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MEASLES SURVEILLANCE: GUIDELINES FOR LABORATORY SUPPORT

Following the commitment by all provinces and territories to eliminate measles by the year 2005, a two-dose measles vaccine schedule has been adopted across the country, augmented by mass vaccination "catch-up" programs in almost all jurisdictions. As the number of cases of measles declines, the importance of surveillance will become even greater. It will be more and more crucial that all suspected cases of measles be reported, and samples from sporadic cases be submitted for full laboratory investigation.

To oversee and document the process of measles elimination, the Laboratory Centre for Disease Control (LCDC) has convened the Working Group on Measles Elimination in Canada (WGMEC). This group will review efforts for the elimination of measles across the country, monitor case incidence, and make recommendations about national surveillance.

The importance of a standard set of laboratory procedures to be used across the country is evident in any assessment of measles surveillance procedures. The WGMEC has therefore developed these guidelines to ensure optimum laboratory surveillance of measles at a time when, with fewer cases, false positive serologic results will be more likely, and it will become increasingly important to detect any importation of virus into a community.

Effective laboratory support for surveillance requires that

- health-care professionals are aware of the system and its requirements;
- appropriate specimens are collected and sent to a laboratory capable of performing the necessary tests;
- reliable equipment is used and tests are performed correctly;
- timely feedback is provided to the appropriate authorities; and
- the integrity of the surveillance system is monitored on an ongoing basis.

Both the public-health authority and the laboratory have a role in ensuring optimum laboratory surveillance of measles in a jurisdiction. The guidelines have been structured to reflect these roles. The role of public health is to educate health-care providers on the importance of laboratory testing, and to make sure that the laboratory resources are accessible. The role of laboratories is to develop and maintain testing resources, standard procedures and quality assurance, and to analyze data and provide feedback of the results to public-health authorities. The following guidelines propose a standard set of responsibilities for adoption in each province or territory to facilitate effective laboratory support for the surveillance of measles.

Laboratory Issues

Laboratory Methods for Diagnosing Measles

- Laboratory diagnosis of measles is done by serologic testing and/or culture.
- Measles specific IgM serology is the standard test of choice for routine diagnosis of measles.
- Demonstration of a significant increase* in measles specific IgG titre is a reliable alternative serologic method for diagnosis.
- Measles virus isolates are important for surveillance purposes; therefore, collection of appropriate specimens for culture is recommended for all sporadic cases and a sample of cases in an outbreak.

All clinical and suspected cases of measles should be confirmed by a laboratory. If an epidemiologic link to an already confirmed case has been established, laboratory confirmation is not necessary

* A fourfold rise in IgG titre using such assays as complement fixation (CF) or hemagglutination (HI) has traditionally been used to define significant increases in antibody titres. These tests have mostly been replaced by enzyme immunoassays (EIA), which may or may not permit quantitative measurement. Many commercial IgG EIAs, such as the Behring Enzygnost test, use a slightly modified procedure to demonstrate a significant rise in antibody titre between acute and convalescent serum specimens. Alternatively, paired specimens can be referred to a reference centre for CF, HI, or plaque reduction neutralization testing.

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for the case to meet the “confirmed” case definition (see Appendix B). To detect cases of measles and to avoid misdiagnosis of rash illness, it is important to use a laboratory testing protocol to screen routinely for common red rash illnesses.

Information on Measles Serologic Testing

- Measles specific IgM antibodies appear around the time of rash onset and persist for at least 28 days.
- Measles specific IgG antibodies appear around the same time as IgM antibodies.
- A single blood specimen collected 3 to 28 days after rash onset is usually satisfactory for IgM serology.
- IgG serology using paired "acute" and "convalescent" specimens is a reliable test for diagnosing measles, provided that specimens are collected at the appropriate times.
- For IgG serology, the first (acute) sample should be obtained as soon as possible after the onset of the rash, and in any event no later than 7 days afterwards. The second (convalescent) sample should be collected 10 to 20 days after the first sample. These paired sera must be tested simultaneously.

