2266

Draft test protocol for the evaluation of commercial kits for AIDS-related virus antibody screening - (8th March 1985)

Introduction

The virus or closely related viruses HTLV 3, LAV and ARV (hereafter referrred to as HTLV 3) are the primary cause of AIDS. Infection with the virus is much more prevalent than AIDS itself, and HTLV 3 has infected many British homosexuals and haemophiliacs, some drug abusers and perhaps other individuals outside these recognized risk groups.

There is a growing demand from many sections of the Health Service for access to tests for antibody to HTLV 3 (anti HTLV 3). It is thought that most people infected with HTLV 3 develop anti HTLV 3 within two months. In most individuals studied anti HTLV 3 persists, though some patients who on clinical or epidemiological grounds are thought to have been infected lack anti HTLV 3. It is unclear whether this represents failure to make an antibody response, termination of the response, or inability of assays to detect low concentrations of antibody.

Concern has been expressed about the specificity and sensitivity of 'prototype' commercial assays for anti HTLV 3, and the DHSS wishes to evaluate kits that are to be sold in the United Kingdom in order to establish that they reach minimum standards of accuracy. This evaluation will be under the direction of an expert working group appointed by DHSS with the following terms of reference:-

BDX41

[redacted]

105

[redacted]

1) To receive and approve a test protocol for kit evaluation prepared by [redacted] of the Virus Reference Laboratory, CPHL Colindale.

2) To consider if necessary any revisions or developments of the protocol and advise on the production and use of a standardised form of reporting the results of evaluation tests.

3) To advise on

i) Selection of panels of suitable test sera.

ii) Criteria for acceptance of kits for listing by DHSS.

iii) The conduct of follow-up studies and co-ordination and verification tests assessment of longer term field trials.

iv) Interpretation of data supplies by manufacturers in support of performance claims.

The evaluation process will begin as follows:-

Manufacturers will be asked to notify the Supplies Division of DHSS Scientific and Technical Branch of their intention and ability to sell kits in UK. The division will ask them to co-operate in the evaluation in the terms set out below:-

i) DHSS will, for evaluation, purchase kits for 1020 tests from each manufacturer and lease ancillary equipment.

ii) Each manufacturer will be asked to provide an initial training programme to personnel at PHLS Virus Reference Laboratory (VRL) who have been appointed to do the evaluation work. The manufacturer must satisfy himself that the programme has been completed, after which VRL will be left to evaluate the kits purchased.

Panels of sera

Panels of aliquotted sera will be set up before the evaluation process starts by [redacted] and [redacted]. The panels will be coded a) to e) and their constituents not revealed to the workers carrying out the assays, not to the manufacturers, until the evaluation process is complete.

Sera for evaluation will be separated into 12 aliquots of >150 ul (requring >2 ml of each serum). The aliquots will be distributed in the wells of 4 x 5 well plastic trays. Each tray will be marked with its code and covered with a thick adhesive plastic cover. These trays will be stored in sandwich boxes and placed in a -30°C freezer dedicated to this purpose.

The sera used in the evaluation will be of two sorts a) those of previously unknown anti HTLV 3 status drawn from blood donors, from patients in high anti HTLV 3 risk groups and from patients with diseases in which non-specific reacton may be expected to arise; ii) those previously identified by testing at VRL as reactive for anti HTLV 3. Each set of aliquots will include classes a, b, c under (i) and d, e under (ii).

Class a) 200 blood donors aliquotted into 10 plastic trays.

b) 40 sera from patients with AIDS, ARC or attendining STD clinics and haemophilia centres and in the high risk groups (2 trays).

c) 10 rheumatoid factor positive and 10 heterophile antibody positive sera (1 tray)

d) 20 strongly and 20 weakly anti HTLV 3 positive sera (2 trays).

e) Double volume aliquots of dilutions of four strongly anti HTLV 3 positive sera (/100, /200, /400, /800, /1600) (1 tray) (assayed x 2). Total a) - e) 16 trays x 12 = 192 trays.

Total number of tests per evaluation	=	340
if in duplicate	=	680
if also following treatment at 56°C for 30 minutes	=	1020

When an evaluation is complete a report will be prepared for the expert working group. The report will consider the following aspects:-

i) The quality of the written instructions, training programme and 'back-up' provided by the company.

ii) The ease of use of the assay and its safty.

iii) The compatibility of the assay to the needs of diagnostic, blood transfusion and research laboratories.

iv) The reproducibility, specificity and sensitivity of the kit, based on interpretation of a standardized report of the results of the assays.

v) The feasibility of arrangements for verifying positive and borderline results in the assay.

The working group will then be convened and asked to decide whether or not the assay kit is acceptable for using by DHSS.

Appendix: equipment required for the evaluation.

Freezer -30°C - £2,500

Abbott type 20 well plates x 200 -

Plate covers x 1000

Plastic tips large x 5000

small x 10000

Finn pipettes (or similar) 2 x 5 - 5 ul
3 x 5 - 50 ul
2 x 50 - 200 ul
1 x 1000 ul
} £1,500

Waterbath capacity at least 10 trays - £500.

etc