CTK BIOTECH
SIMPLIFYING DIAGNOSTICS



COVID-19 IgG/IgM Rapid Test Tech Support

833-919-0617

CTK-MK-PPT-R0180C Rev. 1.0

Contents

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Currently available IVD methods for COVID-19

	RT-PCR	Ab Rapid Test	Ab ELISA	Ab CLIA
Test principle	Molecular test detects virus nucleic acid	**Lateral flow immunoassay detects IgG/IgM antibodies against virus**	Immunoassay detects IgG/IgM antibodies against virus	Immunoassay detects IgG/IgM antibodies against virus
Specimen type	Swab	**Serum/Plasma/Whole Blood**		
Ideal testing window	During initial stages of infection first 2-3 weeks	**After IgG/IgM antibodies are generated starting a few days to weeks after infection**		
Cost	High	**Low**	Medium	High
Time-to-result	Time-consuming, takes several hours	**Fast results within 15 minutes**	Time-consuming, takes several hours	Fast results within 30 minutes
Complexity	• Requires specialized equipment • Requires trained personnel	• **Does not need equipment** • **Easy to use**	• Requires specialized equipment • Requires trained personnel	• Requires specialized equipment • Easy to use
Limitation	Specimen collection issues (false negative)	**Not advisable to use in the first week of illness**	Very few products on the market	Closed system

When to use a COVID-19 IgG/IgM rapid test

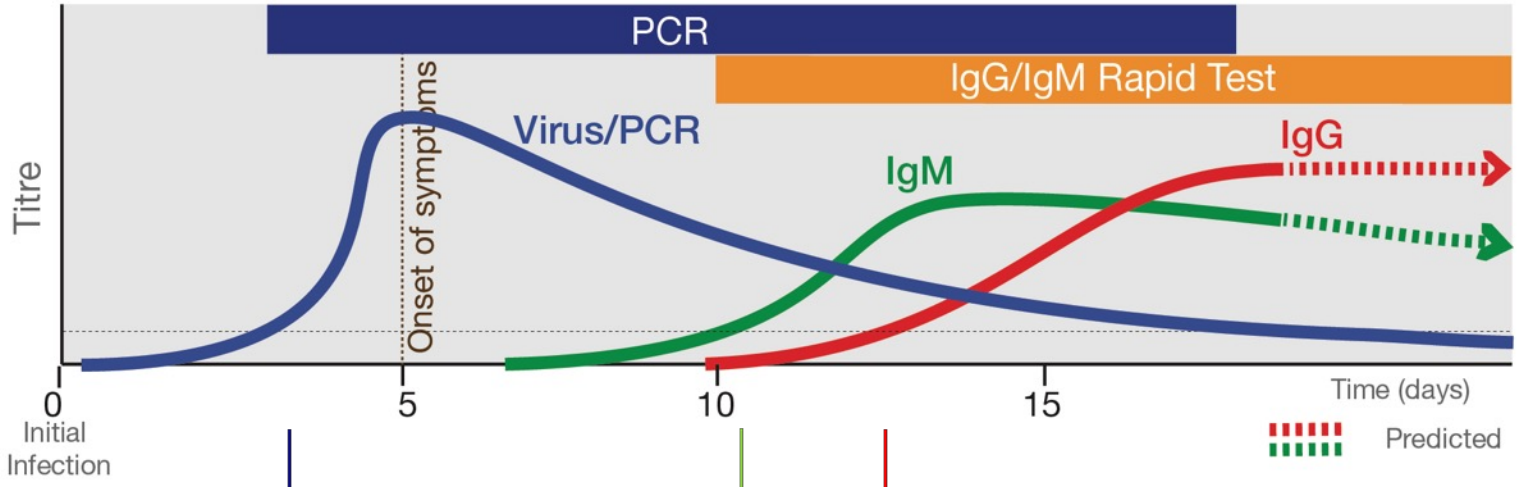
- **RT-PCR**
  - ✓ Confirms the presence of infection
  - ✓ Doesn't provide information on immune response and likely immunity