In order to maximize the probability of obtaining laboratory confirmation, the provincial or territorial epidemiologist may recommend that a sample of blood be drawn between 3 and 7 days after rash onset. This sample would be appropriate for IgM serology and could serve as the acute sample for IgG serology. If indicated, a second sample should be drawn 10 to 20 days after the first to facilitate retesting for the presence of IgM as well as testing for an increase in IgG titre.

Samples from the early acute phase (i.e. those drawn before 3 days after rash onset) are more likely to test falsely IgM negative compared with those drawn 3 to 28 days after rash onset. For this reason a second blood sample is indicated if the IgM serologic results from an early acute phase are inconclusive or negative for measles, rubella, and parvovirus B19, and the person meets the clinical case definition for measles.

Both false positive and false negative IgM serology results may occur with commercial test kits. Therefore, it is important to confirm IgM serology results using the IgM capture assay, the reference gold standard test available at LCDC. Samples sent to LCDC must be accompanied by the required clinical and patient information (see Appendix A).

Information on Virus Isolation and/or Culture

Measles virus is present in throat and nasopharyngeal secretions during the acute stage, and excreted in urine for at least 7 days after rash onset. Virus isolation should be attempted for all sporadic cases of measles and for cases occurring early in an outbreak. With the identification of a suspected measles case, the attending physician should collect at least one specimen for virus isolation, along with blood for serology. If blood is not collected and the specimen obtained for virus isolation is required for laboratory confirmation of the case, the laboratory should be notified by phone. This should be documented on the requisition.

The measles virus isolation procedure may not always be successful. In an outbreak, specimens should be collected from several individuals to increase the possibility of achieving the goal of genotyping.

The Public-Health Role

The provincial or territorial epidemiologist should ensure that the following policies and procedures are in place locally.

1. A method for informing and updating all physicians and local public-health authorities about the issues surrounding measles surveillance, specifically as follows.
   - Any case of rash illness meeting the "suspect" case definition for measles must be immediately reported to the local public-health authority.
   - Laboratory confirmation is essential for all sporadic cases of measles and all outbreak cases where there is no epidemiologic link to a confirmed case. A blood sample of at least 3 mL (e.g. full pediatric tube) should be taken for submission to the laboratory.
   - The blood sample should be taken early in the illness, ideally between 3 and 7 days after onset of rash (at most, 28 days after rash onset). If blood drawn before 3 days after rash onset is found to be negative for specific IgM antibodies against measles, rubella, and parvovirus in a person who meets the clinical case definition for measles, a second specimen is indicated.
   - Blood from suspected measles cases will also be screened for parvovirus B19 and rubella specific IgM. Although the differential diagnosis of rash is not limited to these viral illnesses, these are the most likely to be confused with measles and therefore the most important to rule out in Canada.
   - In addition to the blood sample, a urine specimen, and/or nasopharyngeal or throat swab should be obtained for virus isolation. A nasopharyngeal or throat swab should be obtained within 4 days after onset of the rash and/or approximately 50 mL of sterile urine within 7 days after onset of rash.
   - In order to maximize the possibility of successfully isolating the measles virus, the specimen must be collected as described in Appendix C and transported on ice (4^{o} C) to the laboratory as soon as possible. Specimens must be processed by the laboratory within 48 hours after collection. LCDC can perform the sample processing and virus isolation should this be necessary.
   - If blood is not collected from a suspected measles case and a specimen obtained for viral isolation is available, the laboratory should be notified by phone that virus isolation will be required for laboratory confirmation of the case. This should be documented on the requisition.
   - It is essential for successful epidemiologic analysis that the information listed below be submitted to the laboratory with all specimens (see Appendix A):
     - name of institution sending specimen
     - patient identifier
     - patient name
     - date of birth
     - sex
     - city, county (municipality)
     - date of fever onset
     - date of rash onset.

