REPORT

HANDS-ON TRAINING/WORKSHOP ON THE LABORATORY DIAGNOSIS OF MEASLES VIRUS INFECTION

Melbourne, Australia
24-27 May 2005

Manila, Philippines
October 2005
REPORT

HANDS-ON TRAINING/WORKSHOP ON THE LABORATORY DIAGNOSIS OF MEASLES VIRUS INFECTION

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NOTE

The views expressed in this report are those of the participants in the Hands-on Training/Workshop on the Laboratory Diagnosis of Measles Virus Infection and do not necessarily reflect the policies of the World Health Organization.

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Keywords:

Measles laboratory testing, IgM ELISA, Dried blood spots (DBS), Quality assurance (QA)

This report has been printed by the Regional Office for the Western Pacific of the World Health Organization for the participants in the Hands-on Training/Workshop on the Laboratory Diagnosis of Measles Virus Infection, Melbourne, Australia, from 24 to 27 May 2005.
SUMMARY

A workshop on laboratory diagnosis of measles virus infection was held at the Victorian Infectious Diseases Reference Laboratory (VIDRL), Melbourne, Australia from 24 to 27 May 2005. The workshop was attended by seven participants from national measles laboratories (NML) from Cambodia, Fiji, French Polynesia, Guam, New Caledonia, the Lao People's Democratic Republic and Papua New Guinea, and by an observer from Guam. In addition to support from the WHO secretariat, the workshop was conducted with support from three temporary advisers and five resource persons from VIDRL.

The objectives of the workshop were:

1. to introduce WHO standardized methods for laboratory diagnosis of measles infection;
2. to familiarize participants with practical procedures of measles immunoglobulin class M (IgM) enzyme immunoassay (EIA) and dried blood samples (DBS) as an alternative sampling technique;
3. to familiarize participants with laboratory quality assurance (LQA) inclusive of standard operating procedures (SOPs) and internal quality control (QC);
4. to introduce the participants to the WHO network laboratory accreditation scheme and its criteria to be met; and
5. to introduce laboratory data management and reporting to the Western Pacific Regional Office.

The workshop, which consisted of lectures and practical sessions, focused on the anti-measles IgM EIA, its procedures, interpretation of results and troubleshooting.

Overall, the participants were positive in their feedback and considered the workshop to have met its objectives and the schedule and administrative arrangements to be well organized.

The workshop participants were encouraged to remain in contact with each other and with the facilitators as a future resource for technical advice and support.
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<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>DBS</td>
<td>dried blood spots</td>
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<tr>
<td>EIA</td>
<td>enzyme immunoassay</td>
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<td>ELISA</td>
<td>enzyme-linked immunosorbent assay</td>
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<td>IgM</td>
<td>immunoglobulin class M</td>
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<tr>
<td>LQA</td>
<td>laboratory quality assurance</td>
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<td>PCR</td>
<td>polymerase chain reaction</td>
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<td>PIHOA</td>
<td>Pacific Island Health Officers Association</td>
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<td>QAP</td>
<td>quality assurance panel</td>
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<td>QC</td>
<td>quality control</td>
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<tr>
<td>SOPs</td>
<td>standard operating procedures</td>
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1. INTRODUCTION

The Western Pacific Region of the World Health Organization (WHO) has declared a goal of regional measles elimination with a target date of 2012, recommended by a Measles Task Force in July 2004 and a Technical Advisory Group meeting in June 2005. The Regional Committee for the Western Pacific will consider this target date at its fifty-sixth session in September 2005. The Pacific island countries and areas conduct active hospital-based surveillance for patients with acute fever and rash, in order to detect measles and rubella. WHO recommends that the clinical diagnosis of measles be confirmed by the detection of measles immunoglobulin class M (IgM) using an enzyme immunoassay (EIA). To increase familiarity of some laboratory staff in the Region to measles IgM EIA testing and the use of dried blood samples (DBS) as an alternative method of sampling, the WHO Western Pacific Regional Office held a workshop at the Victorian Infectious Diseases Reference Laboratory in Melbourne, Australia from 24 to 27 May 2005.

1.1 Objectives

(1) To introduce WHO standardized methods for laboratory diagnosis of measles infection.

(2) To familiarize participants with practical procedures of IgM EIA and DBS as an alternative sampling technique.