- **IgG/IgM rapid test** is suited for POC testing:
  - ✓ Provides information on previous infection
  - ✓ Detects immune response and provides indication of likely immunity
  - ✓ Aids in verifying if people can be released from quarantine and/or return to work

- There is a clear benefit in testing asymptomatic patients before they are released from quarantine.[1]

1. Novel coronavirus (SARS-CoV-2) - Discharge criteria for confirmed COVID-19 cases. (2020, March 10). Retrieved from https://www.ecdc.europa.eu/en/publications-data/novel-coronavirus-sars-cov-2-discharge-criteria-confirmed-covid-19-cases

When to use a COVID-19 IgG/IgM rapid test



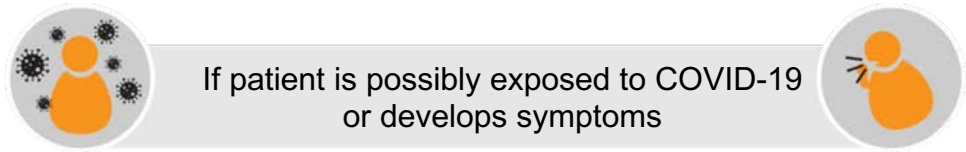
IgG can be detected 1-2 weeks after onset of symptoms, and persist for months or longer

IgM can be detected a few days after symptoms and typically persists for several weeks

In general, **PCR** sensitivity is higher in the initial stages of infection, when the virus is present.

Lauer, S. A., Grantz, K. H., Bi, Q., Jones, F. K., Zheng, Q., Meredith, H. R., ... & Lessler, J. (2020). The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Annals of internal medicine*.

When to use a COVID-19 IgG/IgM rapid test



If patient is possibly exposed to COVID-19
or develops symptoms

If the result is positive, the patient was likely:

- Infected at the time specimen was collected, or
- Previously infected and has developed immune response

Positive results must be confirmed by PCR

If PCR result is positive, the patient must go into quarantine.

Antibody testing after quarantine can track possible immunity over time.

If PCR result is negative, the patient has likely developed immunity.

If the result is negative, the patient was likely:

- Not infected at the time specimen was collected, or
- In the early infection stages, and could test positive later

The patient is at risk of exposure and developing illness. Therefore, negative test results do not rule out getting sick later.

+ Positive; - Negative

Interpretation of test results

Test results			Clinical significance
PCR	IgM	IgG	
+	-	-	Patient likely in the window period of infection.
+	+	-	Patient likely be in the early stages of infection.
+	+	+	Patient is in the active phase of infection.
+	-	+	Patient may be in late or recurrent stage of infection.
-	+	-	Patient likely in the early stage of infection.
-	-	+	Patient likely had a past infection, and has recovered.
-	+	+	Patient likely in recovery stage of infection.

1. Lauer, S. A., Grantz, K. H., Bi, Q., Jones, F. K., Zheng, Q., Meredith, H. R., ... & Lessler, J. (2020). The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Annals of internal medicine*.
2. [Nucleic acid and antibody detection] Dongliang Li: Analysis and interpretation of SARS-CoV-2 nucleic acid and specific antibody detection. (n.d.). Retrieved from https://mp.weixin.qq.com/s/jsDNi3jG24orHwYg3Xpczw

+ Positive; - Negative

Interpretation of test results

No test is 100% accurate. There's a trade-off between sensitivity and specificity of a rapid test: an increasingly sensitive test will potentially lose specificity. This trade-off has important implications for interpreting COVID-19 population trends based on testing to date and moving forward.

	Potential Causes of Erroneous Results
False positive	1. Potential cross-reactivity with other related respiratory virus 2. Potentially interfering drugs and medicines 3. Human anti-mouse antibody (HAMA) present in patients who have received immunotherapy with a murine monoclonal antibody 4. Poor technique in sampling or testing 5. Operator variability in interpreting test results
False negative	1. Low test sensitivity 2. Low levels of antibodies in the sample, due to poor immune response 3. Poor technique in sampling or testing (e.g, didn't wipe off the first droplet of fingertip blood) 4. Operator variability in interpreting test results

ALTA® Rapid Test Reader

Eliminating subjective interpretation by operator
Quantitative differentiation between negative & weak positive results