In addition, the public-health authority will need to know
- whether the case meets the clinical or suspect case definition (see Appendix B)
- number of doses of measles vaccine received
- date of last measles vaccination
- date of collection.

2. A means of transporting and processing blood samples for the serologic screen of rash.
3. A means of transporting and processing samples taken for virus isolation.
4. A policy for the laboratory to notify the public-health authority of all positive measles and rubella results within 24 hours of the results becoming available.
5. A policy for the public-health authority to notify the provincial or territorial public-health authority of all positive measles and rubella results within 1 business day of the results becoming available.

The Laboratory's Role

The provincial or territorial laboratory must ensure the following regarding serologic testing.

1. All serum specimens submitted from suspected measles cases are also screened for specific IgM antibodies against parvovirus B19 and rubella, constituting a "red rash screen", with a turnaround time of no more than 72 hours. Ideally, these tests would all be done in a single laboratory.
2. Health professionals are aware of the appropriate timing of specimen collection for serologic testing and know that at least 3 mL of blood (e.g. one full pediatric tube) should be collected.
3. Only kits recommended by LCDC are used to test for measles specific IgM (see Appendix D).
4. All serum specimens that yield positive or indeterminate IgM serology results along with 5% to 10% of serum specimens that yield negative results are forwarded to LCDC for confirmation by IgM capture assay. Also, IgM negative specimens from all persons meeting the clinical case definition of measles are forwarded to LCDC. For successful serologic and/or genetic epidemiologic analysis it is essential that all samples sent to LCDC have all the clinical information included (see Appendix A).
5. The laboratory that performs the serologic tests reports all results to the physician who ordered the test on the day they become available, and all positive results for measles and rubella to the local public-health authority within 24 hours of the results becoming available.

The provincial or territorial laboratory must ensure the following regarding virus isolation and/or culture.

1. Laboratories are prepared to advise clients as to the optimal time for specimen collection and provide handling instructions, specifically as follows.
   - A nasopharyngeal or throat swab must be collected within 4 days after onset of the rash and a sterile urine specimen (approximately 50 mL) within 7 days after rash onset, in order to increase the probability of isolating the virus.
   - All specimens should be placed on ice and immediately transported to the laboratory for proper processing (see Appendix C).
   - Specimens should be processed within 48 hours or frozen at -70^{o} C in viral transport medium (see Appendix C).
2. A procedure is in place for transferring specimens to a laboratory where virus isolation can be undertaken, and clients and the local public health authorities are made aware of this procedure. (For laboratories that do not undertake virus isolation, the LCDC Viral Exanthema Laboratory can provide sample processing and virus isolation services. Prior arrangements with LCDC should be made.)
3. Procedures are in place to send measles virus isolates from the testing laboratory to LCDC, where arrangements for genotypic analysis of the isolate(s) will be made. LCDC should ensure that the results of the genotypic analysis are forwarded to the isolating laboratory within 1 business day of receipt of the results. The isolating laboratory should provide the results to the local public-health authority and to the provincial or territorial public-health authority within 1 business day of LCDC's notification.
4. If the viral isolation was required for laboratory confirmation of a case (i.e. if no serology was carried out), then
   - the result of the viral isolation attempt is communicated to the physician who ordered the test on the day it becomes available; and
   - positive results are reported to the local public-health authority within 24 hours of their becoming available.

The provincial or territorial laboratory should ensure the following regarding proficiency testing.

Since it is important to maintain a high level of proficiency in providing measles diagnostic services across the country, LCDC will offer proficiency testing programs. All laboratories providing measles diagnostic services should participate in these.

