

PRESS WORKSHOP

Sensitivity of Antigen Tests to the Omicron Variant

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Exemplary analysis by the
Paul-Ehrlich-Institut (PEI), Robert Koch-Institut (RKI),
Bundeswehr Institute of Microbiology
(InstMikroBioBw)

Manufacturer Inquiry by the BfArM

Cichutek, Nübling, Scheiblaue
Paul-Ehrlich-Institut
Presse-Workshop
Langen, 24.03.2022



*Das Paul-Ehrlich-Institut ist ein Bundesinstitut im Geschäftsbereich
des Bundesministeriums für Gesundheit.*

*The Paul-Ehrlich-Institut is an Agency of the
German Federal Ministry of Health.*



Panel: Speakers and Experts

- Prof Klaus Cichutek, President of the Paul-Ehrlich-Institut
- PD Dr Micha Nübling, Head of the Division Major Policy Issues, Coordination
- Dr Heinrich Scheiblaue, Head of the Testing Laboratory for In Vitro Diagnostics at the Paul-Ehrlich-Institut
- Carola Lübbling-Raukohl, Head of Public Relations and Spokesperson



AGENDA

Sensitivity of Antigen Tests

Exemplary Analysis by the Paul-Ehrlich-Institute,
Robert Koch-Institute, Bundeswehr Institute of Microbiology

- Structure of the exemplary experimental test
Prof Klaus Cichutek
- Results
PD Dr Micha Nübling
- Manufacturer information about test design
PD Dr Micha Nübling
- Discussion
Dr Heinrich Scheiblauber et al.



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SARS-CoV-2 In vitro diagnostics (IVD)

- Antigen tests versus PCR tests -



PCR Test

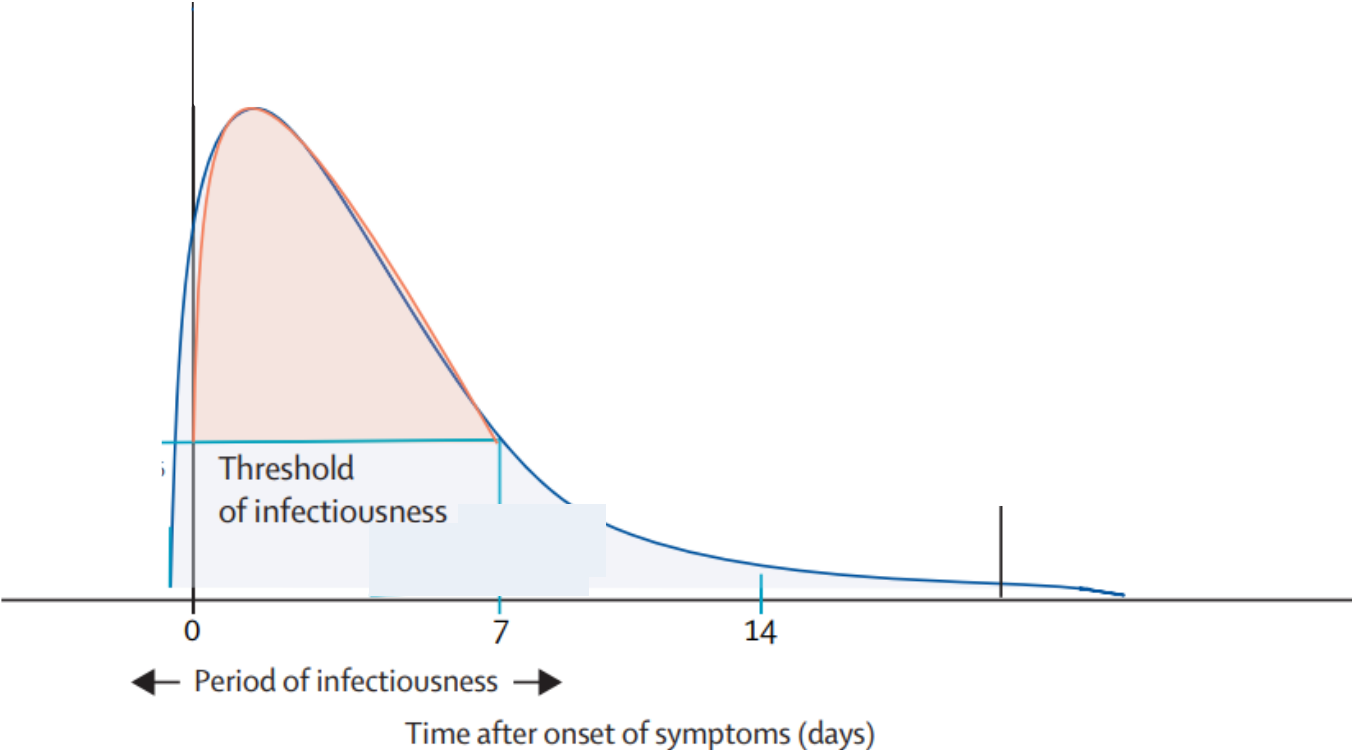
- sensitive detection of infection, even at low viral load in the nasopharyngeal cavity
- SARS-CoV-2 RNA concentration (Ct value) indicates viral load in the nasopharyngeal cavity
- Infectiousness (risk of transmission to contact persons) is assumed to be an RNA copy number corresponding to the Ct value of 25 (10^6 virus particles per ml respiratory sample)
- *>24 hours until results (laboratory infrastructure)*

