Version 24 september 2020

Checklist 1.
Laboratory preparedness and response

EVD-LabNet

ENIVD, 2014. 5.1.2e, 5.1.2e
5.1.2e

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Checklist laboratory preparedness and response.

A. Patients.

Sampling and test interpretation.

1) What are the infection dynamics of the pathogen of interest? (e.g. kinetics immune response, kinetics of pathogen shedding; duration viremia; incubation period) Course of clinical manifestations. Presence of asymptomatic infections? Is there a panel of tests that can be done in case of "pathogen of interest" is negative and where?
2) What pathogens have to be considered for differential diagnosis (dependent on geographic situation)?
3) What is the role of each of the diagnostic tests in the case definitions (probable vs confirmed).
4) Which specimens need to be collected and how? (dependent on choice of diagnostic test, see 7-14)?

4.1 Type of specimens:

- ☐ whole blood
- ☐ serum/plasma
- ☐ blood cells
- ☐ CSF
- ☐ sputum
- ☐ bronchial lavage
- ☐ swab (e.g. nasopharyngeal, nasal, oral, rectal, conjuctival, uterus, other).
- ☐ skin biopsy
- ☐ necropsy
- ☐ saliva
- ☐ urine
- ☐ feces
- ☐ other

4.2 What is the minimum quantity required for each specimen? ((milli)grams or milliliter)?

4.3 Quantity of aliquots are needed?

4.4 Tools and containers for sampling? (e.g. cotton swabs, EDTA tubes etc.)

4.5 Storage and transport of specimens.

Required temperatures transport

- ☐ -78 °C (dry ice)
- ☐ - 20°C - 4°C (frozen sample with ice packs)
- ☐ Ambient temperature .

Required packaging

- ☐ Category A (UN2900,animals; UN2814, humans)
- ☐ Category B (UN3373)
- ☐ Exemptions

☐ Permits required?
(e.g. import animal products from outside EU).

Storage temperature
☐ -78 °C
☐ -20 °C
☐ 4 °C
☐ ambient tempretaure

5) Biosafety category
REAL5.1 Risk group classification: risk group (2, 3, 4)
5.2 Containment requirements: Containment level facilities (BSL) and operational practices for work involving infectious or potentially infectious material.
5.3 Protective clothing
☐ gloves (single/double)
☐ gown
☐ goggles
☐ FFP2 masks
☐ FFP3 masks

6) What is the minimum patient data set required for interpretation/ what data need to be filled in on diagnostic request form?

Diagnostic methods.
(in case of zoonoses, address both veterinary and human diagnostics).

7) Which tests are available for diagnosis in humans/animals with clinical illness?

Viral genome detection:
☐ PCR ☐ real-time ☐ conventional
☐ single ☐ multiplex
☐ in-house ☐ commercial

☐ NGS
☐ hybridization

☐ rapid test ☐ in-house ☐ commercial

Virus/antigen detection:
☐ capture ELISA ☐ in-house ☐ commercial
☐ immunoblot
☐ EM
☐ virus isolation (tissue culture/suckling mice)
☐ immuno histochemistry

☐ rapid test ☐ in-house ☐ commercial

Antibody detection:

☐ IgM ☐ IgG ☐ both

☐ ELISA ☐ in-house ☐ commercial
☐ IFA ☐ in-house ☐ commercial
☐ virus neutralization
☐ immunoblot
☐ hemaglutination inhibition

☐ rapid test ☐ in-house ☐ commercial

For each type of test:

8) Confirmatory testing by a single test or confirmation by additional testing necessary?
9) Where are the diagnostic tests available (national/international)? Check for both primary testing and secondary/confirmative testing.
10) Assess the quality of the available diagnostic tests:
    - ☐ Sensitivity (detection limit) ? ☐ manufacturer ☐ field (11)
    - ☐ Specificity? ☐ manufacturer ☐ field
    - ☐ Positive predictive value? ☐ manufacturer ☐ field
    - ☐ Negative predictive value? ☐ manufacturer ☐ field
    - ☐ Performance in external quality panels? ☐ manufacturer ☐ field
11) Are the available diagnostic methods standardized?
12) Do publications on these tests and their performance exist?
13) Are commercial tests CE marked/registered?
14) Shelf life of the tests? Order limitations?
15) Are there any specific issues regarding implementation or interpretation? (e.g. need for special expertise and equipment). What kind of issues need to be introduced to personel? What education is required?