Appendix A

REQUISITION FOR VIRAL EXANTHEMATA / DEMANDE RELATIVE AUX EXANTHÈMES VIRAUX

NATIONAL LABORATORY FOR SPECIAL PATHOGENS
BUREAU OF MICROBIOLOGY, LCDC

ADDRESS:
Laboratory for Surveillance, Influenza and Viral Exanthemata
Virus Bldg. 10, P.L. 1001C
Tunney's Pasture
Ottawa, Ontario K1A 0L2

LABORATOIRE NATIONAL POUR DES PATHOGÈNES SPÉCIAUX
BUREAU DE MICROBIOLOGIE, LLCM

ADRESSE :
Laboratoire de Surveillance, grippe et exanthèmes viraux
Laboratoire de Virologie, Imm. 10, L.P. 1001C
Pré Tunney
Ottawa (Ontario) K1A 0L2

SENDER / EXPÉDITEUR INFORMATION

Sender / Expéditeur – Lab. No. / N° du labo. : _____

Name / Nom : _____

Address / Adresse : _____

_____

_____

_____

City / Ville : _____

Province : _____

Postal Code / Code postal : _____

Telephone / Téléphone : _____

PATIENT INFORMATION / INFORMATIONS SUR LE PATIENT

Name / Nom : _____

Date of birth / Date de naissance : _____

Sex / Sexe: M ☐ F ☐

City / Ville : _____

Type of specimen / Type du spécimen : _____

_____

_____

Date taken / Date de prélèvement : _____

Test requested / Test requis : _____

_____

Date of Onset of Disease / Début de la maladie : _____

Symtoms, Clinical Diagnosis / Symptômes, diagnostic cliniques : _____

_____

_____

MEASLES ONLY / LA ROUGEOLE SEULEMENT

For laboratory confirmed measles cases / Pour les cas de rougeole confirmés en laboratoire

Date of rash onset / Date de survenue de l'éruption : _____

Date of fever onset / Date de survenue de la fièvre : _____

No. of doses of measles vaccine received / N° de doses de vaccins antirougeoleux reçues : _____

Date of last measles vaccination / Date de la dernière vaccination antirougeoleuse : _____

Appendix B

MEASLES CASE DEFINITIONS

Measles case definitions were developed at the Measles Consensus Conference (1992), reworked by the Advisory Committee on Epidemiology, and released with the 1995 *Guidelines for control of measles outbreaks in Canada*[1]. The case definitions below have been reviewed and approved by the WGMEC.

Confirmed Case

One of the following:

- a significant increase in serum antibody level between acute and convalescent serum samples or the presence of measles-specific IgM in cases with compatible clinical or epidemiologic features
- clinical measles in a person who is a known contact of a laboratory-confirmed case
- detection of measles virus in appropriate specimens.

Clinical Case

All of the following symptoms:

- fever ≥ 38.3° C
- cough, coryza, or conjunctivitis followed by
- generalized maculopapular rash for at least 3 days.

Suspect Case

All of the following symptoms:

- fever ≥ 38.3° C
- cough, coryza, or conjunctivitis followed by
- onset of generalized maculopapular rash.

Appendix C

MEASLES VIRUS ISOLATION

Background

Measles virus isolation is a definitive means of establishing the diagnosis of measles. Measles culture has become a more reliable tool with the use of the B95-8 cell line, an Epstein-Barr virus-transformed lymphoblastoid line known to be quite sensitive in isolating measles virus from clinical specimens. As progress is made toward elimination of measles in the Americas, it will be critical to examine virus isolates from as many outbreaks and sporadic cases as possible for strain surveillance, and to identify the source of the virus. From this standpoint, viral isolation is important. Automated DNA sequencing techniques are now available for rapid genetic characterization of viral isolates. This, together with the existence of a database of nucleic acid sequence information, now makes it possible to identify the source of wild-type viruses and rapidly differentiate between wild-type and vaccine strains.

Virus isolation can take several days to weeks. Therefore, **IgM serology should always be the first priority in the laboratory diagnosis of measles.** Specimens for virus isolation should be taken at the same time that blood is obtained, since a delay in collection will reduce the chance of isolating the virus. **Nasopharyngeal or throat swab or urine specimens should not be substituted for blood, which is required for serologic diagnosis**.

