.

Appendix I

Note: All saliva, nasopharyngeal swab and oropharyngeal swab were collected from individuals with Covid-19 symptoms within seven days of symptom onset.

No	Assessment reagent test results	Nucleic acid test
		RT-PCR result
1	+	+
2	+	+
3	+	+
4	+	+
5	+	+
6	+	+
7	+	+
8	+	+
9	+	+
10	+	+
11	+	+
12	+	+
13	+	+
14	+	+
15	+	+
16	+	+
17	+	+
18	+	+
19	+	+
20	+	+
21	+	+
22	+	+
23	+	+
24	+	+
25	+	+
26	+	+
27	+	+
28	+	+
29	+	+
30	+	+
31	+	+
32	+	+
33	+	+
34	+	+
35	+	+
36	+	+
37	+	+

38	+	+
39	+	+
40	+	+
41	+	+
42	+	+
43	+	+
44	+	+
45	+	+
46	+	+
47	+	+
48	+	+
49	+	+
50	+	+
51	+	+
52	+	+
53	+	+
54	+	+
55	+	+
56	+	+
57	+	+
58	+	+
59	+	+
60	+	+
61	+	+
62	+	+
63	+	+
64	+	+
65	+	+
66	+	+
67	+	+
68	+	+
69	+	+
70	+	+
71	+	+
72	+	+
73	+	+
74	+	+
75	+	+
76	+	+
77	+	+
78	+	+
79	+	+

80	+	+
81	+	+
82	+	+
83	+	+
84	+	+
85	+	+
86	+	+
87	+	+
88	+	+
89	+	+
90	+	+
91	+	+
92	+	+
93	+	+
94	+	+
95	+	+
96	+	+
97	+	+
98	+	+
99	+	+
100	+	+
101	+	+
102	+	+
103	+	+
104	+	+
105	+	+
106	+	+
107	+	+
108	+	+
109	+	+
110	+	+
111	+	+
112	+	+
113	+	+
114	+	+
115	+	+
116	+	+
117	+	+
118	+	+
119	+	+
120	+	+
121	+	+

122	+	+
123	+	+
124	+	+
125	+	+
126	+	+
127	+	+
128	+	+
129	+	+
130	+	+
131	+	+
132	+	+
133	+	+
134	+	+
135	+	+
136	+	+
137	+	+
138	+	+
139	+	+
140	+	+
141	+	+
142	+	+
143	+	+
144	+	+
145	+	+
146	+	+
147	+	+
148	+	+
149	+	+
150	+	+
151	+	+
152	+	+
153	+	+
154	+	+
155	+	+
156	+	+
157	+	+
158	+	+
159	+	+
160	+	+
161	+	+
162	+	+
163	+	+

164	+	+
165	+	+
166	+	+
167	+	+
168	+	+
169	+	+
170	+	+
171	+	+
172	+	+
173	+	+
174	+	+
175	+	+
176	+	+
177	+	+
178	+	+
179	+	+
180	+	+
181	+	+
182	+	+
183	+	+
184	+	+
185	+	+
186	+	+
187	+	+
188	+	+
189	+	+
190	+	+
191	+	+
192	+	+
193	+	+
194	+	+
195	+	+
196	+	+
197	+	+
198	+	+
199	+	+
200	+	+
201	+	+
202	+	+
203	+	+
204	+	+
205	-	+

206	-	+
207	-	+
208	-	+
209	-	+
210	-	+
211	-	+
212	-	+
213	+	-
214	+	-
215	+	-
216	+	-
217	+	-
218	+	-
219	-	-
220	-	-
221	-	-
222	-	-
223	-	-
224	-	-
225	-	-
226	-	-
227	-	-
228	-	-
229	-	-
230	-	-
231	-	-
232	-	-
233	-	-
234	-	-
235	-	-
236	-	-
237	-	-
238	-	-
239	-	-
240	-	-
241	-	-
242	-	-
243	-	-
244	-	-
245	-	-
246	-	-
247	-	-

