The standardization of diagnostic assays for parasitic diseases

Background: Serological and NAT based assays are applied in the diagnosis of parasitic diseases. However, the relative sensitivity, specificity and reproducibility of these assays is uncertain due to the lack of appropriate reference materials. The WHO Expert Committee for Biological Standardisation recognises the need to improve the quality of diagnoses for parasitic diseases and so have encouraged the development of primary reference materials or International Standards for specific diseases. At NIBSC, we have undertaken a programme of producing reference materials to support diagnosis of Malaria, Chagas Disease and Toxoplasmosis.

Material/methods: NIBSC prepared candidate reference materials for the serological diagnosis of Toxoplasma (IgG standard and IgG, IgM and IgA standard), Malaria (P.falciparum) antibody reference reagent and Chagas disease one for T. cruzi type 1 and the other for T. cruzi type 2. For NAT based diagnostic assays, we prepared candidate reference materials for P. falciparum and Toxoplasma gondii. Candidates for each standard underwent detailed evaluation and analysis in international collaborative studies involving at least 14 laboratories worldwide. Bio-statistical analysis of data generated was performed at NIBSC. The data were reviewed by the WHO ECBS prior to establishment.

Results: Freeze dried preparations of parasites performed equally with frozen preparations in NAT assays generating almost identical values in either end-point dilution or directly quantitative NAT assays. The use of the selected lyophilized preparation as a reference to establish the relative potency of other candidate preparations improved the comparability of estimates from participating laboratories in the case of Toxoplasma reference from 3.2 log_{10} to 1.8 log_{10} irrespective whether end-point dilution or quantitative assays were applied.

Conclusions: The establishment of International Standards for diagnostic assays of parasitic disease encourages the standardization of these assays. Improving the quality of this data enables effective comparison between clinical studies that assess different approaches to the clinical management of individuals at risk of or infected these agents. NIBSC is continuing this programme by beginning the development of 3 new International Standards in the area of parasitology over the next 3 years. These standards will be an International Standard for Plasmodium vivax NAT assays, an International Standard for T. cruzi NAT assays as well as a sub-type panel for T. cruzi and an International Standard Plasmodium falciparum HRP2 for development, validation and quality control of rapid diagnostic tests (RDTs) for malaria.