Protocols for Isolation of Measles Virus†

Specimens for virus isolation should be obtained as soon as possible after the onset of rash. Always collect a urine specimen and, if possible, attempt to collect a nasopharyngeal or throat specimen.

Specimen Collection and Processing

Respiratory Specimens (nasopharyngeal or throat swabs)

1. Obtain the sample as soon as possible after onset of rash but no later than 4 days afterwards.
2. Use sterile swabs to obtain nasopharyngeal or throat specimens. The virus is cell-associated, so attempt to swab the throat and nasal passages to collect epithelial cells. Place the swabs in a tube containing 2 mL to 3 mL of VTM (viral transport medium: PBS or suitable isotonic solution such as Hank's BBS containing antibiotics [100 units/mL penicillin, 100 µg/mL streptomycin] and, either 2% fetal bovine serum [FBS] or 0.5% gelatin).
3. Keep all specimens under refrigeration (approximately 4° C), and ship as soon as possible on wet ice to the laboratory for processing.
4. In the laboratory, remove swabs from the VTM after allowing at least an hour for elution of the virus. Centrifuge the eluant at 2,500 x g for 15 minutes at 4° C. Resuspend the pellet in 1 mL of tissue culture medium. If possible, save the supernatant in a separate tube. Either proceed directly with virus isolation (specimens may be held at 4° C for up to 24 hours) or freeze the samples at -70° C, and ship on dry ice to the appropriate laboratory for virus isolation.

Urine Specimens

1. Collect 50 mL to 100 mL of urine within 7 days after rash onset.
2. Keep urine at 4° C and process within 48 hours at the latest.
3. In the laboratory, centrifuge 50 mL of urine at 2,500 x g for 15 minutes at 4° C to pellet the sediment. Resuspend the sediment in 2 mL VTM or any cell culture medium (e.g. DMEM, EMEM, RPMI plus antibiotics). Either proceed directly with virus isolation or freeze the samples at -70° C and ship on dry ice to the appropriate laboratory for virus isolation.

   If centrifugation cannot be done, **do not freeze the urine sample**. The entire urine specimen should be held under refrigeration and shipped to the appropriate laboratory on wet ice. Seal the specimen container to prevent leakage.

† Original protocols, except shell vial method, were based on the method of Dr. William Bellini, Measles Section, Centers for Disease Control and Prevention, USA.

Virus Isolation

B95-8 (B95-a) cell line

B95-8 is the preferred cell line for primary isolation of measles virus[2], and this cell line is available from the American Type Culture Collection (#CRL 1612). Note that **this cell line should be handled as an infectious cell line capable of yielding Epstein-Barr virus**.

The B95-8 cells grow lightly attached to the culture surface when grown in DMEM supplemented with 1x antibiotics (100 units/mL penicillin, 100 mg/mL streptomycin), 0.25 µg/mL amphotericin (fungizone), and FBS. Under these conditions, when B95-8 cells grow as an adherent monolayer, the cell line is referred to as B95-a cells. Cell growth is sustained by adding 5% to 10% FBS. FBS is used at a 2% concentration for cell maintenance during viral isolation. Grow cells in a moist CO_2 incubator at 37° C. Cell stocks can be stored frozen at -70° C using a standard cryoprotection medium (50% FBS, 10% DMSO, 40% DMEM).

The B95-a cells can be passaged by briefly treating the cell monolayers with 0.05% trypsin-EDTA to release cells from the tissue culture surface. Be careful not to over-trypsinize. Neutralize trypsin by adding DMEM containing 10% FBS. Usually the cells from a single monolayer culture can be split in a ratio of 1:3. The cells tend to become "floaters", growing in clumps suspended in the medium as the cell density increases. These cells are viable and can be passaged by gentle pipetting to break up the clumps, then replating to a lower cell density.