Independent evaluation - 1

Specimen			CTK Rapid Test		Test A		Test B (NMPA approved)	
ID	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM
308	+	+	+	+	+	+	+	+
309	+	+	+	-	+	+	+	-
310	+	+	+	-	+	-	+	-
311	+	+	+	+	+	+	+	-
312	+	+	+	-	+	+	+	-
517	+	+	+	+	+	-	+	-
518	+	+	+	+	+	-	+	-
519	+	+	+	+	+	+	+	-
520	+	+	+	+	+	+	+	+
521	+	+	+	+	+	+	+	+
522	+	+	+	+	+	+	-	+
523	+	+	+	-	+	-	+	-
524	+	+	+	-	+	-	+	-
525	+	+	+	+	+	+	-	-
526	+	+	+	+	+	+	+	+
527	+	+	+	+	+	+	+	+
528	+	+	+	+	+	+	-	-
529	+	+	+	+	+	+	+	-
530	+	+	-	-	-	-	-	-
533	+	+	+	+	+	+	+	-

✓ The specimens missed by CTK tests are weak positive. It matches the claim of the limited detection in IFU.

CTK COVID-19 Rapid Test shows highest sensitivity

+ Positive; - Negative

Independent evaluation - 2

Antibody rapid tests from 3 companies were evaluated. 25 specimens (whole blood in EDTA tube) were tested.
Note: It is not advisable to use antibody test on individuals in the first week of illness.

PCR Test		CTK Test		Test A		Test B	
Results	No. of samples	+	-	+	-	+	-
Positive (recent infection 1-2 days)	5	0	5	0	5	0	5
Positive	10	8	2	8	2	6	4
Negative (with history of positive COVID-19)	5	4	1	4	1	0	5
Negative (healthy people)	5	0	5	0	5	0	5
Total	25	12	13	12	13	6	19
Conclusion		88% concordance to the PCR results		88% concordance to the PCR results		64% concordance to the PCR results	

Appearance of virus specific antibodies start later in the course of infection, around 5-7 days post-infection.

CTK COVID-19 Rapid Test has 88% concordance with PCR results

Independent evaluation - 3

China NMPA Quality Inspection Panel

Specimen		CTK Test		Test A		Test B		Test C
ID	Value	IgG	IgM	IgG	IgM	IgG	IgM	Total antibody
2081	-	-	-	-	-	-	-	-
2082	-	-	-	-	-	-	-	-
2083	+	+	+	-	+	-	-	+
2084	-	-	-	-	-	-	-	-
2085	+	-	+	-	-	-	-	+
2086	-	-	-	-	-	-	-	-
2087	+	-	+	-	-	-	+	-
2088	+	+	-	+	+	+	-	-
2089	+	+	-	+	+	+	+	+
2090	-	-	-	-	-	-	-	-

✓ CTK test picked all 5 positive specimens.

✓ Tests A, B and C all picked 3 positive specimens, and missed 2 positive specimens.

- CTK COVID-19 Rapid Test has higher sensitivity
- CTK COVID-19 Rapid Test shows 100% sensitivity to the quality inspection panel