(3) To familiarize participants with laboratory quality assurance (LQA) inclusive of standard operating procedures (SOPs) and internal quality control (QC);

(4) To introduce the participants to the WHO network laboratory accreditation scheme and its criteria to be met.

(5) To introduce laboratory data management and reporting to the Western Pacific Regional Office.

1.2 Organization

The workshop included seven participants from national laboratories from two South-East Asian countries (Cambodia and the Lao People's Democratic Republic), four countries from the Pacific island network (Fiji, French Polynesia, Guam and New Caledonia), and Papua New Guinea. An observer from Guam (Pacific Island Health Officers Association [PIHOA] Regional Laboratory Coordinator) also participated in the workshop. In addition to support from the Secretariat, the workshop was conducted with assistance from three temporary advisers and five resource persons from the measles regional reference laboratory (including one resource person from the polio reference laboratory) at the Victorian Infectious Diseases Reference Laboratory, Melbourne (Annex 1).
2. PROCEEDINGS

2.1 Workshop programme

A timetable of the workshop is presented in Annex 2.

Dr Mike Catton, Medical Director of VIDRL, who welcomed the participants and introduced them to VIDRL staff, opened the workshop. An introductory speech from the WHO Regional Director for the Western Pacific Region, Dr Shigeru Omi, was read by Dr Kazunobu Kojima, the Regional Laboratory Coordinator, WHO Western Pacific Regional Office.

The workshop consisted of lectures and practical sessions. On each of the four days, the workshop focused on the anti-measles IgM EIA, its procedure, interpretation of results and troubleshooting. These were largely based on results from practical work.

A set of practical notes for the workshop, which included copies of all presentations made during the workshop, was distributed.

2.2 Practical sessions

The hands-on portion of the workshop was conducted in the serology laboratory at VIDRL and included three components. Participants worked in pairs for the first two components of the workshop and independently for the third session.

The first component was a theoretical and practical introduction to the EIA technique, specifically using the Dade Behring Enzygnost Anti-Measles Virus/IgM assay. All participants successfully completed the introductory assay, which consisted of the kit positive and negative controls, an in-house positive control and positive and negative measles IgM samples, tested in duplicate. All results passed validation criteria and were within acceptable ranges, as specified by the manufacturer.

The second component involved groups of two people processing four different DBS that had been collected and stored at -20°C as part of enhanced measles and rubella screening in Victoria. The DBS panel included four measles IgM confirmed cases and two other positive samples: one from a recently vaccinated child and the other a convalescent sample from a patient with measles who had seroconverted to IgG but whose IgM was not detected in serum. All other samples, including four samples that were rubella IgM positive and one that was human parvovirus B19 positive, were measles IgM negative. Each group achieved satisfactory results for the panel, including detecting measles specific IgM in the convalescent DBS of the case who had seroconverted to measles and the DBS collected from the recent vaccine recipient.

The third exercise, where all participants worked independently, involved processing 12 serum samples, consisting of six measles IgM positive and six negative specimens, all of which had previously been included in the WHO global measles quality assurance panel (QAP). The DBS panel included specimens that were positive for rubella and human parvovirus B19 specific IgM, both of which are known to cross-react with measles IgM. All participants achieved satisfactory results for the panel.

The host laboratory had organized a workstation within the serology laboratory with adequate equipment, test reagents and kits, and stationery for easy flow of practical activities. Details on kits and preparation and storage of reagents, required for optimal performance were discussed intensely.
Details of products for ordering were also provided. Maintenance of the automated plate washer to provide optimal performance was discussed.

2.3 Lecture sessions

The lecture sessions covered all of the topics performed in the practical sessions including EIA troubleshooting. Participants were given a wide range of examples of when the validation criteria of an EIA may not be met, why this may have happened, and what would be the appropriate response.

Demonstrations for alternative methods for measles diagnosis were presented. These included antigen detection by immunofluorescence, viral culture and the detection of measles specific RNA by polymerase chain reaction (PCR).

Presentations were made on good laboratory practice including record keeping, laboratory quality assurance, data management in the laboratory and transporting infectious and diagnostic material. Informal discussion in all sessions encouraged participants to share ideas and develop networks.

