To: 5.1.2e [5.1.2e @rivm.nl]; 5.1.2e [5.1.2e @rivm.nl]; 5.1.2e [5.1.2e @rivm.nl]
From: 5.1.2e
Sent: Mon 11/29/2021 5:11:29 PM
Subject: RE: antigen tests - self and professional use
Received: Mon 11/29/2021 5:11:30 PM

Er staat op 5.1.2h wel literatuur maar niet hierover

5.1.2e

From: 5.1.2e < 5.1.2e @rivm.nl>
Sent: maandag 29 november 2021 18:05
To: 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e < 5.1.2e @rivm.nl>
Subject: RE: antigen tests - self and professional use

Hi collegae,

Wellicht is er in contact met de Bibliotheek (5.1.2e) iets mogelijk.
Ik vraag me af of zij ook, via een online search, op MedRxiv etc. kunnen zoeken.
Ik krijg inmiddels meermaals Bibliotheek-searches van online berichten binnen op geselecteerde thema's.
Vaak zijn dat nieuwsberichten maar de vraag kan even bij 5.1.2e gesteld worden.

Groet!

5.1.2e

From: 5.1.2e < 5.1.2e @rivm.nl>
Sent: maandag 29 november 2021 18:01
To: 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e < 5.1.2e @rivm.nl>
Cc: 5.1.2e < 5.1.2e @rivm.nl>
Subject: RE: antigen tests - self and professional use

Hoi, 5.1.2e

Ik heb nog geen specifieke vraag die doorzocht moet worden, misschien @ 5.1.2e verwachten we een verzoek voor een zelftestendocument vanuit de OMT of VWS?

Maar als iemand tijd heeft om de nieuwe publicaties (kort termijn - laatste week of zo) over de opsporing van varianten in het algemeen: door antigeentesten en PCR (voor omicron) in de gaten te houden, zal dat heel fijn zijn *

Ik ben ook dit week bezig de ECDC corona-EQA rapport en kan niet veel de laatste literatuur lezen.

Groeten,
5.1.2e

From: 5.1.2e < 5.1.2e @rivm.nl>
Sent: 29 November 2021 17:43
To: 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e < 5.1.2e @rivm.nl>
Subject: RE: antigen tests - self and professional use

Dear 5.1.2e

Do you need help to search for more literature about RAT and variants?
I could ask one of the current aios if they can help?

5.1.2e

From: 5.1.2e < 5.1.2e @rivm.nl>
Sent: maandag 29 november 2021 16:15
To: 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e < 5.1.2e @rivm.nl>

Subject: RE: antigen tests - self and professional use

Hi, all,

Attached an update to the RATs comparison table. Thanks, 5.1.2e for sharing the delta performance manuscript. I included the tests from it in the table, if the professional use versions are also on the EU common list. A few comments on the test that I didn't include:

- Mologic Ltd - COVIOS Ag COVID-19 Antigen Rapid Diagnostic Test - professional test currently under review for inclusion in the EU common list (confidential: favorable data from clinical validation study in DE, pending formal confirmation by DE and acceptance for inclusion in the list) → **test to keep an eye on, will soon be on the EU common list**
- Nal von minden GmbH NADAL COVID -19 Ag Test - professional test on the EU common list, no self-test version found? →**of interest if they come up with self-test**
- CTK Biotech, Inc OnSite COVID-19 Ag Rapid Test - professional test on the EU common list, no selftest version found? → **of interest if they come up with self-test**

- Premier Medical - Sure Status COVID-19 Antigen Card Test - professional use only, NOT on the EU common list: reviewed and rejected 20 July 2021, no EU data presented for review, no PEI evaluation. WHO-EUL emergency use looks like it's used in Asia/India by Unicef
- Beijing Tigsun Diagnostics - Tigsun COVID-19 Saliva Antigen Rapid Test - **saliva** test, rejected by EU common list on 6 July 2021, passed PEI in-vitro evaluation in Germany →**be wary of it, rejected due to saliva setup, might try to pass the German PEI as universal EU approval**

And a few comments in purple below:

Groeten,
5.1.2e

From: 5.1.2e <5.1.2e@rivm.nl>
Sent: 29 November 2021 14:31
To: 5.1.2e <5.1.2e@rivm.nl>; 5.1.2e <5.1.2e@rivm.nl>; 5.1.2e <5.1.2e@rivm.nl>
Subject: RE: antigen tests - self and professional use