The B95-a cells can be transported at room temperature in a 75 cm^2 or 25 cm^2 tissue culture flask with additional medium added to help keep cells attached. After shipment, look at the cell sheet. If many cells are free-floating, a light spin of the medium will recover cells, which can be added back to the flask or to another flask for passage. For maintenance, add 30 mL to 50 mL of DMEM with 2% FBS to a 75 cm^2 flask.

B95-a cells infected with measles virus can show syncytium formation and giant-cell cytopathic effect (CPE) as early as 48 hours after inoculation. However, isolation-attempt cultures should be followed for 7 to 8 days with two to three blind passages before isolation of measles virus is ruled out.

Inoculation of Specimens for Measles Isolation (Flask Method – CDC)

1. Passage cells, split into 25 cm^2 flasks at 1:3 or 1:4, and incubate for 24 to 48 hours. Cells should be at 75% to 85% confluency when the specimen is inoculated.
2. For inoculation, decant medium, add 1.0 mL to 1.5 mL DMEM with 2 x antibiotics and add 0.1 mL to 1.0 mL of specimen, depending on the concentration. Save all leftover specimens, as they may still be useful for analysis by polymerase chain reaction (PCR).
3. Incubate at 37° C for 1 hour.
4. Decant medium into bleach water, replace medium with 5 mL to 10 mL of DMEM containing 2% FBS and 2 x antibiotics.
5. Change medium every 3 to 4 days, and passage cells by splitting at 1:3 every 7 to 9 days. Check for CPE daily.
6. Attempt at least three blind passages before terminating isolation attempt.
7. If CPE is visible, continue to feed the cells until the CPE becomes extensive. It may be necessary to passage the cells one more time to allow the CPE to progress. When CPE is maximal, pellet the cells, resuspend the pellet in 1 mL of DMEM and freeze at -70° C.
8. If a culture becomes contaminated, the original specimen can be diluted in DMEM, passed through a 0.45 µm nitrocellulose filter, and used to inoculate fresh B95-a cells.
9. Confirmation of culture can be achieved by using fluorescent antibody staining or PCR.

Please remember to save some of the original clinical specimen. This material can be used for a second isolation attempt if problems occur with the first one, and it can provide a specimen for direct PCR analysis.

Inoculation of Specimens for Virus Isolation (Shell Vial Method)

The shell vial method has been found to be quite convenient and highly successful by some laboratories in Canada. This method involves the following.

Maintenance of B95-8 cells

1. B95-8 cells are routinely maintained in a 25 cm^2 flask in an upright position. The cells, contained in 10 mL of RPMI growth medium, settle to the bottom of the flask.
2. Without disturbing the cells, each week carefully remove 9 mL of growth medium and discard, leaving 1 mL of cell suspension. Add 9 mL of fresh growth medium (formula below). If additional cells are required, each flask can be split 1:3.
3. Trypsinization is not required because these cells do not attach. Reduction in the density of the cells can be accomplished by harvesting the cells through centrifugation and resuspending them in the fresh medium to the required density.
4. These cells can be maintained at -70° C in an appropriate cryoprotectant and easily retrieved when required.

Growth medium for B95-8 cells

- 500 mL RPMI 1640 (Gibco Cat. No. 21870-076 without glutamine).
- Aseptically remove and save 56 mL of the medium for other use.
- Add 50 mL FBS (heat inactivated) to the remaining 444 mL medium.
- Add 1 mL penicillin-gentamicin solution (final concentration penicillin 100 units/mL; gentamicin 10 µg/mL).
- Add 5 mL 300 mM glutamine.

Inoculation

1. Inoculate two shell vials with coverslips per specimen with 10^6 cells in 0.2 mL growth medium and 0.2 mL of specimen.
2. Centrifuge 1,000 x g for 45 minutes at room temperature.
3. Following centrifugation, remove inoculum and add 1 mL of maintenance medium containing 2% FBS.
4. Incubate at 37° C and observe for syncytium formation at 48 hours and daily for up to 6 days.
5. When CPE is observed (at least 50% cells) or after 6 days' incubation, centrifuge one vial at 900 x g for 10 minutes.