248	-	-
249	-	-
250	-	-
251	-	-
252	-	-
253	-	-
254	-	-
255	-	-
256	-	-
257	-	-
258	-	-
259	-	-
260	-	-
261	-	-
262	-	-
263	-	-
264	-	-
265	-	-
266	-	-
267	-	-
268	-	-
269	-	-
270	-	-
271	-	-
272	-	-
273	-	-
274	-	-
275	-	-
276	-	-
277	-	-
278	-	-
279	-	-
280	-	-
281	-	-
282	-	-
283	-	-
284	-	-
285	-	-
286	-	-
287	-	-
288	-	-
289	-	-

290	-	-
291	-	-
292	-	-
293	-	-
294	-	-
295	-	-
296	-	-
297	-	-
298	-	-
299	-	-
300	-	-
301	-	-
302	-	-
303	-	-
304	-	-
305	-	-
306	-	-
307	-	-
308	-	-
309	-	-
310	-	-
311	-	-
312	-	-
313	-	-
314	-	-
315	-	-
316	-	-
317	-	-
318	-	-
319	-	-
320	-	-
321	-	-
322	-	-
323	-	-
324	-	-
325	-	-
326	-	-
327	-	-
328	-	-
329	-	-
330	-	-
331	-	-

332	-	-
333	-	-
334	-	-
335	-	-
336	-	-
337	-	-
338	-	-
339	-	-
340	-	-
341	-	-
342	-	-
343	-	-
344	-	-
345	-	-
346	-	-
347	-	-
348	-	-
349	-	-
350	-	-
351	-	-
352	-	-
353	-	-
354	-	-
355	-	-
356	-	-
357	-	-
358	-	-
359	-	-
360	-	-
361	-	-
362	-	-
363	-	-
364	-	-
365	-	-
366	-	-
367	-	-
368	-	-
369	-	-
370	-	-
371	-	-
372	-	-
373	-	-

374	-	-
375	-	-
376	-	-
377	-	-
378	-	-
379	-	-
380	-	-
381	-	-
382	-	-
383	-	-
384	-	-
385	-	-
386	-	-
387	-	-
388	-	-
389	-	-
390	-	-
391	-	-
392	-	-
393	-	-
394	-	-
395	-	-
396	-	-
397	-	-
398	-	-
399	-	-
400	-	-
401	-	-
402	-	-
403	-	-
404	-	-
405	-	-
406	-	-
407	-	-
408	-	-
409	-	-
410	-	-
411	-	-
412	-	-
413	-	-
414	-	-
415	-	-

416	-	-
417	-	-
418	-	-
419	-	-
420	-	-
421	-	-
422	-	-
423	-	-
424	-	-
425	-	-
426	-	-
427	-	-
428	-	-
429	-	-
430	-	-
431	-	-
432	-	-
433	-	-
434	-	-
435	-	-
436	-	-
437	-	-
438	-	-
439	-	-
440	-	-
441	-	-
442	-	-
443	-	-
444	-	-
445	-	-
446	-	-
447	-	-
448	-	-
449	-	-
450	-	-
451	-	-
452	-	-
453	-	-
454	-	-
455	-	-
456	-	-
457	-	-

458	-	-
459	-	-
460	-	-
461	-	-
462	-	-
463	-	-
464	-	-
465	-	-
466	-	-
467	-	-
468	-	-
469	-	-
470	-	-
471	-	-
472	-	-
473	-	-
474	-	-
475	-	-
476	-	-
477	-	-
478	-	-
479	-	-
480	-	-
481	-	-
482	-	-
483	-	-
484	-	-
485	-	-
486	-	-
487	-	-
488	-	-
489	-	-
490	-	-
491	-	-
492	-	-
493	-	-
494	-	-
495	-	-
496	-	-
497	-	-
498	-	-
499	-	-