+ Positive;
- Negative

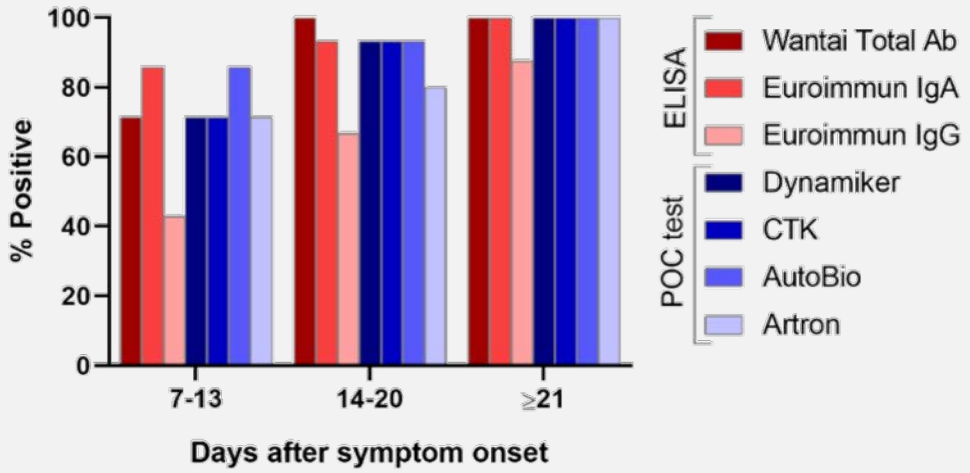
Independent evaluation - 4

Assay	Number (%) of serum samples: Case sera testing positive	Control sera testing negative	PPV (%)	NPV (%)
ELISA				
Wantai Total Ab	28/30 (93)	82/82(100)	28/28 (100)	82/84 (98)
Euroimmun IgA[a]	28/30 (93)	76/82 (93)	28/34 (82)	76/78 (97)
Euroimmun IgG[a]	20/30 (67)	79/82 (96)	20/23 (87)	79/89 (89)
Point-of-care test				
Dynamiker	27/30 (90)	32/32 (100)	27/27 (100)	32/36 (89)
CTK Biotech	27/30 (90)	32/32 (100)	27/27 (100)	32/36 (89)
AutoBio Diagnostics	28/30 (93)	32/32 (100)	28/28 (100)	32/25 (91)
Artron Laboratories	25/30 (83)	17/17 (100)	25/25 (100)	17/23 (74)
Acro Biotech	4/5 (80)[b]	12/15 (80)	4/7 (57)	12/13 (92)
Alltest Biotech	1/1 (100)[b]	13/15 (87)	Too few tested	Too few tested

[a]Borderline data were considered negative.

[b]Due to comparatively poorer assay performance in an initial round of testing, further testing were suspended.

CTK COVID-19 Rapid Test has good analytical sensitivity and specificity for SARS-CoV-2 antibody detection



CTK COVID-19 Rapid Test has good analytical sensitivity of SARS-CoV-2 antibody in relation to the duration of illness

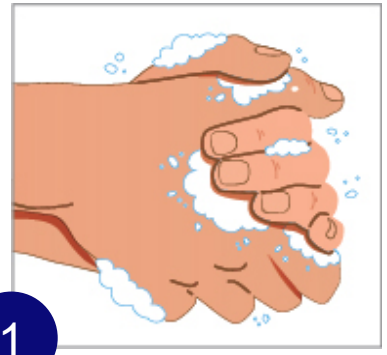
CTK COVID-19 Rapid Test shows 100% specificity to Adv, Flu A/B, RSV, and Dengue.

Lassaunière, R., Frische, A., Harboe, Z. B., Nielsen, A. C., Fomsgaard, A., Krogfelt, K. A., & Jørgensen, C. S. (2020). Evaluation of nine commercial SARS-CoV-2 immunoassays. *medRxiv*.

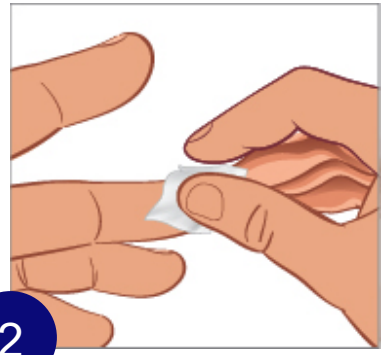
FAQs

Q: What is the proper procedure for a finger prick test?

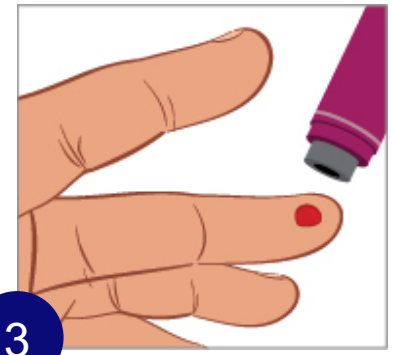
A:



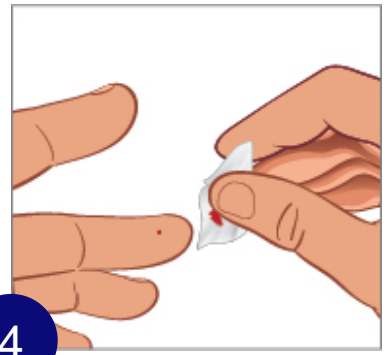
1 Wash hands thoroughly, and then dry them with an appropriate towel.