Hi 5.1.2e
Dank voor deze update- ik vroeg me alleen nog af hoe dit zich verhoud tot de testen die 5.1.2e hebben meegenomen in hun testen (zie email 5.1.2e zondag 11;54): *Er zijn 6 zelftesten uit aanbesteding gekomen en die zijn ook door onze ballotage heen gekomen. Roche en Abbott die we meegenomen hebben zijn proffesionele testen, niet zelftesten. Roche en Abbott hebben geen zelftesten aanbesteed of zijn niet door de aanbesteding ballotage gekomen. Dat weet ik niet.*

Roche and Abbot have both self-test version, not sure why they were not considered in this tender, maybe due to high price? All 6 tests that were tested are on the EU common list (see attached table for their details).

Het rapport is onderdeel van de aanbesteding en weet niet of ik dat dan vrijelijk mag delen.
Gebruiken van leftovers om met Omicron te testen zouden we even met DT/VWS moeten kortsluiten, zodat zij en wij dan niet in de problemen komen. Er zijn zeer strikte contractueel vastgelegde afspraken over wat met die testen in aanbesteding wel en niet gedaan mocht worden. Vooraf juridisch behoorlijk wat gesteggel over geweest.

Mbt je vragen 5.1.2e

1. the loss of sensitivity in self-use. Wasn't the latest estimate around 10%? In de Lindner study(ik heb alleen de preprint doi: https://doi.org/10.1101/2021.01.06.20249009); staat

The positive percent agreement between self-testing and professional testing on Ag-RDT was 91.4% (95% CI 77.6-97.0), and negative percent agreement 99.1% (95% CI 95.0- 100). At high viral load (>7.0 log_{10} SARS-CoV-2 RNA copies/ml), sensitivity was 96.6% (28/29; 95% CI 82.8-99.8) for both self- and professional testing.
NB: het betrof volwassenen met symptomen.

2. In the long-run, however, use of professional tests with clinical validation data is "safer" as they have better chances to remain longer on the list. The question is whether we take the same considerations for the corresponding self-tests? Clinical validation is per se closer as setup (real-life professional sampling) than the in-vitro conditions.

Difficult- I think the information is limited about the clinical validation- even information about symptoms or where and how the patients were selected often is missing.I have seen many of the clinical validation reports from the producers for the ontheffingen – and sometimes the information is very poor or even strange.
It is indeed difficult to judge with certainty. The latest EU common list criteria do ask for unselected participants and proper description of the study population. However, some of the tests approved in the early months of the list could have passed with less stringency on their clinical studies.

3. If using the professional tests as reference, what thresholds (respectively after correction) to set?

I thought you have criteria for the EU list: >90-% for Ct<25 etc.?
That's in follow up to 1, would we be happy with 90%-(4 or 5%?) = 85%, for example?

4. Do you know of other self-tests that might of the interest now?

No I have no idea but maybe there is information which tests are used in Germany or Belgium (as we are lacking that information for the Netherlands)?

I hope 5.1.2e has new information – hope to hear more tomorrow at 14:00

I really miss the information about what is ongoing in the covid department 5.1.2e was going to organize something- but I have not heard yet.

5.1.2e

From: 5.1.2e <5.1.2e@rivm.nl>
Sent: vrijdag 26 november 2021 13:53
To: 5.1.2e <5.1.2e@rivm.nl>; 5.1.2e <5.1.2e@rivm.nl>; 5.1.2e <5.1.2e@rivm.nl>
Subject: antigen tests - self and professional use

Hi all,

I'm writing in English to avoid mistakes in those slightly convoluted explications. Attached is an Excel spreadsheet I made for our reference to get an idea of the antigen tests with ontheffing.

