INSTITUT NATIONAL
DE SANTÉ PUBLIQUE
DU QUÉBEC

# Report of the Sous-comité Épreuves de détection de la syphilis

**HIGHLIGHTS**

Québec

**AUTHORS**

**Claude Fortin**, MD, Microbiologist-infectious disease specialist and Co-chair of the Sous-comité Épreuves de détection de la syphilis
Hôpital Notre-Dame, Centre hospitalier de l'Université de Montréal

**Bouchra Serhir**, Microbiologist and Co-chair of the Sous-comité Épreuves de détection de la syphilis
Laboratoire de santé publique du Québec, Institut national de santé publique du Québec

**Évelyne Fleury**, Coordinator of the Comité sur les infections transmissibles sexuellement et par le sang (CITSS) and the Sous-comité Épreuves de détection de la syphilis
Direction des risques biologiques et de la santé au travail, Institut national de santé publique du Québec

**LAYOUT**

**Amélie Dugué**, Administrative Officer
Direction des risques biologiques et de la santé au travail, Institut national de santé publique du Québec



LEGAL DEPOSIT – 2nd QUARTER 2011
BIBLIOTHÈQUE ET ARCHIVES NATIONALES DU QUÉBEC
LIBRARY AND ARCHIVES CANADA
ISBN: 978-2-550-57787-4 (FRENCH PDF)
ISBN: 978-2-550-61494-4 (PDF)

# Background

Since 2000, the resurgence of syphilis in Québec has led to increased screening and resulted in a greater number of reported cases, particularly in the Montréal area. To meet the growing demand for laboratory testing, some medical diagnostic laboratories have introduced an enzyme immunoassay (EIA) test into their syphilis detection algorithm. This situation raised concerns among general practitioners, microbiologists and infectious disease specialists with regards to the interpretation of screening results and the diagnosis and confirmation of syphilis infections.

In response to these concerns, the Comité sur les infections transmissibles sexuellement et par le sang (CITSS) of the Institut national de santé publique du Québec (INSPQ) established the Sous-comité Épreuves de détection de la syphilis whose mandate was to make recommendations for optimizing syphilis diagnosis in Québec.

# Methodology

To fulfill its mandate, the subcommittee:

- conducted a literature review on syphilis detection tests;
- compiled an inventory of syphilis detection tests used by medical diagnostic laboratories in Québec;
- reviewed serodiagnostic algorithms for syphilis detection used in other Canadian provinces and in other countries;
- reviewed the data analysis from a 2008 validation study conducted by the Laboratoire de santé publique du Québec (LSPQ) on the use of INNO-LIA as a confirmatory test and performed a retrospective analysis of screening and confirmatory test results for 2,132 serum samples analyzed by LSPQ between January and December 2007.

Based on the aforementioned, the subcommittee proposed and validated two syphilis detection algorithms. An accompanying interpretation of results chart was also developed.

# Results

## Two new algorithms

The first algorithm (Figure 1) starts with RPR and the second (Figure 2) starts with EIA. These algorithms constitute a significant update for the detection of syphilis in Québec. They take into account recent changes made by the LSPQ (replacement of the FTA-ABS-DS by the INNO-LIA and the TRUST by the RPR).

The new algorithms propose changes to the testing sequence and the tests used by both medical diagnostic laboratories and the LSPQ. These changes require that medical diagnostic laboratories performing the RPR quantitative test or request the RPR titer from a service laboratory[1]. When both the EIA and the RPR test results are simultaneously reactive, the laboratories will be able to immediately report the final results. These algorithms will reduce the number of samples sent to the LSPQ and the number of tests required to confirm a result.

[1] Service laboratories are defined as public laboratories which perform biomedical tests for institutions in their regions, organisations and/or institutions with which a service agreement has been established.

