Call for partners
Sample sharing for a FIND initiative to conduct standardized evaluation of typhoid and scrub typhus diagnostics

BACKGROUND

General

Typhoid fever is one of the most common bacterial causes of acute febrile illness in the developing world, with an estimated 10.9 million new cases and 116,800 deaths in 2017. The disease is most common in South Asia and sub-Saharan Africa, with one third of cases occurring in young children. There are various aspects of *S. Typhi* biology that makes diagnosis by standard laboratory methods challenging. A Cochrane review of the accuracy of the commercially available antibody-based rapid diagnostic tests showed moderate sensitivity and specificity for commonly used assays such as the TUBEX colorimetric test, the Typhidot immunodot assay and the Test-it Typhoid immunochromatographic lateral flow assay. Our understanding of the performance of currently available immunoassays is hindered by the lack of a gold standard reference and the absence of systematic studies that simultaneously evaluate performance of multiple assays in samples obtained from patients in various regions.

Scrub typhus is a reemerging acute febrile disease that affects predominantly the Asia-Pacific region. Without a specific antibiotic treatment (doxycycline), the fatality rate is as high as 50%. It is estimated that 1 million persons are infected every year and the World Health Organization considers scrub typhus as an underdiagnosed disease. This may be explained by the lack of affordable, easy to use and rapid tests in endemic countries. The current gold standard for the disease diagnosis is the indirect immunofluorescence assay (IFA). This test is expensive, requires experienced staff and appropriate facilities. Although the test shows a high sensitivity and specificity, results are usually obtained several days after patient admission and therefore using IFA cannot ensure rapid and appropriate patient management and care. Alternatives include ELISA assays which are less expensive and easier to perform than IFAs, but also less accurate. Point-of-care tests with high performance would be a solution to improve scrub typhus diagnosis and patient care. However, development of new scrub typhus tests and evaluation of their performance depend on access to specimens (serum, plasma, blood) from diverse endemic regions to improve reagent selection and assay optimization.

In conclusion, for both typhoid and typhus there is a distinct need for well-characterized specimens (evaluation panels) to enable a **standardized evaluation** of currently available and emerging immunologic diagnostic tests as well as specimens that could be used in product development efforts to accelerate the development of improved tools.

OBJECTIVES AND REQUIREMENTS

Objectives of the call: To collect information on the availability of well-characterized typhoid and/or scrub typhus (and other causes of acute febrile illness) specimens for inclusion in an evaluation panel to be used to assess the performance of current and "in development" immunologic assays for typhoid or scrub typhus. In addition, a small number of samples will be stored in FIND's dedicated specimen bank with a governance structure to support diagnostic development for poverty related diseases under global access terms. FIND currently hosts a specimen repository for TB, malaria and general fever samples (characterized for host marker diagnostics) and the aim is to expand this biobank by adding small well-characterized panels

of specimens for these two neglected high burden diseases (https://www.finddx.org/specimen-bank/).

The vision is to provide comparative data for different assays and have small volumes to support very high priority developments.

Requirements: To leverage previous efforts, we would like to collect existing, retrospective specimens; however, if this is not a feasible approach, we are also keen to evaluate the interest of potential partners to prospectively collect typhoid, scrub typhus, or both specimens for the above purpose.

Sample requirements

- Adequate specimen volume per sample (at least 1.0 ml)
- Sample type: serum and plasma
- Stored frozen
- Demographic information about patient (age, sex, country)
- For typhoid specimens: blood culture results confirmed
- For scrub typhus: acute samples with presence of IgM detected by IFA, ELISA, PCR or another high-performing test
- Information about other assays performed on the specimen and results
- Samples collected following GCP, the Declaration of Helsinki, and local laws and regulations; informed consent provided.
- Permission to use the samples in future development or evaluation studies has been (or can retrospectively be) granted with consent forms available for review if needed

Partner requirements

- Ability and willingness to enter into agreement with FIND
- Ability and willingness to export samples to the central biobank/storage partner in the USA
- Willingness to share samples for diagnostic evaluation and inclusion in a biobank to support evaluation of current and future diagnostic assays for typhoid and scrub typhus

Specimens of special interest for inclusion in the biobank

We are especially interested in specimens from:

- Sub-Saharan Africa, South Asia, Southeast Asia, and/or South America
- Endemic and non-endemic regions for both typhoid and scrub typhus
- Both adults and children
- Patients with blood culture confirmed *S. Paratyphi* and non-typhoidal Salmonellosis
- Typhoid patients who have been tested with the TPTest (Typhoid/Paratyphoid Diagnostic Assay)
- Patients with evidence of infection with scrub typhus (acute specimens)
- Patients with evidence of infection with other causes of acute febrile illness such as murine typhus, dengue, brucellosis, malaria, and leptospirosis

RESPONSIBILITIES

FIND will be responsible for any shipment (or other) costs and the partner is responsible for provision of specimen and local permissions, with the support of FIND, if appropriate.

BENEFITS

Benefits of participating in this FIND initiative include:

- Early access to results from the evaluation of current and future immunoassays for the diagnosis of typhoid and scrub typhus
- Authorship on manuscripts presenting results from studies assessing the performance of currently used immunologic assays for typhoid and scrub typhus
- Authorship (as applicable) on manuscript(s) describing the development and utility of a reference panel, sharing framework and data analysis interface to accelerate the development and access of diagnostics

TIMELINES

Complete the questionnaire online (https://www.surveygizmo.com/s3/5217670/Call-for-partners-Sample-sharing-for-a-FIND-Initiative-to-conduct-standardized-evaluation-of-Typhoid-and-Scrub-Typhus-Diagnostics) and send submission before 11th October 2019

Priority activities include:

- Responses to the call by 11 October 2019
- MTAs signed with partners by 15 December 2019
- Initial panels available by early 2020
- Initial draft of the sample sharing framework available for feedback by mid-2020

FOR QUESTIONS, CONTACT:

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