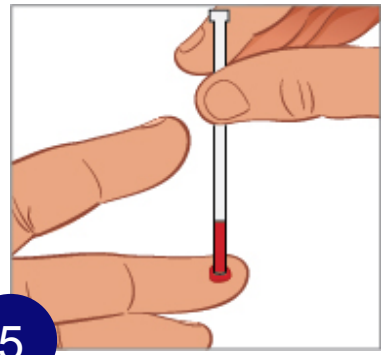
2 Warm and massage the fleshy portion of the finger gently. Clean the finger with the alcohol pad.



3 Quickly puncture it with a sterile lancet in a position slightly lateral to the center of the fingertip.



4 Wipe off the first droplet of blood with a sterile gauze or cotton ball.



5 Draw the blood into the capillary tube and run the test.

6 Safely dispose all supplies and used reagents.

FAQs

Q: What is the general benefit of using a COVID-19 IgG/IgM Rapid Test?

A: COVID-19 IgG/IgM Rapid Test has high sensitivity and specificity, does not need equipment, is easy to use and cost efficient, and can get results within 15 minutes.

Q: We already have COVID-19 PCR test. Why we still need antibody test for COVID-19?

A: As a highly sensitive test for COVID-19, PCR test requires high-quality swabs containing sufficient amounts of SARS-CoV-2 RNA. It's a challenge since the amount of viral RNA not only varies between patients, but also varies at different stages of infection. Besides, nasopharyngeal swabs are not pleasant to the patient, and the sampling techniques vary significantly from nurse to nurse. Without sufficient viral RNA, PCR may return false negative results.

IgG/IgM rapid test has advantages over PCR. First, the antibody test detects IgG/IgM antibodies which are more stable than viral RNA, and therefore less sensitive to degradation during collection, transport and storage than PCR specimens. Second, since antibodies are uniformly distributed in the blood, IgG/IgM specimens have much less variations than viral RNA specimens, and can be collected easily. Third, unlike PCR, serological tests can detect past infection because SARS-CoV-2 specific antibodies can persist in the blood for several months/years after onset of symptoms.

Q: Why should the first drop of blood be wiped away when performing a finger puncture?

A: The first drop of fingertip blood may be diluted and/or contaminated with tissue fluid and/or debris (sloughing skin). Also, avoid squeezing the finger or heel too tightly because this dilutes the specimen with tissue fluid and increases the probability of hemolysis.[1]

Q: How to Interpret Test Results?

A: Based on current knowledge of COVID-19, IgG/IgM rapid tests are recommended to be used after a few days to 1 week after symptoms.[1, 2] The results of PCR and IgG/IgM tests do not necessarily need to agree. Overall, while PCR testing is appropriate for COVID-19 detection during the window period of infection, IgG/IgM tests are appropriate tests during the active and chronic phases. Since the exact phase of infection is often unknown, combining PCR and IgG/IgM testing can improve the accuracy of the COVID-19 diagnosis.

1. World Health Organization. (2010). *WHO guidelines on drawing blood: best practices in phlebotomy*. World Health Organization.

FAQs

Q: Are Rapid Tests confirmatory tests?

A: A Rapid test is an IVD test that is meant to be used as a diagnostic aid. Any use or interpretation of these results must also rely on other clinical findings, and alternative test methods such as ELISA or PCR test should be used to confirm positive rapid test results.

Q: Why would the intensity of the color on a rapid test vary from patient to patient?

A: Line intensity can vary with different parameters, such as specimen type, composition, storage conditions, and many other factors. Line intensity is not directly proportional to the number of detecting antibodies or antigen present in the sample. The formation of a line other than the control line, regardless of intensity, indicates a positive result.

Q: Why is specimen flow on a rapid test slow or not happening?