If viral isolation is needed to confirm the case, follow steps 6 and 7.

6. Aspirate the maintenance medium from the vial, fix by adding 1 mL acetone, and allow to sit for 15 minutes. Remove the acetone and wash with PBS to remove residual acetone.
7. Aspirate PBS and stain the coverslip (within the vial) with measles immunofluorescent stain according to the manufacturer's instructions (Light Diagnostics – Chemicon; distributed in Canada by Bio/Can).

Otherwise inoculate fresh B95-8 cells in 75 cm² flask with virus until CPE is observed, and follow steps 7 and 8 of Flask Metbod protocol.

8. If CPE is not observed after 6 days, the monolayer in the second shell vial can be scraped and passed to a fresh vial(s) for further incubation.

Please remember to save some of the original clinical specimen. This material can be used for a second isolation attempt if problems occur with the first one, and it can provide a specimen for direct PCR analysis.

Shipping of Measles Virus Isolates

For shipping measles virus isolates, it is best to use a 25 cm^2 tissue culture flask. Cells should be seeded and infected just prior to shipping. Once cells have been infected, fill the flask to the top with DMEM (plus antibiotics and 2% FBS). Screw the top on tightly, and seal with parafilm. It is best to place the flask in a leak-proof container, such as a ziplock plastic bag, and ship at room temperature.

Alternatively, infected cells can be pelleted, resuspended in a small volume of DMEM and frozen at -70° C before shipping on dry ice.

Please contact LCDC concerning shipment of sera and other clinical specimens and measles virus isolates.

Viral Exanthema Laboratory, Room 108, Virus Laboratories, LCDC, Building #10, Postal Locator 1001C, Tunney's Pasture, Ottawa, ON K1A 0L2, Telephone: (613) 957-9068 Fax: (613) 954-0207. Head, Viral Exanthema Laboratory, Dr. Graham Tipples, Telephone: (613) 946-1488, e-mail: graham_tipples@hc-sc.gc.ca

Note: After June 1, 1998, the new address will be: Viral Exanthema Laboratory, Bureau of Microbiology, Federal Laboratories, Room H5790, 1015 Arlington St., Winnipeg, Manitoba R3E 3R2.

Appendix D

CURRENT RECOMMENDATION REGARDING COMMERCIAL MEASLES IgM SEROLOGY TEST KITS

Commercial measles IgM serology tests give both false positive and false negative results. An evaluation of a few commercial measles IgM enzyme immunoassay kits (indirect assays) was conducted in late 1996. The products evaluated included those of Behring Enzygnost (Marburg, Germany), Chemicon International, Inc. (Temecula, CA), Clark Laboratories, Inc. (Jamestown, NY), Gull Laboratories, Inc. (Salt Lake City, UT), and Pan-Bio (East Brisbane, Australia). Of these, overall the Behring Enzygnost test correlated best with both the clinical condition and the gold standard CDC IgM capture assay. (The CDC IgM capture assay has the advantage of better sensitivity and specificity, and tends to suffer less than indirect EIA assays from false positive results; hence, it is important as the gold standard.) Chemicon has a new generation kit based on IgM capture technology. This new kit is currently being evaluated. However, until further notice, WGMEC recommends the use of the Behring Enzygnost test for measles IgM serology.

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1. LCDC. *Guidelines for control of measles outbreaks in Canada.* CCDR 1995;21:189-95.
2. Kobune F, Sakata H, Sugiura A. *Marmoset lymphoblastoid cells as a sensitive host for isolation of measles virus.* J Virol 1990;64:700-05.

Source: *Working Group on Measles Elimination in Canada, Laboratory Issues Subgroup (Drs. J Carlson [Chairperson], H Artsob, M Douville-Fradet, P Duclos, M Fearon, S Ratnam, G Tipples, P Varughese, B Ward, and Ms J Sciberras).*

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