Local implementation

16) Decide which test(s) to use for diagnostics.
17) How reliable are results with this test and is additional confirmatory testing required?
18) Decide where testing is done (both primary and confirmatory testing).
19) Discuss role of diagnostic testing in outbreak control: identification of each infected individual? Identification of sufficient cases for (non)human reservoir identification? Identification of sufficient cases to measure effect control measures?

Laboratory capacity.

20) What is the current capacity (number of samples processed every day) of the diagnostic tests? (own laboratory, nation-wide, European level). Sufficient or up scaling necessary?
21) What level of (de) centralization of testing is necessary?
22) What is the required turn-around time? What is the realistic turn-around time? Is 24/ 7 testing necessary?
23) What is the delay to provide first line results vs confirmed results?
24) What are the logistic problems that need to be addressed to maintain/raise capacity (availability qualified personnel, reagents, sampling materials, timely communication of test results etc.).
25) Is laboratory reponse for own laboratory necessary? If yes, which aspects need to be addressed by own laboratory?

In case development, implementation new diagnostic tests:

- Who decides the need for a laboratory response effort? Who is responsible for the laboratory response? Who is back-up? Who decides whether a tests needs to be run and at what speed? What are the criteria to do it "on call"?
- How is the first contact with the laboratory done with first suspected cases (who? timing, before shipment of samples)? What questions (anamneses) are to be asked at that point?
- Who communicates with other response groups at institute/national/international level?
- What materials are required to set up diagnostics? Are they available (e.g. through EVA: what is the capacity of EVA and dispersal time EVA?)? How to get these materials? Who is actually going to set-up the methodology in the laboratory?
- Who is going to perform diagnostics once implemented? (take into account expertise, availability for 24/7 testing, licensed in quality system/biosafety level training).
- Who is responsible for logistics ? (orders, provision of sampling materials in the field, registration in laboratory databases, shipments, work protocols)
- What is the required biosafety level? Are there any matters that need to be addressed based on the biosafety level? What PPE is necessary? Have laboratory acquired infections been described? Any special hazards? What medical precautions need to be taken? (immunization, prophylaxis, surveillance for symptoms, treatment). What happens to the samples of the suspect patient in other diagnostic testing (ciinical chemistry, other clinical microbiology tests)?
- Who has the final responsibility for the diagnostic results? (approval of test results)
- What is the tipping point to upscale capacity? (Capacity needs to be increased before maximum of current capacity has been reached).
- What are the costs? Who pays for the costs?
- Is there a need to reprioritize ongoing work? Who needs to be informed in case of reprioritization?

Pathogen typing/molecular epidemiology

26) Is pathogen typing possible ?
27) What is the added value of typing in the current situation (outbreak response)? (relevant ? aim?)
28) Where is pathogen typing available (national, international ?) and by what methods?
29) If typing is not available: how long will it take to develop basal typing?
30) What is the quality of the typing methods? (f.i. resolution,ability to identify clusters)
31) What clinical samples are suitable for typing? (not only matrix but also timing of sampling with respect to first day of illness). See 4-6.
32) Are available typing tools standardized? Are typing results from different laboratories comparable?
33) What is known from literature about the typing methods?
34) What is known about background? reference data?
35) Are there any specific points that need to be addressed with respect to performance, implementation, interpretation? (f.i. location central database with results).
36) Decide which test to use for typing.
37) How reliable are results with this test and is additional confirmatory testing required?
38) Decide where testing is done, both primary and confirmatory testing.
39) Decide where database for data collection and analysis is housed.
40) Discuss role of typing in outbreak control. Typing of pathogen in each infected individual? Typing of sufficient cases for (non)human reservoir identification?

Laboratory capacity for typing.

41) What is the current capacity of the typing method? (own laboratory, nation-wide, European level). Sufficient or up scaling necessary?
42) What are the logistic problems that need to be addressed to maintain/raise capacity (availability qualified personnel, reagents, sampling materials, timely communication of test results etc.).
43) Is typing necessary for own laboratory? If yes, which aspects need to be addressed by own laboratory?