Antigen Test

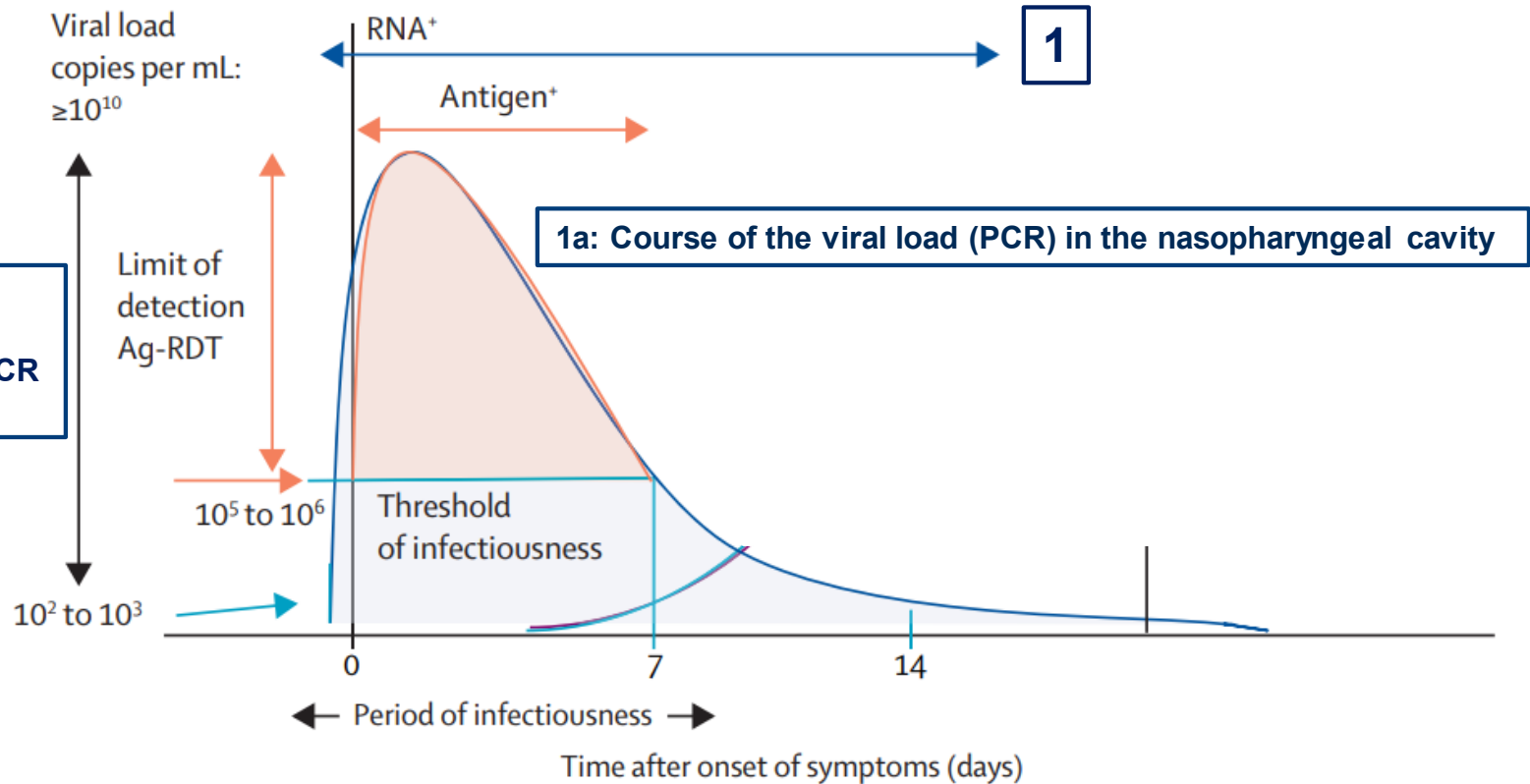
- Antigen test positive only at very high viral load in the nasopharyngeal cavity (Ct value ≤ 25)
- Result correlates with potential infectiousness of an infected person (risk of transmission to contact persons)
- *< 30 minutes until results ("rapid tests", also available as self-tests)*