A few general comments first:

- There is no common list of antigen self-tests in the EU. Thus it is practically a free market open to whichever producer obtains a CE-marking (based on their own submitted data).
- The Dutch Ontheffingen antigeentesten | Publicatie | Rijksoverheid.nl expire end of this year for self-tests that were temporarily allowed in the NL without CE-mark.
- There is, however, an EU common list for the antigen tests for professional use, updated by the Technical working group on COVID-19 diagnostic tests | Public Health (europa.eu) that 5.1.2e and I take part in. Some of the exclusion criteria for this list are self-tests in general, no CE-mark, use of alternative samples like saliva.
- Regarding the tests for professional use on the EU common list, the current criteria still allow in-vitro validation, which is done mainly by the German PEI. However, it is expected that at a future moment it will no longer be accepted, thus tests that only have it and no prospective clinical field evaluation, could be removed from the list. I marked them in orange in the spreadsheet (also orange in the EU common list study listing).
- Also regarding the tests for professional use on the EU common list, a few tests in the early months of the list were registered based on "proper" samples (nasal, NP, OP), but it was known they also market themselves for other samples like saliva. In the current version they are marked with red/yellow (see specimen column), while JRC contacted the manufacturers to remove those alternative sampling methods from the IFUs and overall documentation. If they refuse to comply, they might be considered for removal from the list in the future too. The current advice to MS is to always check the recommended sample of the antigen tests and

beware that alternative samples were not reviewed/approved by the EU common list committee.
•

Coming now to the attached spreadsheet:
- I included tests that either had in the past or currently have an ontheffing (see column Selftest_ontheffing) . I also included a few tests that were recently of interest to Dienst Testen (see column Selftest_notes)
- Interestingly, all of the self-tests on the list display the CE mark on their packaging (googling their IFU and box images on European websites). I could easily locate the actual CE mark number of the granting notified body for just 2 tests. We could (with some degree of uncertainty) all the other have a real CE-marking too.
- I tried to trace corresponding antigen tests for professional use (by checking the IFU's text on the manufacturer). Quite often from my experience reviewing the antigen tests for professional use, the manufacturers leave the IFU vague, or even straightforward mention in the documentation that the same test cassette is used for the self-test version. Thus again with some degree of uncertainty we can assume the self-tests in question roughly correspond to the tests for professional use.
- I copied the current information (EU common list update: 10 November 2021) on the antigen test for professional use. And took out some interesting information like the lowest and highest sensitivity, and lowest specificity in clinical/in-vitro validations. Where the information comes only from in-vitro studies the colour is orange, and green if a clinical fields study was performed.
- Two of the self-tests currently on the ontheffings list have a corresponding professional use test that uses saliva sampling, both flagged in the EU common list. When googling the self-tests they marketed their saliva versions as "RIVM-approved"…

Finally on the discussion what is a "good" antigen self-test and how to score them without validating them all:
- In my opinion, we can, with certain caveats, assume that most self-tests correspond/are practically the same tests casettes as the tests for professional use. The only way to check this is to ask for declarations of conformity or something similar from the manufacturers.
- If using the EU common list as data source for self-tests, we need a certain correction factor for the loss of sensitivity in self-use. Wasn't the latest estimate around 10%?
- In my opinion, in the short-term use of only in-vitro validated professional tests is "safe". It will be a few months until the criteria are updated and a grace period for the manufacturers passes. In the long-run, however, use of professional tests with clinical validation data is "safer" as they have better chances to remain longer on the list. The question is whether we take the same considerations for the corresponding self-tests? Clinical validation is per se closer as setup (real-life professional sampling) than the in-vitro conditions.
- We need to be wary of the professional tests with alternative sampling like saliva. They might be removed from the list sooner. Besides they seems to be more prone to shady practices like marketing their saliva kits as "approved", even though they only passed in-vitro evaluation and were added to the list for standard samples use. I would say same caution should apply to the self-test versions.
- If using the professional tests as reference, what thresholds (respectively after correction) to set? See the columns Prof_test_lowest_sensitivity, Prof_test_highest_sensitivity, Prof_test_lowest_specificity for an idea of the current range. Highest specificity is almost always 100%, so I didn't add it as column.

Do you know of other self-tests that might of the interest now? Let me know, so I check if they have professional counterparts on the EU common list.

What do you think?
5.1.2e: We need to be very careful with any recommendations on the self-tests, as all is basically all extrapolated information and assumptions. At the same time, we can't advise to validate everything on the vast EU marker either…

Commentaar in het Nederlands welkom, het was gewoon sneller om het in het Engels uit te leggen *

Groeten,
5.1.2e