**Figure 1** **Proposed syphilis screening and serologic confirmation algorithm: Algorithm I, starting with RPR**

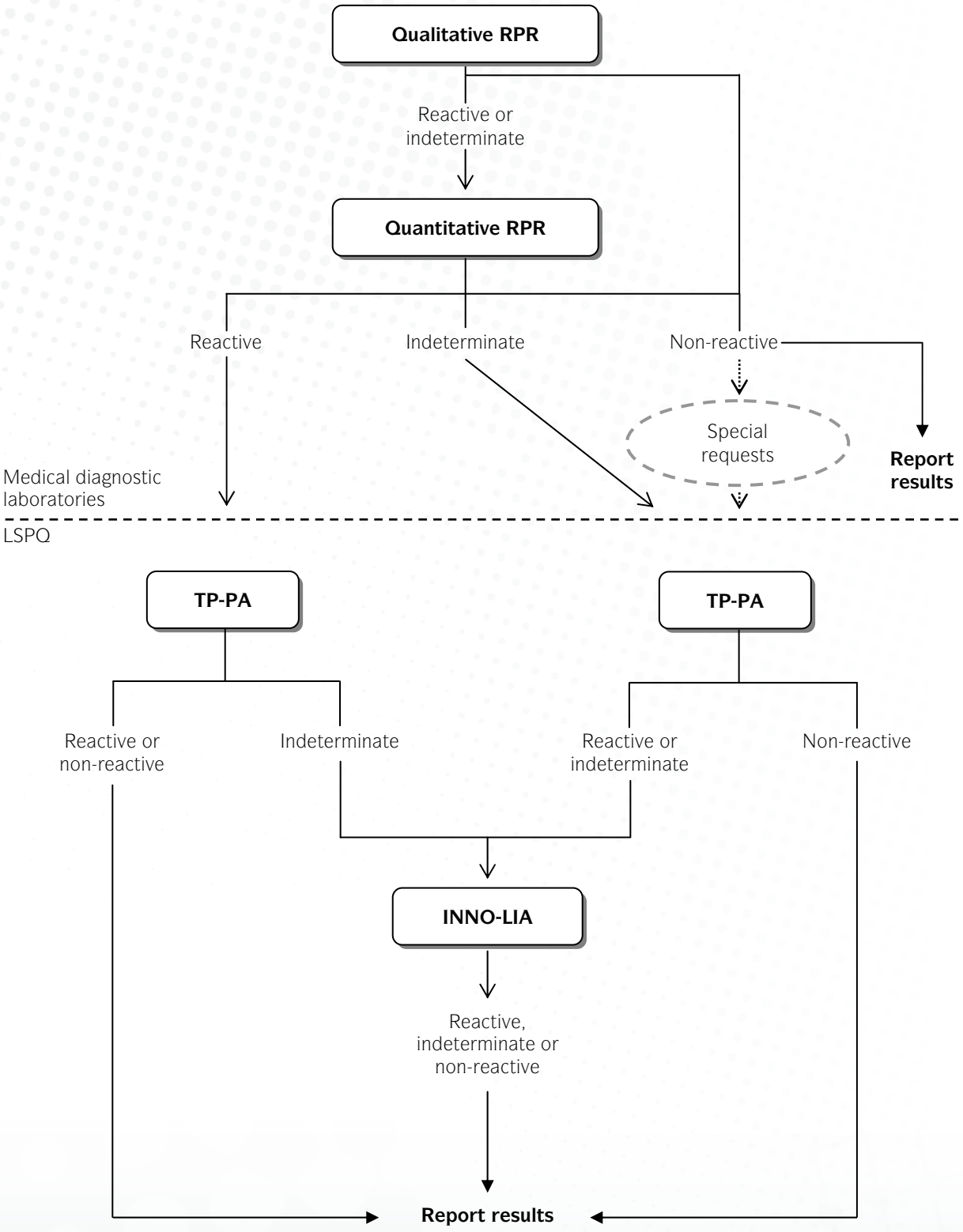
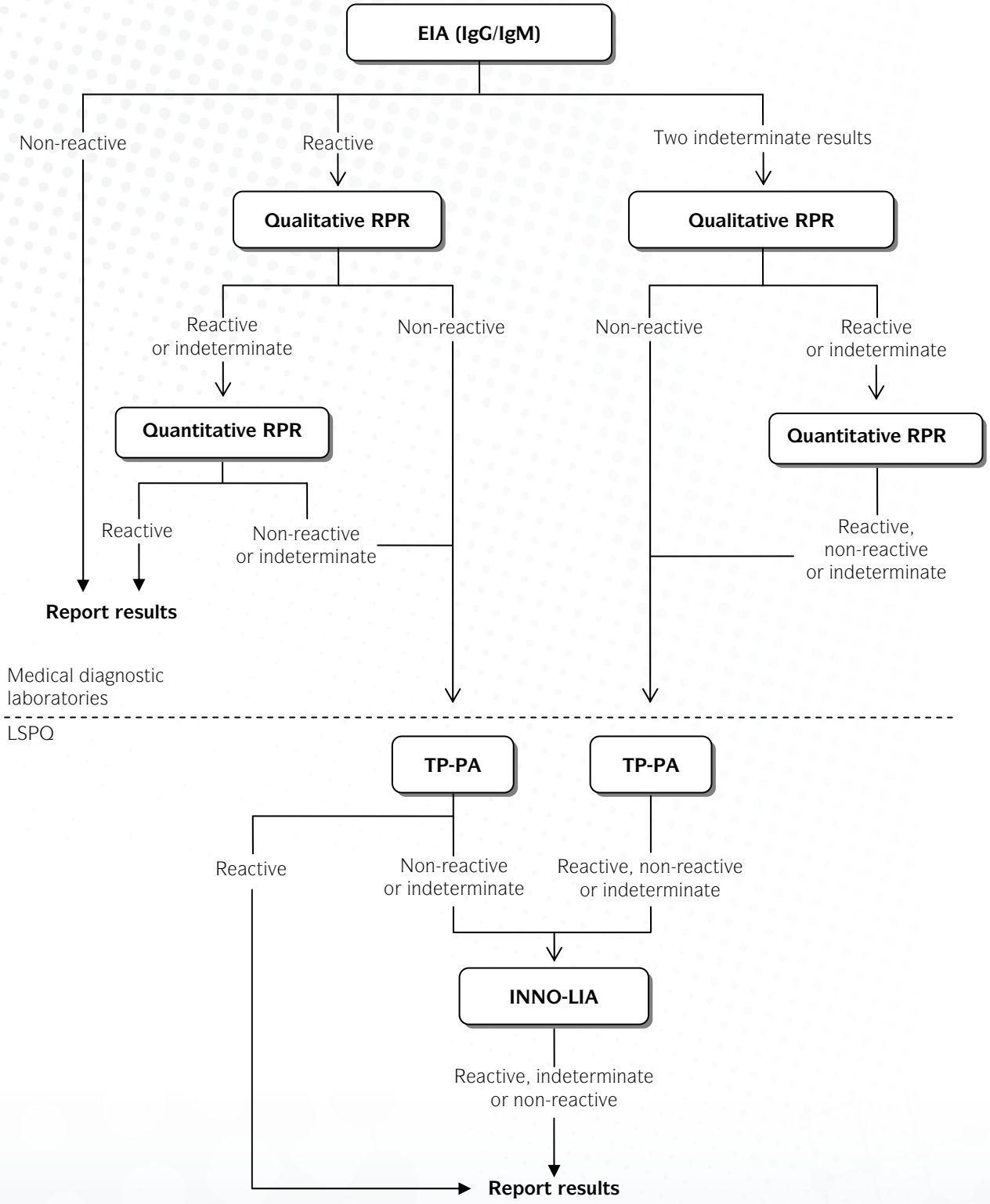