500	-	-
501	-	-
502	-	-
503	-	-
504	-	-
505	-	-
506	-	-
507	-	-
508	-	-
509	-	-
510	-	-
511	-	-
512	-	-
513	-	-
514	-	-
515	-	-
516	-	-
517	-	-
518	-	-
519	-	-
520	-	-
521	-	-
522	-	-
523	-	-
524	-	-
525	-	-
526	-	-
527	-	-
528	-	-
529	-	-
530	-	-
531	-	-
532	-	-
533	-	-
534	-	-
535	-	-
536	-	-
537	-	-
538	-	-
539	-	-
540	-	-
541	-	-

542	-	-
543	-	-
544	-	-
545	-	-
546	-	-
547	-	-
548	-	-
549	-	-
550	-	-
551	-	-
552	-	-
553	-	-
554	-	-
555	-	-
556	-	-
557	-	-
558	-	-
559	-	-
560	-	-
561	-	-
562	-	-
563	-	-
564	-	-
565	-	-
566	-	-
567	-	-
568	-	-
569	-	-
570	-	-
571	-	-
572	-	-
573	-	-
574	-	-
575	-	-
576	-	-
577	-	-
578	-	-
579	-	-
580	-	-
581	-	-
582	-	-
583	-	-

584	-	-
585	-	-
586	-	-
587	-	-
588	-	-
589	-	-
590	-	-
591	-	-
592	-	-
593	-	-
594	-	-
595	-	-
596	-	-
597	-	-
598	-	-
599	-	-
600	-	-
601	-	-
602	-	-
603	-	-
604	-	-
605	-	-
606	-	-
607	-	-
608	-	-
609	-	-
610	-	-
611	-	-
612	-	-
613	-	-
614	-	-
615	-	-
616	-	-
617	-	-
618	-	-
619	-	-
620	-	-
621	-	-
622	-	-
623	-	-
624	-	-
625	-	-

626	-	-
627	-	-
628	-	-
629	-	-
630	-	-
631	-	-
632	-	-
633	-	-
634	-	-
635	-	-
636	-	-
637	-	-
638	-	-
639	-	-
640	-	-
641	-	-
642	-	-
643	-	-
644	-	-
645	-	-
646	-	-
647	-	-
648	-	-
649	-	-
650	-	-
651	-	-
652	-	-
653	-	-
654	-	-
655	-	-
656	-	-
657	-	-
658	-	-
659	-	-
660	-	-
661	-	-
662	-	-
663	-	-
664	-	-
665	-	-
666	-	-
667	-	-

668	-	-
669	-	-
670	-	-
671	-	-
672	-	-
673	-	-
674	-	-
675	-	-
676	-	-
677	-	-
678	-	-
679	-	-
680	-	-
681	-	-
682	-	-
683	-	-
684	-	-
685	-	-
686	-	-
687	-	-
688	-	-
689	-	-
690	-	-
691	-	-
692	-	-
693	-	-
694	-	-
695	-	-
696	-	-
697	-	-
698	-	-
699	-	-
700	-	-
701	-	-
702	-	-
703	-	-
704	-	-
705	-	-
706	-	-
707	-	-
708	-	-
709	-	-

710	-	-
711	-	-
712	-	-
713	-	-
714	-	-
715	-	-
716	-	-
717	-	-
718	-	-
719	-	-
720	-	-
721	-	-
722	-	-
723	-	-
724	-	-
725	-	-
726	-	-
727	-	-
728	-	-
729	-	-
730	-	-
731	-	-
732	-	-
733	-	-
734	-	-
735	-	-
736	-	-
737	-	-
738	-	-
739	-	-
740	-	-
741	-	-
742	-	-
743	-	-
744	-	-
745	-	-
746	-	-
747	-	-
748	-	-
749	-	-
750	-	-
751	-	-