Course of SARS-CoV-2 viral load in the nasopharyngeal cavity

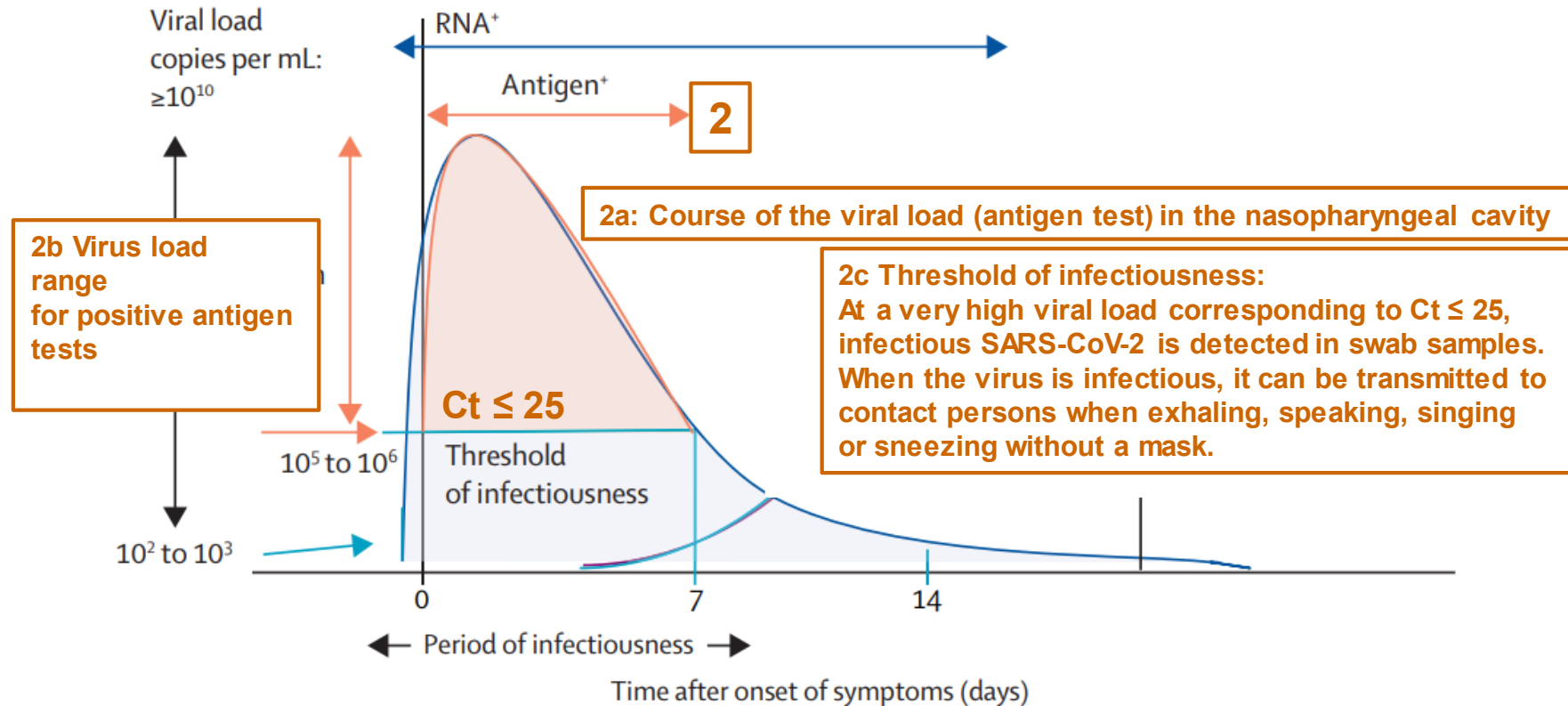
- Detection of infection with PCR or antigen test correlates with high viral load -