**Figure 2** **Proposed syphilis screening and serological confirmation algorithm: Algorithm II, starting with EIA**



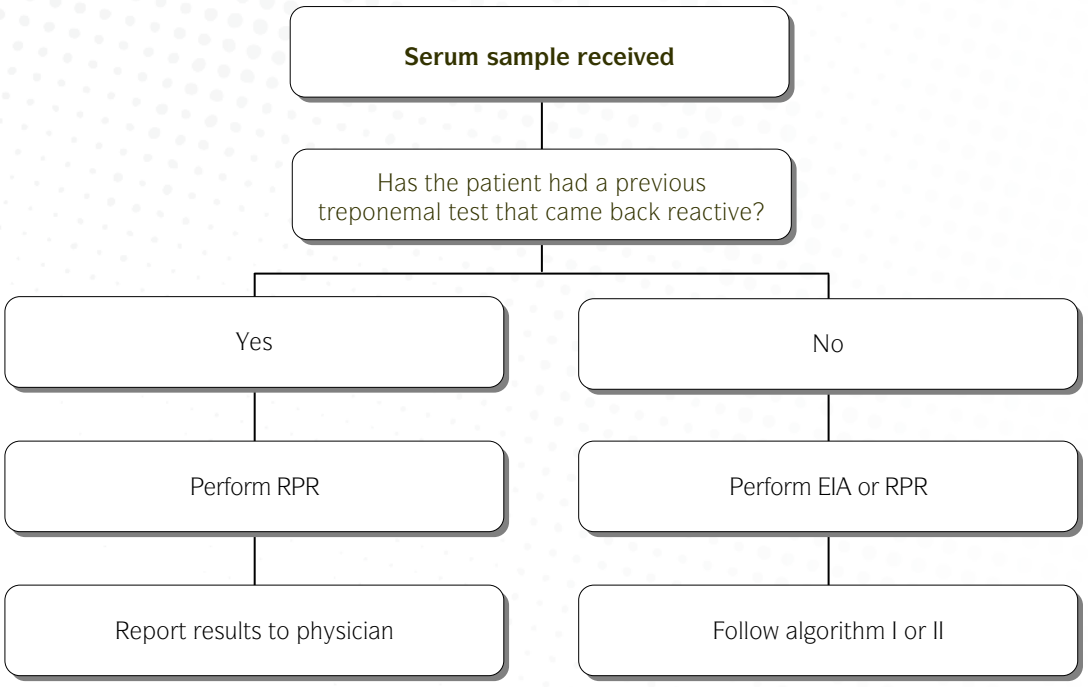
When a serum sample is received, prior to using algorithm I or II, it is necessary to search for prior test results (see Figure 3). The search will reveal whether the patient has had a previous reactive treponemal test (EIA, TP-PA, FTA-ABS-DS, INNO-LIA). This, in turn, determines which tests should be performed.

If the patient has had a previous reactive treponemal test, the medical diagnostic laboratory will perform qualitative RPR and, if necessary, quantitative RPR.

Then the medical diagnostic laboratory will report the results. Treponemal tests are not considered useful when there have been previous reactive results because, in most cases, treponemal antibodies remain detectable for life.

If, however, the patient has never had a reactive treponemal test, the medical diagnostic laboratory will follow algorithm I or II.

**Figure 3 Research of previous results before using algorithms I and II**




## Interpretation chart

The proposed interpretation chart (see Table 1) presents and interprets the serologic profiles possible with the proposed algorithms. The chart was developed to support clinicians in interpreting complex serologic profiles that may be reflective of more than one clinical situation.

For ease of use, the chart does not include special cases or congenital syphilis.

Widespread use of the chart by laboratories may assist in standardized reporting.