A: This could be due to a variety of reasons such as: no sample diluent, not enough sample diluent, not enough specimen, specimen that is too thick (increased lipids, hemolysis, etc.), and a number of other conditions that could affect the specimen.

Q: I may have overloaded the cassette with too much specimen, does this invalidate the test?

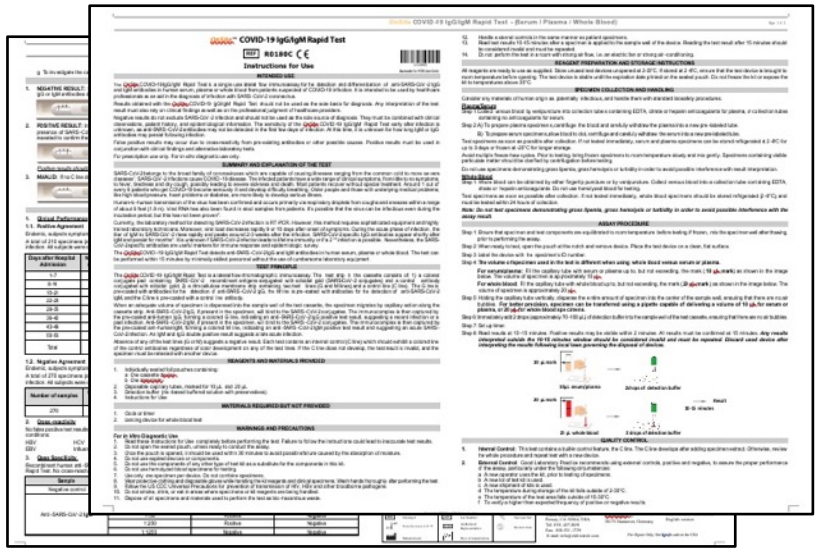
A: If the cassette has been overloaded, it means either too much specimen or too much buffer was used. In either case the performance characteristics of the test could be different because it is outside of the recommended use. The test should be repeated, ensuring that the cassette is loaded correctly.

Q: How can I get additional information on CTK's other tests?

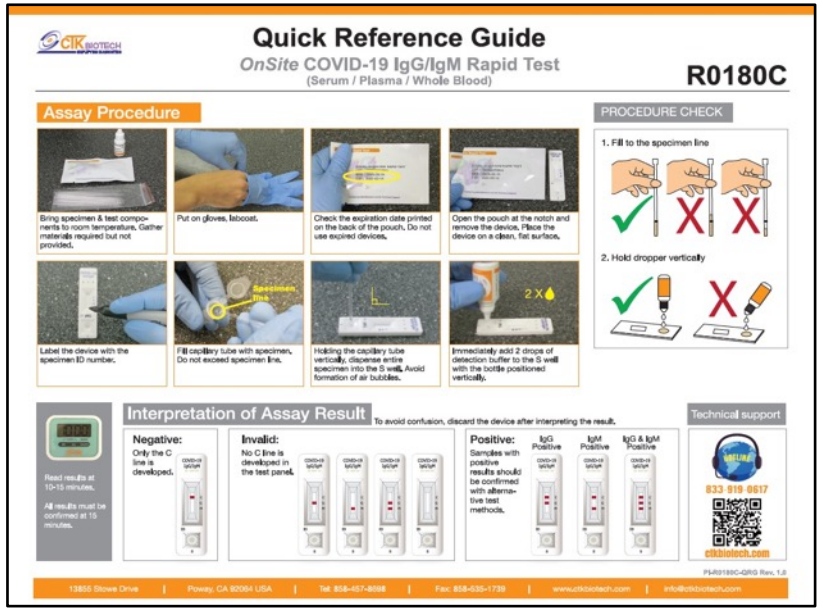
A: CTK offers a broad range of diagnostic test kits covering many disease states and formats. We can provide any information you need and you can visit their website for specific details on ALL their products at ctkbiotech.com

1. Lauer, S. A., Grantz, K. H., Bi, Q., Jones, F. K., Zheng, Q., Meredith, H. R., ... & Lessler, J. (2020). The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Annals of internal medicine*.
2. To, K. K. W., Tsang, O. T. Y., Leung, W. S., Tam, A. R., Wu, T. C., Lung, D. C., ... & Lau, D. P. L. (2020). Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *The Lancet Infectious Diseases*.