In case development, implementation typing:

- Who is responsible for the typing response? Who is back-up?
- Who communicates with other response groups at institute/national/international level?
- What materials are required to set up typing? Are they available? How to get these materials? Who is actually going to set-up the methodology in the laboratory?

- Who is going to perform typing once implemented? (take into account expertise, availability for 24/7 testing if necessary, licensed in quality system/biosafety level training).
- Who is responsible for logistics ? (orders, provision of sampling materials in the field, registration in laboratory databases, shipments, work protocols)
- What is the required biosafety level? Are there any matters that need to be addressed based on the biosafety level? What PPE is necessary? Have laboratory acquired infections been described? Any special hazards? What medical precautions need to be taken? (immunization, prophylaxis, surveillance for symptoms, treatment).
- Who has the final responsibility for the typing results? (approval of typing results)
- What is the tipping point to upscale capacity? (Capacity needs to be increased before maximum of current capacity has been reached).
- What are the costs? Who pays for the costs?
- Is there a need to reprioritize ongoing work? Who needs to be informed in case of reprioritization?

B. Exposed
C. Asymptomatic carriers.

Diagnostic methods.

44) What diagnostic tests are available to exclude infection in contact cases? Are these tests different from tests used to confirm infection in symptomatic cases? Have these test been validated for this purpose?
45) What diagnostic tests are available to identify carriers and to determine the end of carrierstate in symptomatic and asymptomatic cases? Are these tests different from tests used to confirm infection in symptomatic cases? Consider the same for testing of blood donations.

For each type of test:
46) Confirmatory testing by a single test or confirmation by additional testing necessary?
47) Where are the diagnostic tests available (national/international)? Check for both primary testing and secondary/confirmative testing.
48) Assess the quality of the available diagnostic tests:
    - 4a) Sensitivity (detection limit) ?
    - 4b) Specificity?
    - 4c) Positive predictive value?
    - 4d) Negative predictive value?
    - 4e) Performance in external quality panels?
49) Are the available diagnostic methods standardized?
50) Do publications on these tests and their performance exist?

51) Are there any specific issues regarding implementation or interpretation? (f.i. need for special expertise and equipment).

Sampling and test interpretation.

52) How important is the identification of exposed individuals and asymptomatic carriers for outbreak control. Do they play a role in transmission? What is known?
53) What are the infection dynamics of the pathogen of interest? ? (e.g. kinetics immune response, kinetics of pathogen shedding; duration viremia; incubation period) Course of clinical manifestations. Presence asymptomatic infections.
    i. What is the differential diagnosis? What are the available diagnostic tests for these pathogens with similar clinical manifestations?
54) What is the role of each of the diagnostic tests in the case definitions (probable vs confirmed).
55) Which materials need to be sampled? What is the minimum quantity for each sample type? What is needed for sampling? (kind of materials, transport temperatures/packaging).
56) What personal protection is required for sampling and laboratory analysis?

57) Decide, based on the above, which test to use for diagnostics
58) How reliable are results with this test and is additional confirmatory testing required?
59) Decide where testing is performed (both primary and confirmatory testing).
60) Discuss role of diagnostic testing in outbreak control: identification of each infected individual? Identification of sufficient cases for (non) human reservoir identification? Identification of sufficient cases to assess effect of control measures?
61) Discuss what other samples besides human diagnostics need to be collected: environmental, veterinary, wildlife, entomological, food chain etc. These type of sampling often needs to be considered asap, not to be postponed by bureaucratic information reporting lines.

Laboratory capacity.
See laboratory capacity A.

Communication (addressed at national level)

- Who is the contact person in case of suspicion of case?
- Who are involved in the investigation? Who are responsible contacts/focal points? What are their contact details?
- Have superiors been informed?
- Who needs to be notified? Identify the stakeholders, e.g. public health domain, veterinary health domain, food chain domain, entomology etc.)

☐ National level
☐ International level

- Who releases information? What is the role of the laboratory?

References.
http://apps.who.int/iris/bitstream/10665/78075/1/WHO_HSE_GCR_2012.12_eng.pdf