**Table 1 Interpretation chart for serodiagnosis of syphilis**

| Results of tests performed by medical diagnostic laboratories | | Results of tests performed by the Laboratoire de santé publique du Québec (LSPQ) | | | |
|---|---|---|---|---|---|
| **EIA** | **RPR** | **TP-PA** | **INNO-LIA** | **VDRL on CSF** | **Comments** |
| Non-reactive | | | | | 1 |
| Reactive | Reactive | | | | 2 |
| Reactive | Non-reactive | | | | 3 |
| Reactive | Non-reactive | Reactive | | | 4 |
| Reactive | Non-reactive | Non-reactive or indeterminate | Reactive | | 4 then 5 |
| Reactive | Non-reactive | Non-reactive or indeterminate | Non-reactive | | 6 then 5 |
| | Non-reactive | | | | 7 |
| | Reactive | | | | 8 |
| | Reactive | Reactive | | | 2 |
| | Reactive | Non-reactive | | | 9 |
| | Reactive | Indeterminate | Reactive | | 2 then 5 |
| | Reactive | Indeterminate | Non-reactive | | 9 then 5 |
| For any other serologic findings or unusual serologic findings | For any other serologic findings or unusual serologic findings | For any other serologic findings or unusual serologic findings | For any other serologic findings or unusual serologic findings | | 10 |
| | | | | Reactive | 11 |
| | | | | Non-reactive | 12 |

**Comment 1**

No evidence of treponematosis.

If incubating or primary syphilis is suspected, a second serum sample should be collected in 2 to 4 weeks.

**Comment 2**

Syphilitic treponematosis. The clinical presentation and previous treatment history are needed to clarify the interpretation:

a) infectious syphilis: primary, secondary or early latent (i.e. less than one year);
b) late latent syphilis;
c) tertiary syphilis;
d) treated syphilis with persistent reactive RPR.

**Comment 3**

Serum sample sent to LSPQ for the confirmatory tests required for final interpretation.

**Comment 4**

1) Syphilitic treponematosis. The clinical presentation and previous treatment history are needed to clarify the interpretation:
   a) primary syphilis prior to RPR seroconversion;
   b) secondary syphilis with RPR prozone phenomenon;
   c) late latent syphilis after RPR seroreversion;
   d) treated syphilis.
2) Possible non-syphilitic treponematosis (bejel, yaws or pinta).

**Comment 5**

The INNO-LIA test kit has not been approved by Health Canada.

**Comment 6**

1) No evidence of treponematosis. False reactive EIA.
2) If incubating or primary syphilis is suspected, a second serum sample should be collected in 2 to 4 weeks.

**Comment 7**

1) No evidence of treponematosis.
2) If incubating or primary syphilis is suspected, a second serum sample should be collected in 2 to 4 weeks.
3) If secondary syphilis is suspected, inform the laboratory so that the possibility of a prozone phenomenon can be examined.

**Comment 8**

The serum sample of a patient who has never had a reactive treponemal test is sent to the LSPQ. Confirmatory test results are required for the final interpretation.

**Comment 9**

1) No evidence of treponematosis. False reactive RPR.
2) If incubating or primary syphilis is suspected, a second serum sample should be collected in 2 to 4 weeks.

**Comment 10**

Contact the laboratory for results interpretation.

**Comment 11**

If the treponemal test on the serum sample is reactive, a reactive CSF-VDRL is an indicator of neurosyphilis.

**Comment 12**

Because the sensitivity of CSF-VDRL is poor, a non-reactive VDRL does not necessarily rule out neurosyphilis.

**A notifiable disease report must be submitted in the following situations:**[2]

- Visualization of *Treponema pallidum* from samples taken from a chancre or lymphatic ganglion using dark-field microscopy or any other specific recognized test for *T. pallidum*.
- All positive non-treponemal test results (VDRL, RPR, TRUST or other) for serum samples of any titer, confirmed by a treponemal test (TP-PA, MHA-TP, EIA, INNO-LIA or other recognized test). The report must include the dilution titer of the RPR result (1/1, 1/2, 1/4, 1/8, etc.).
- All positive treponemal test results (TP-PA, MHA-TP, EIA, INNO-LIA or other recognized test) should be reported when the clinical information on the requisition suggests a recent acquisition of syphilis even in the presence of a negative non-treponemal test result.
- All CSF-VDRL positive results using a validated diagnostic procedure for neurosyphilis. This particular test is usually performed in a reference laboratory.

