INESSS
LE SAVOIR PREND FORME

Assessment mechanism for medical biology test at INESSS - Overview

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Répertoire québécois et système de mesure des procédure de biologie médicale

- Every year, the Ministère de la Santé et des Services sociaux (MSSS) publishes the *Répertoire québécois et système de mesure des procédures de biologie médicale*

- This index contains information on interpreting and managing hospital laboratory tests

- When a laboratory test entered into the index, it means that the test must be available to everyone in Québec should a doctor or qualified person prescribe it

- In 2012–2013, 1 709 tests were listed in the index

CHANGES TO THE INDEX (1)

- **To make changes to the index, an application must be sent to the MSSS**

- **Until very recently, to enter a new lab test, the applicant had to :**
  - **complete a form for the addition of a new test**
  - **submit two scientific articles on the technology in question**

- **Using this model, all tests submitted for entry into the system were automatically accepted**

CHANGES TO THE INDEX (2)

Santé et Services sociaux Québec

FORMULAIRE D'ADDITION
D'UNE NOUVELLE ANALYSE DE BIOLOGIE MÉDICALE AU RÉPERTOIRE QUÉBÉCOIS ET SYSTÈME DE MESURE DES PROCÉDURES DE BIOLOGIE MÉDICALE DU MINISTÈRE DE LA SANTÉ ET DES SERVICES SOCIAUX (MSSS)

DATE DE LA DEMANDE : Année | Mois | Jour

IDENTIFICATION DE L'ANALYSE DE BIOLOGIE MÉDICALE

Nom ou description de la nouvelle analyse

Technique de la nouvelle analyse (préciser si résultat qualitatif ou quantitatif)

Valeur pondérée de la nouvelle analyse : _____
(Inclure le formulaire *Ajout ou révision de la valeur pondérée d'une procédure de biologie médicale* en annexe)

Hiérarchie proposée de la nouvelle analyse : ◯ locale ◯ régionale ◯ suprarégionale

Sous-section proposée du répertoire : _____

CARACTÉRISTIQUES DE LA NOUVELLE ANALYSE DE BIOLOGIE MÉDICALE

Quelle(s) analyse(s) présentement en usage dans le répertoire du MSSS cette nouvelle analyse remplacera-t-elle (inclure également si elle peut remplacer une analyse d'électrophysiologie ou d'imagerie) ?

Quels seront les avantages cliniques de cette nouvelle analyse au niveau de son efficacité, de son efficience et de son optimisation ?

Quelles seront les indications cliniques pour lesquelles l'analyse peut être prescrite ?

Quelles seront les restrictions qui vont s'appliquer (ex. : algorithme, types de renseignements cliniques écrits, etc.) ?

Quels seront le temps de réponse (phase analytique) et la périodicité attendus ?

Est-ce une analyse court délai ? ☐ Oui ☐ Non

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CONTRÔLE DE QUALITÉ

Quelle est votre approche pour assurer la fiabilité et la sécurité des résultats ?

Est-ce que les réactifs ou la trousse ont été homologués par Santé Canada ?

Avez-vous prévu participer à des contrôles externes ? ☐ Oui ☐ Non (si oui, lequel ? si non, pourquoi ?)

UTILISATION CLINIQUE ATTENDUE

Volume provincial annuel attendu pour les trois prochaines années

Si l'utilisation est reliée à la détermination d'un diagnostic, quelles sont la prévalence et l'incidence de ce diagnostic au Québec ?

Si l'utilisation est reliée au monitoring d'un médicament, quelles sont les recommandations à ce sujet ?

IDENTIFICATION DU REQUÉRANT ET DU PRODUCTEUR DU SERVICE

Nom du médecin requérant : _____
Nom du chef de département requérant : _____
Discipline du département requérant : _____
Nom du professionnel responsable de l'analyse (niveau technique) : _____
Nom de l'établissement producteur : _____
Nom du chef de département producteur : _____

