Development of diagnostics and validated reference materials

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A scientific framework for epidemic and pandemic research preparedness
Vaccine research response to Pathogen X

Third consultation - January 19, 2024
1 pm – 5:30 pm Central European Time (CET)
DRAFT Agenda
SARS-CoV-2

- First genome release: Jan 11, 2020
- WHO technical guidance on diagnostic RT-PCR published on January 15, 2020
What priority research should be triggered immediately after the declaration of the pandemic?

• Diagnostics (direct detection) = Cornerstone of response activity → only reliable identification allows for assessment of the situation, public health measures, prevention of (nosocomial) spread, knowledge on state of the epidemic, understanding transmission etc.

• As immediate response: Less **research**, more **implementation** challenges

• Rapid diagnostic development such as (RT-)PCR is possible & diagnostics were quickly available in recent outbreaks

• It is implementation & building up diagnostic capacity brings challenges
Early implementation - challenges

• Sharing of diagnostic materials: Positive controls and reference materials are key (inactivated RNA/DNA, plasmids, *in vitro* transcribed RNA)

• Role of cultured pathogens? Sharing of isolates in an emergency: many challenges: global repositories as one solution (EVA, WHO Biohub)

• Obstacles for sharing reference materials: Production in sufficient quantity & quality, shipping, regulatory aspects (e.g. Nagoya protocol), biosafety regulations, organization/workload (especially for academic partners), speed!

• In house vs. commercial assays: Technical expertise, implementation, quality control, also: reimbursement (private laboratories), time delay until commercial assays are available
Research priorities: Diagnostic assays

• Which use case for type of assay: individual patient diagnosis vs. public health tool, laboratory-based vs. POCT vs. community

• Independent validations and public availability of such data (e.g. FIND, WHO, national public health agencies)

• Viruses: Diagnostic tests for infectious virus are lacking → VL as surrogate

• Align research on diagnostics with other areas: Clinical course of disease, surveillance, public health decision making (at a later stage also: vaccine break-through, therapy monitoring)

• Serological assays for epidemiology: validation, reference sera, quantitative vs. qualitative

• Continuous monitoring as pathogen evolves (commercial assays: targets often not known)

• Environmental impact
(Diagnostic) Assays for vaccine research

- Development of assays to measure antibody and cellular responses
- Binding vs. neutralizing antibodies, challenges: biological assays, hereogenicity between laboratories, development of surrogate assays (cell-free assays), partly overlap with diagnostic assays & surveillance
- Alignment with assays used in animal models
- T cell assays: more restricted to specialized laboratories
- Reference materials: Standardized sera, peptide pools, antigens
- Well-characterized human specimens from cohorts with defined immunity background
- Correlates of protection
Creating synergies between diagnostics, surveillance and research

Outpatient testing centre of the hospital & emergency room
- Collection of clinical data (incl. vaccination status)
  - > 125,000 consultations

Diagnostic validation:
- Clinical studies on Ag-RDTs molecular POCT

Convalescent period (+ informed consent)
- Convalescent biobank
  - Post-vaccine sera/plasma
  - Hybrid immunity sera

Routine diagnostic testing
- Full genome sequencing
  (National genomic surveillance, led by our reference lab in Geneva)

Data analysis
- > 387,000 RT-PCRs
- > 65,000 positive specimens

Clinical specimens biobank
- > 15,000 sequences to GISAID

Virus isolate biobank
- B.1, B.1.610, B.1.258 (pre-VOC)
- Alpha
- Beta
- Gamma
- Zeta
- Delta, incl. Delta AY.4.2, Delta E484Q
- Mu
- Lambda
- XE
- Omicron (e.g. BA.1, BA.2, BA.5, BA.2.75, BQ.1, BA.4.6, XBB, XBB.1.5, BA.2.86, JN.1...)

Validation & development of serological assays
- SARS-CoV-2 +
  - VOC/VOI

Swiss FOPH
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Diagnostic validation for emerging viruses

- 2020: Independent validation of 22 molecular SARS-CoV-2 assays
- Clinical validation of 15 different antigen-based rapid diagnostic tests (> 4500 participants enrolled), including clinical & epidemiological data
- All reports continuously published www.finddx.org, shared with WHO & national/international stakeholders
- Analytical studies using live virus isolates to study impact of variants

- Continuous validation of Ag-RDTs for latest SARS-CoV-2 variants (EG.5 and JN.1)
- Ongoing: Analytical validation of molecular diagnostics and Ag-RDTs for monkeypox virus

Thank you!