Cases that have previously been reported and which present with serologic findings suggestive of a new infection should be reported. *For example, if the titer of a non-treponemal test increases by four times in relation to the previous titer, or if a non-treponemal test is reactive at 1/2 or higher and the previous test is non-reactive—this suggests a new infection (new episode of syphilis).*

[2] Adapted from a MSSS publication entitled *Déclaration des résultats de tests de laboratoire en lien avec la syphilis*, published in 2003. The proposed changes are as follows:

- The FTA-ABS-DS test was replaced by INNO-LIA. Since February 2009, the LSPQ has used INNO-LIA instead of FTA-ABS-DS; and
- The criteria for identifying the acquisition of a new infection have been clarified.

# Recommendations

## Regarding the use of syphilis detection tests

### *RPR tests*

We recommend:

- that RPR tests be used by medical diagnostic laboratories to detect syphilis, especially laboratories with a low volume of tests; and
- that medical diagnostic laboratories using an RPR test to detect syphilis adopt algorithm I.

### *EIA tests*

We recommend:

- that EIA tests be used by medical diagnostic laboratories to detect syphilis, especially laboratories with a high volume of tests;
- that EIA tests that detect total antibodies (IgG and IgM) be used instead of those that detect IgG only; and
- that laboratories using an EIA test adopt algorithm II.

### *Syphilis detection tests on cerebrospinal fluid*

We recommend:

- In patients with a serologic reactive treponemal test result that VDRL continue to be the gold standard test for detecting neurosyphilis; and
- that no changes be made to the current algorithm for detecting neurosyphilis in CSF.

## Syphilis detection and confirmation algorithms

We recommend:

- that medical diagnostic laboratories use one of the two proposed algorithms based on their volume of tests and their requirements;
- that medical diagnostic laboratories or service laboratories perform quantitative RPR;
- that RPR titer results be sent to the LSPQ with all requests for confirmation;
- that the LSPQ stop performing RPR tests; and
- that the proposed algorithms be re-evaluated some time after being implemented.

## Interpretation of results

We recommend:

- that the LSPQ and all medical diagnostic laboratories in Québec use the proposed interpretation chart.

## External quality audits

We recommend:

- that the Comité d'assurance qualité en microbiologie médicale increase the frequency of external quality control of syphilis detection tests.

## Impact on syphilis surveillance

We recommend:

- that the Direction générale de la santé publique (DGSP) of the Ministère de la Santé et des Services sociaux (MSSS) adopt the proposed changes to the document entitled *Déclaration des résultats de tests de laboratoire en lien avec la syphilis* (deleting and adding test names, and clarifying the definition of acquisition of a new infection; see footnote on page 7);
- that the DGSP remind medical diagnostic laboratories of which types of syphilis are to be reported;
- that the DGSP remind those filing notifiable disease reports (treating physicians and laboratories) of the identifying elements to include in the reports; and
- that the LSPQ ensure that possible duplicates due to the reporting of the same episode of syphilis by more than one public health department are detected, and that the regions concerned are notified.

# Conclusion

We believe that these algorithms, interpretation chart and recommendations are adapted to the situation in Québec and fit in with the roles and responsibilities of medical diagnostic laboratories and the LSPQ. We hope they will help improve syphilis detection by limiting the number of tests required for a final report and by reducing turnaround time.

For more information, see the following:

- the **full report in French** at www.inspq.qc.ca in the section "Publications"
- an **interactive electronic version of the algorithms and the interpretation grid in French** at www.inspq.qc.ca/syphilis in the section "Sous-comité Épreuves de detection de la syphilis" and at www.inspq.qc.ca/lspq/ in the section "Répertoire des analyses" then "Treponema pallidum."

PUBLICATION N°: 1232

EXPERTISE
CONSEIL

INFORMATION

FORMATION

www.**inspq**.qc.ca

RECHERCHE
ÉVALUATION
ET INNOVATION

COLLABORATION
INTERNATIONALE

LABORATOIRES
ET DÉPISTAGE

*Institut national de santé publique* Québec