752	-	-
753	-	-
754	-	-
755	-	-
756	-	-
757	-	-
758	-	-
759	-	-
760	-	-
761	-	-
762	-	-
763	-	-
764	-	-
765	-	-
766	-	-
767	-	-
768	-	-
769	-	-
770	-	-
771	-	-
772	-	-
773	-	-
774	-	-
775	-	-
776	-	-
777	-	-
778	-	-
779	-	-
780	-	-
781	-	-
782	-	-
783	-	-
784	-	-
785	-	-
786	-	-
787	-	-
788	-	-
789	-	-
790	-	-
791	-	-
792	-	-
793	-	-

794	-	-
795	-	-
796	-	-
797	-	-
798	-	-
799	-	-
800	-	-
801	-	-
802	-	-
803	-	-
804	-	-
805	-	-
806	-	-
807	-	-
808	-	-
809	-	-
810	-	-
811	-	-
812	-	-
813	-	-
814	-	-
815	-	-
816	-	-
817	-	-
818	-	-
819	-	-
820	-	-
821	-	-
822	-	-
823	-	-
824	-	-
825	-	-
826	-	-
827	-	-
828	-	-
829	-	-
830	-	-
831	-	-
832	-	-
833	-	-
834	-	-
835	-	-

836	-	-
837	-	-
838	-	-
839	-	-
840	-	-
841	-	-
842	-	-
843	-	-
844	-	-
845	-	-
846	-	-
847	-	-
848	-	-
849	-	-
850	-	-
851	-	-
852	-	-
853	-	-
854	-	-
855	-	-
856	-	-
857	-	-
858	-	-
859	-	-
860	-	-
861	-	-
862	-	-
863	-	-
864	-	-
865	-	-
866	-	-
867	-	-
868	-	-
869	-	-
870	-	-
871	-	-
872	-	-
873	-	-
874	-	-
875	-	-
876	-	-
877	-	-

878	-	-
879	-	-
880	-	-
881	-	-
882	-	-
883	-	-
884	-	-
885	-	-
886	-	-
887	-	-
888	-	-
889	-	-
890	-	-
891	-	-
892	-	-
893	-	-
894	-	-
895	-	-
896	-	-
897	-	-
898	-	-
899	-	-
900	-	-
901	-	-
902	-	-
903	-	-
904	-	-
905	-	-
906	-	-
907	-	-
908	-	-
909	-	-
910	-	-
911	-	-
912	-	-
913	-	-
914	-	-
915	-	-
916	-	-
917	-	-
918	-	-
919	-	-

920	-	-
921	-	-
922	-	-
923	-	-
924	-	-
925	-	-
926	-	-
927	-	-
928	-	-
929	-	-
930	-	-
931	-	-
932	-	-
933	-	-
934	-	-
935	-	-
936	-	-
937	-	-
938	-	-
939	-	-
940	-	-
941	-	-
942	-	-
943	-	-
944	-	-
945	-	-
946	-	-
947	-	-
948	-	-
949	-	-
950	-	-
951	-	-
952	-	-
953	-	-
954	-	-
955	-	-
956	-	-
957	-	-
958	-	-
959	-	-
960	-	-
961	-	-

962	-	-
963	-	-
964	-	-
965	-	-
966	-	-
967	-	-
968	-	-
969	-	-
970	-	-
971	-	-
972	-	-
973	-	-
974	-	-
975	-	-
976	-	-
977	-	-
978	-	-
979	-	-
980	-	-
981	-	-
982	-	-
983	-	-
984	-	-
985	-	-
986	-	-
987	-	-
988	-	-
989	-	-
990	-	-
991	-	-
992	-	-
993	-	-
994	-	-
995	-	-
996	-	-
997	-	-
998	-	-
999	-	-
1000	-	-
1001	-	-
1002	-	-
1003	-	-

1004	-	-
1005	-	-
1006	-	-
1007	-	-
1008	-	-
1009	-	-
1010	-	-
1011	-	-
1012	-	-
1013	-	-
1014	-	-
1015	-	-
1016	-	-
1017	-	-
1018	-	-
1019	-	-
1020	-	-