Medicines & Healthcare products Regulatory Agency

NIBSC

National Institute for Biological Standards and Control
Blanche Lane, South Mimms, Hertfordshire EN6 3QG
United Kingdom

April 2022

Dear Colleague,

Establishment of WHO International Reference Reagents for anti-HLA Flow Cytometry Crossmatch and Luminex Ab assays collaborative study

I am writing on behalf of the World Health Organization and its collaborative centre NIBSC to formally request your assistance in the establishment of the International Reference Reagents for anti-HLA Flow Cytometry Crossmatch (FCXM) and Luminex Ab assays.

Preparation of pooled sensitised and non-sensitised human plasma or sera with varying levels of alloreactivity (low and high background negatives, weak positive and strong positive) have been filled into ampoules and freeze-dried. To evaluate these materials, we intend to carry out an international collaborative study with expert Histocompatibility and Immunogenicity laboratories. Participating laboratories will be asked to test coded preparations using FCXM and Luminex Ab assays used to evaluate patient samples. More detail study information is enclosed with this letter.

We intend to dispatch the samples in May 2022 and would like data to be returned as soon as possible but not later than September 2022. The data will then be analysed centrally at NIBSC, and a report will be prepared and circulated to all participants prior to submission to the Expert Committee on Biological Standardization (ECBS) of the WHO for establishment in October 2022 or April 2023.

I would like to formally invite you to participate in this collaborative study. If, you agree to participate, I would be grateful if you would complete the enclosed Shipping Information form and return them to me via e-mail. If you would like more information on the study, then please do not hesitate to contact me as well.

Your assistance with this important project is greatly appreciated.

Best wishes,

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Instructions for CS708 collaborative study participants

1. Receiving samples

Up to 8 freeze-dried coded preparations will be sent to study participants.

Upon receiving the freeze-dried material should be stored at -20°C. The instructions for use (IFU) will be sent to participants with the samples as a hard copy and electronically beforehand. They include safety specifications and the instructions for re-constituting the freeze-dried material. The IFU states that the samples should be used on the day of the reconstitution but short-term storage (up to a week) of the samples after re-constitution at -20°C has been shown not to affect the sample stability. Before using the material that has been re-constituted and then stored it is recommended to spin down any cryoprecipitates that can form in the samples.

2. Performing the bioassays

The collaborative study's aim is to evaluate the performance of the freeze-dried preparations as intra-assay controls and reference material. A number of H&I laboratories will be performing FCXM and anti-HLA Luminex assays. Any participant should specify before the shipment of the samples whether they'll be performing FCXM, Luminex or both assays. Participants are free to test the samples at any additional assays they routinely perform.

FCXM considerations

Please test the samples as you would be testing patient sera, alongside in-house controls. Ideally, and as possible, all received samples should be tested with 3 different donor cells (in 2-3 replicates). Participants can test the samples on more than the recommended 3 different sets of donor cells.

Luminex single antigen assay considerations

Please test the samples as you would be testing patient sera, alongside in-house controls. Ideally, and as possible, samples should be tested for class I and II antibodies using one or both Immucore and OneLambda kits (in accordance with the local SOP). If single antigen kits are not routinely used by the participants, the positive/negative screening kits can be used instead.

Filling in the collaborative study questionnaires

Four questionnaire forms (2 methodology forms and 2 results forms) will be sent to participants. They will include information that will allow appropriate data stratification when performing biostatistical analysis. Only the forms for the assays performed are to be return to NIBSC (not all the participants will be performing all the assays). The participants are asked to return filled in questionnaires as soon as they have finished evaluating the material but not later than September 2022.

3. What happens at the end of the study?

The results of the study (with coded participant details) will be communicated to the participants in the form of WHO report. The participants can be unblinded to the sample codes at the end of the study and their opinion will be requested on the suitability of the preparations as WHO Reference Reagents.
The participation in this study is voluntary and gives the testing laboratories ability to test the material that is developed in order to aid global biological standardisation of FCXM and anti-HLA Luminex assays.
If data collected as a part of this collaborative study is of publishable quality, it may be submitted into a per-review journal and presented at scientific and clinical meetings. All the data used for publications and scientific presentations will be coded and no identity of any participants will be revealed.

The aim of the study is to investigate whether the preparations are fit to be established as WHO Reference Reagents (subject of endorsement by WHO's ECBS) and released onto NIBSC catalogue from where International Reference Reagents can be ordered.