Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel
Federal Institute for Vaccines and Biomedicines

Paul-Ehrlich-Institut

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Information for Manufacturers and Distributors

COVID-19 ANTIGEN TESTS

In response to numerous inquiries, the Paul-Ehrlich-Institut would like to provide information on current responsibilities for the evaluation of rapid antigen tests for professional use.

1. Pursuant to section 1 (1) sentence 5 of the Ordinance on Coronavirus Testing (Coronavirus-Testverordnung, TestV), the Paul-Ehrlich-Institut coordinates with the Robert Koch-Institut (RKI) to determine the minimum criteria that antigen tests must meet in order to be reimbursed. These minimum criteria are published at the following link:

   - www.pei.de/SharedDocs/Downloads/EN/newsroom-en/dossiers/minimum-criteria-for-rapid-sars-cov2-antigen-tests-01-12-2020.pdf?__blob=publicationFile&v=6

   As per section (d) of the criteria, antigen test performance data can be assessed by means of a comparative evaluation by various institutions in Germany (including the Paul-Ehrlich-Institut). The minimum criteria are considered not fulfilled if the Paul-Ehrlich-Institut concludes based on the comparative evaluation that a rapid SARS-CoV-2 antigen test does not correspond with the latest state of technology.

2. The evaluation is designed to identify antigen tests with low sensitivity. The Federal Institute for Drugs and Medical Devices (BfArM) removes these tests from its list of reimbursable rapid tests. The results of the evaluation cannot be used directly to predict the sensitivity of a particular antigen test in a particular clinical environment. The evaluation can therefore not be used to make any conclusions on clinical sensitivities that may occur with potentially different virus distribution and virus loads in various sample types (throat, nose, nasopharyngeal, mouth swab, saliva, etc.).

3. The sample panel comprises a total of 50 samples with different virus concentrations. The criterion of the evaluation refers to the sample panel used

for this purpose and here again to the sensitivity of tests at very high viral load (Cq ≤ 25). This criterion is in line with the purpose of antigen tests, which are meant to detect very high viral loads in persons who, owing to a very high viral load in the nasopharyngeal cavity, pose a high risk of SARS-CoV-2 transmission to persons with whom they come in contact. Such viral loads often occur in the first 5 to 7 days after the onset of symptoms. The criterion established by the Paul-Ehrlich-Institut and the Robert Koch-Institut (RKI) is the detection of at least 75% of the panel samples used that have a virus concentration of Cq = 25 or lower. A low Cq value corresponds to a higher viral load. A higher viral load corresponds to a higher SARS-CoV-2 concentration in a swab sample.

4. Nasopharyngeal swabs (clinical samples) pooled by the RKI and contained in a PBS buffer were used as a panel (sample series) for the comparative investigation of the test sensitivities. The virus concentration in the individual samples of the panel was subsequently determined by means of the same quantitative PCR.

5. The evaluation by the Paul-Ehrlich-Institut and the Robert Koch-Institut is based on a coordinated and standardised approach that ensures the best possible comparability of the data. The antigen tests are carried out exactly according to the respective instructions for use. The sample material is not placed directly on the test cassette. Instead, the evaluation sample is taken just like a "regular" sample (= a swab taken from the nasopharynx using the swab provided in the antigen test, which is placed into the provided sample solution by dipping it in and squeezing it out) using the swab provided in the antigen test. The swab is transferred into the test-specific buffer and then placed on the test cassette.

6. Published results of various experimental studies on the sensitivity of antigen tests often vary. A comparison and transferability of results between different studies is often not possible due to the use of different populations for the clinical swab samples and the variation in methodologies and experimental design.
   Factors such as the viral load of the samples, the presence of symptoms, the time period after the onset of symptoms, sampling methods and types, sample storage, and the conditions under which samples are taken may influence the results, especially if these have not been standardised during the assessment.

The use of different PCR tests for viral load determination can also yield different results.

7. A comparative evaluation is not a batch test. The evaluation is carried out on a batch submitted by the manufacturer/distributor. The Paul-Ehrlich-Institut must accept the antigen tests or batch for evaluation as they are delivered. The result is considered representative of the particular antigen test named in the evaluation. It is assumed that variations between batches of the antigen tests are minor due to the manufacturer's quality checks.

8. Multiple evaluations within a comparative evaluation are avoided to the extent possible. A test that has already been evaluated and can be assigned to an original equipment manufacturer (OEM), which is then resubmitted separately for evaluation by a private label manufacturer (PLM) and/or distributor, or a test design variant that is submitted by the same manufacturer, i.e. identical tests, will therefore not be revaluated. Indication of OEM or PLM status is voluntary and does not always occur prior to submission for evaluation by the Paul-Ehrlich-Institut.

9. The Federal Institute for Drugs and Medical Devices (BfArM) can transfer a successful evaluation by the Paul-Ehrlich-Institut to any identical tests. The evaluation status is transferred to identical tests on the BfArM lists and these antigen tests are listed accordingly (on the BfArM list under the column: "Evaluation PEI": "Yes"). However, identical antigen tests are not listed on the Paul-Ehrlich-Institut lists (tests with a positive or negative evaluation result). The lists of the Paul-Ehrlich-Institut and the BfArM only provide a complete overview of the status of the Paul-Ehrlich-Institut evaluations and the fulfilment of minimum criteria when viewed together.

10. The comparative evaluation of the Paul-Ehrlich-Institut is limited to tests for professional use (by doctors, trained staff in test centres). Only during the period of the BfArM's special approvals (February 2021 to 14.07.2021) of self-tests (lay tests that are carried out and evaluated at home), was this type of test also evaluated experimentally by the Paul-Ehrlich-Institut in individual cases, insofar as there was no identical variant for professional use for a self-test.

11. Background information: In the special approval phase, there were no standardised SARS-CoV-2 self-tests that were evaluated and given a CE marking by a notified body. The BfArM has granted no special approvals since 15 July 2021. From that point onwards, all products declared as self-tests have a CE marking and have therefore been independently checked and certified by a notified body. The Paul-Ehrlich-Institut does not carry out comparative evaluations of antigen self-tests with a CE. The self-tests on the Paul-Ehrlich-Institut list originate from the special approval phase or refer to the identical professional test variant.

12. The comparative evaluation only presents a sample of the SARS-CoV-2 antigen tests included on the BfArM's list of professional tests (which are therefore reimbursable). The Paul-Ehrlich-Institut is not obligated to evaluate any tests.