Marketing Support Materials



Package Insert



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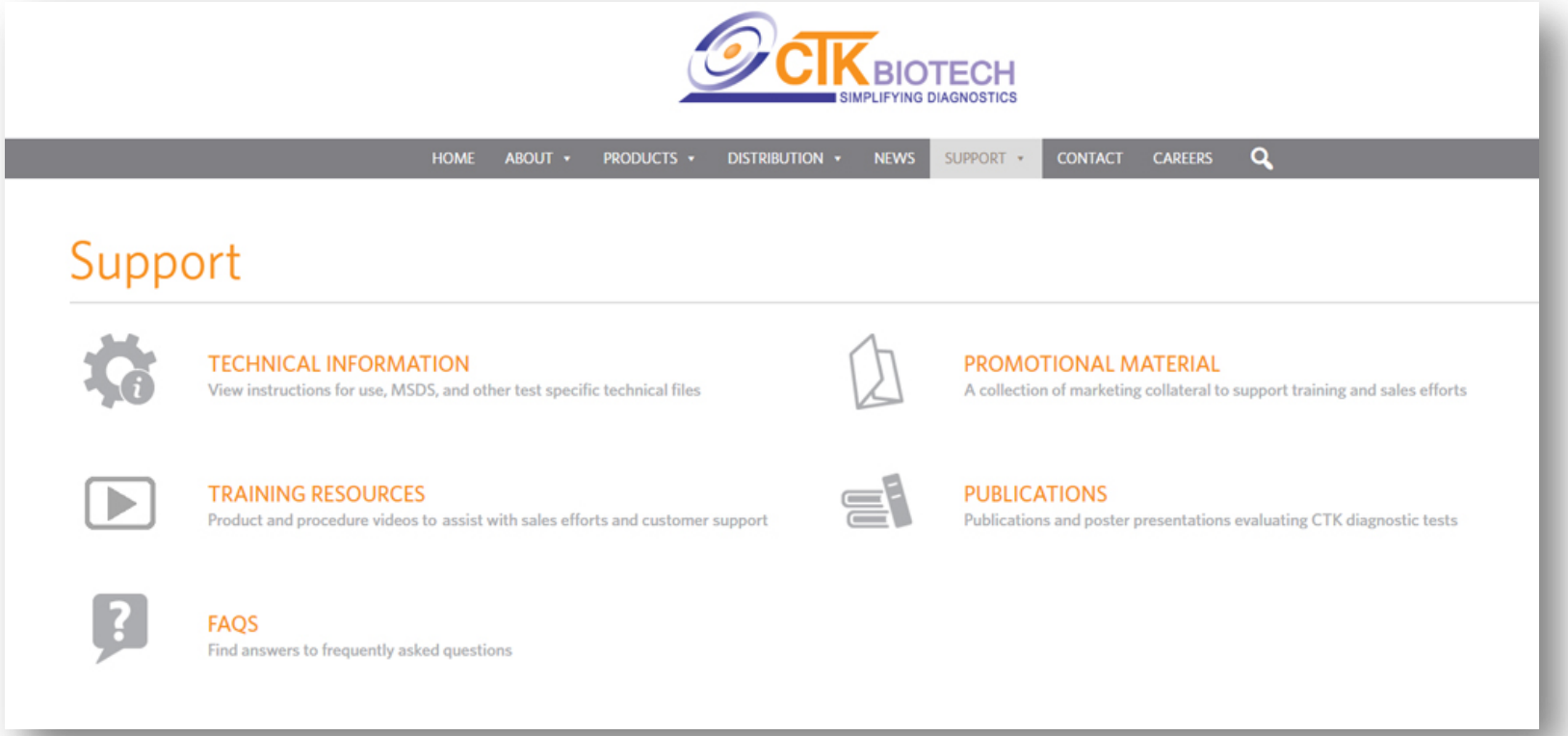

THANK YOU!

HOTLINE 833-919-0617

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