3. CONCLUSIONS

The main conclusions of the workshop were as follows:

3.1 Evaluation of workshop

3.1.1 Overall, the participants were positive in their feedback and considered the workshop to have met its objectives. All but one participant, who was not fluent in the English language, thought that there was sufficient opportunity to exchange knowledge and experience with each other. The participants considered the schedule of the workshop and the administrative arrangements for travel and accommodation to be well organized. All participants regarded their attendance at the workshop as worthwhile on a personal and national level. Three participants recommended that a workshop for rubella testing would be useful to the programme. Overall, organizers and participants were satisfied with the outcome of the workshop.

3.1.2 The seminar on good laboratory practice described the main factors that contribute to the safe handling of specimens in the laboratory, i.e. the principles of biosafety, the appropriate wearing of protective clothing, quality control of both tests and equipment, and good laboratory techniques. Good record keeping of test details, including test controls, maintenance and calibration of equipment, and staff training were also discussed. Participants were also provided with examples of record keeping sheets.

3.1.3 Two aspects of the workshop highlighted by the majority of participants to be most useful were: the measles calculation worksheet and the seminar on good laboratory practice. The worksheet was designed to take participants, step by step, through the calculations required for the assay outlined in the Dade Behring kit insert. It also included a checklist to ensure that the test was valid and that results were interpreted correctly.

3.2 Follow-up of the workshop

3.2.1 At the completion of the workshop, participants, with the necessary import permits from their own countries, carried home the QAP that had been distributed to other laboratories around the world. By 11 July 2005, five of the workshop-participating laboratories had returned the QAP
results to VIDRL and passed the proficiency test. QAP results of the two remaining laboratories are pending.

3.3 General

3.3.1 The workshop ran smoothly throughout both the practical and lecture sessions. All workshop participants were dedicated in their application to all tasks and were keen to understand all topics addressed in the workshop. The topics covered throughout the workshop were relevant to the needs of the participants and covered the principles and procedure of EIA, including calculation, validation and interpretation of results and troubleshooting. Participants were given a wide range of examples of when the validation criteria of an EIA may fail, the reason for test failure, and what would be the appropriate response.

3.3.2 The workshop schedule provided adequate time for performing the practical procedures at a reasonable pace and for information sharing between participants. The duration of each presentation also allowed adequate time for further discussion of theoretical and laboratory-based issues. Informal discussion in all sessions encouraged participants to share ideas and develop networks.

3.3.3 The workshop should result in providing participants from the Western Pacific Regional with the knowledge and capacity to perform accurate measles IgM testing using the Dade Behring EIA for both serum and DBS. It was also an introduction to proficiency testing for the Region.

3.3.4 The main benefits of the workshop were as follows:

(1) Consolidation of the principles and techniques learnt by the workshop participants will be assessed using the QAP.

(2) The provision of worksheets in use at VIDRL may be useful for other laboratories in the implementation of quality control procedures.

(3) The workshop participants were encouraged to remain in contact with each other and with facilitators as a future resource for technical advice and support.
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## TIMETABLE

### Day 1 – 24 May 2005

- **Seminar:** Principles of measles IgM enzyme-linked immunoassay (EIA)
- **Practice:** EIA: technical set up
- **Practice:** Continuation of EIA
- **Practice:** Serology laboratory tour
- **Seminar:** Dried blood spots (DBS)
- **Practice:** First ELISA test until completion
- **Practice:** Elution of dried blood spots

### Day 2 – 25 May 2005

- **Practice:** EIA using dried blood spot eluate: technical set up
- **Seminar:** Interpretation and validation criteria of EIA results
- **Seminar:** Outline of Western Pacific Region measles laboratory network
- **Practice:** Continuation and completion of second EIA

### Day 3 – 26 May 2005

- **Practice:** EIA serum panel: technical set up
- **Seminar:** Good laboratory practice
- **Seminar:** Laboratory quality assurance
- **Practice:** Completion of third EIA, including interpretation and validation of results
- **Seminar:** Shipment of specimens
- **Seminar:** PCR for measles diagnosis and genotyping
- **Practice:** Laboratory tour and measles culture demonstration

### Day 4 – 27 May 2005

- **Seminar:** Review of results and troubleshooting
- **Seminar:** Measles IgM proficiency testing in the global laboratory network
- **Seminar:** Laboratory data management and reporting to the WPR office
- **Practice:** Distribution of workshop materials for quality assurance proficiency test

**Questionnaire:** Workshop evaluation

**Conclusion:** Closing remarks