Virus load range for positive detection with PCR test- infection detection in each infection phase -



Virus load range for positive detection with antigen test- detection of the transmission risk in the presence of very high virus load -



Low Ct value = high viral load

Source: Peeling et al (2022). The Lancet 399, 757-768



Antigen test detects infectious persons with a very high viral load corresponding to $Ct \leq 25$



- Antigen test should be positive if there is a risk of transmissibility of SARS-CoV-2 to contact persons of the tested infected person
 - This risk exists with a very high viral load of $Ct \leq 25$ in swab samples from the nasopharyngeal cavity
 - Isolation of reproducible SARS-CoV-2 in cell culture succeeds at a very high viral load of $Ct = 25$ and lower
- Clinical swab samples with viral load up to 25 may contain infectious SARS-CoV-2

	CT <25 (n=18)	CT 25-30 (n=23)	CT >30 (n=9)
Infectivity in Cell culture	likely (9/18)	unlikely (low reproducibility)	no

Current regulation of SARS-CoV-2 diagnostics- Marketing after certification -



IVD Directive and Medical Devices Act

IVD market entry in the EU takes place after self-certification of the test by the manufacturer (CE mark)

- no independent review foreseen
 - Exception: Notified Body involved in self-test certification

A CE marking means that the manufacturer has declared that the product has been tested in conformity with the applicable EU directives and all legal requirements have been met.



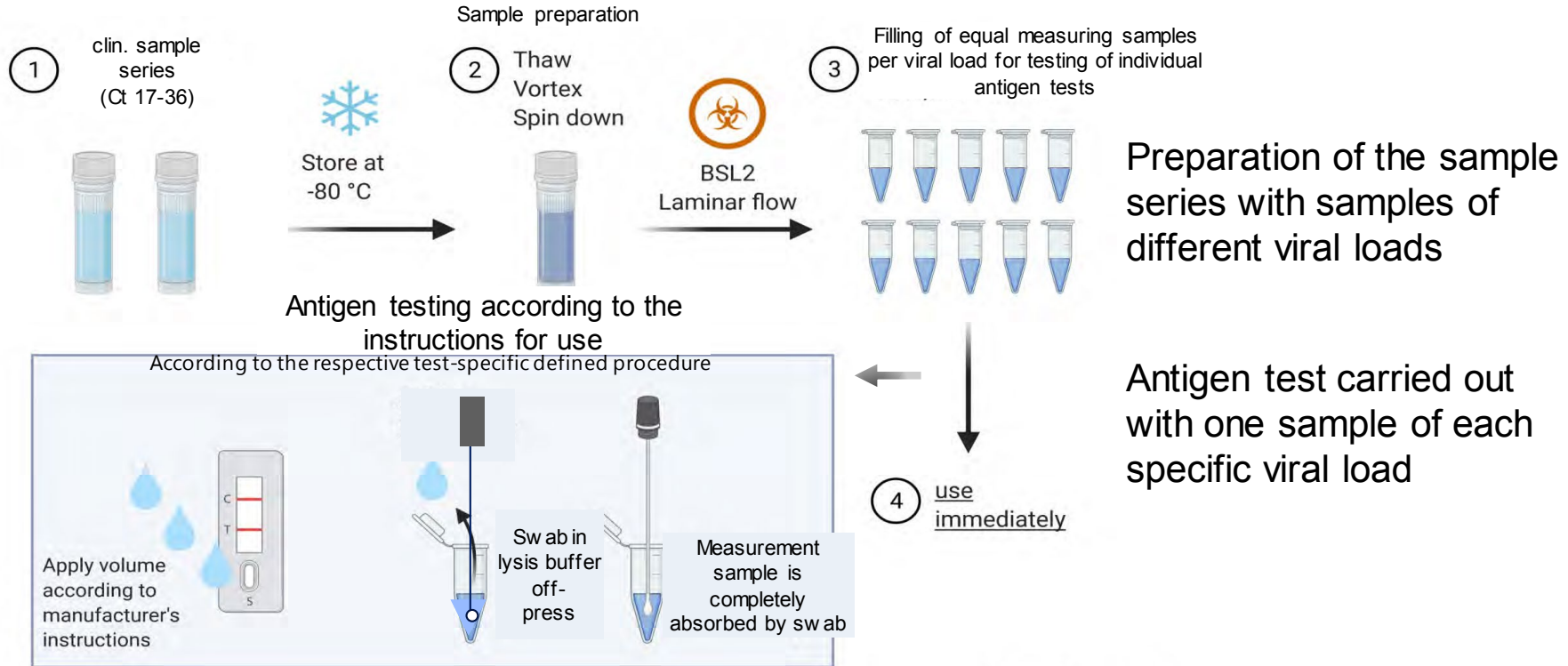
Reimbursement of antigen tests for professional use is subject to minimum criteria in Germany



Coronavirus Testing Ordinance (TestV), section 1.1

- **Reimbursement** of rapid antigen tests in Germany by the federal government, e.g. for test centres, takes place if minimum criteria are met (list on BfArM website)
 - Sensitivity: > 80% of unselected PCR-positive samples from SARS-CoV-2-infected patients within 7 days of onset of symptoms are detected
 - Specificity: > 97% of SARS-CoV-2 negative samples are not detected
 - Cross-reactivity: other samples containing inter alia human CoV types are investigated
- Proof of **compliance with the minimum criteria**
 - Manufacturer confirms fulfilment of minimum criteria
- If necessary, independent evaluation by Paul-Ehrlich-Institut/RKI
- If antigen test is tested in comparative Paul-Ehrlich-Institut/RKI evaluation
 - Pass: Antigen test remains on the BfArM list and on the Paul-Ehrlich-Institut positive list
 - Failure: Antigen test is removed from BfArM list and added to PEI negative list
 - Evaluated tests on the BfArM list are marked with "PEI evaluation: yes"

Procedure of the comparative experimental PEI/RKI evaluation- experimental procedure -



Comparative evaluation of the sensitivity of antigen tests by Paul-Ehrlich-Institute and RKI before the appearance of Omicron



Comparative Sensitivity Evaluation

- 245 tests evaluated (March 2022)
 - 199 passed (reimbursable; on BfArM list)
 - 46 failed (non-reimbursable, removed from BfArM list)

Individual results on the website of the Paul-Ehrlich-Institut

- Basis also for European Commission list
"Common List of COVID-19 rapid antigen tests (RAT)"
 - In the EU: for cross-border mutual recognition of test results
 - Listing only after prior independent review of the tests