DOCUMENTATION

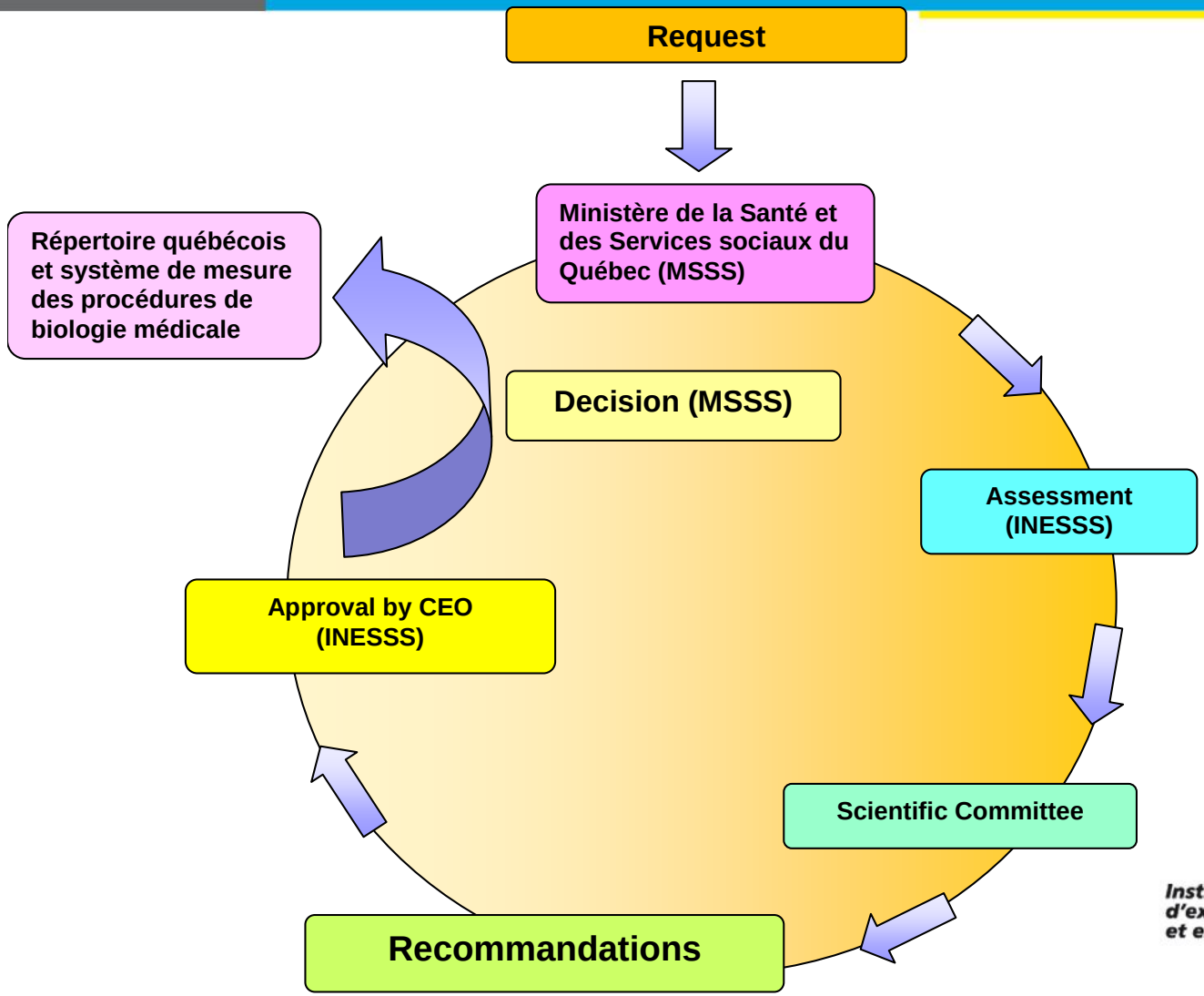
- ✓ Veuillez fournir une photocopie d'au moins deux articles scientifiques publiés traitant de cette analyse avec la présente demande.
- ✓ Veuillez fournir une photocopie de la monographie de la trousse de réactifs homologuée par Santé Canada.

MANDATE FROM MSSS

- **In December 2012, the MSSS requested that the INESSS develop a permanent assessment mechanism that would help the department make informed decisions on whether or not to add new medical biology tests to the index based on their relevance and some specific issues (economics, ethical, clinical practice)**

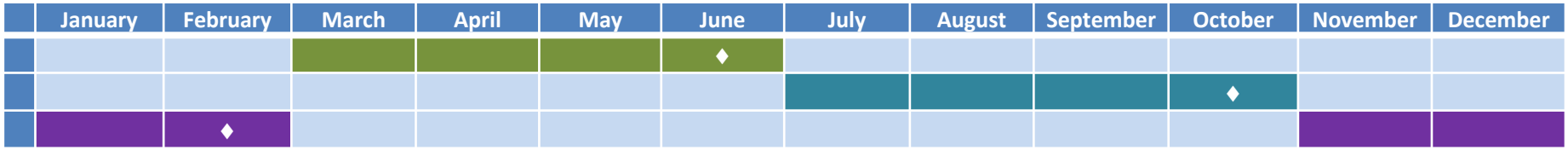
- **In response to the request, INESSS developed an assessment process for medical biology tests, at the end of which a notice is sent to the Minister of Health and Social Services**

ASSESSMENT PROCESS



ASSESSMENT PROCESS

- The assessment mechanism has several steps that are completed over a period of approximately **4 months**



Transmission to INESSS	**March 1** **July 1** **November 1**
Assessment (INESSS)	**March to May** **July to September** **November to January**
Scientific Committee and recommendations to the Minister (♦)	**February** **June** **October**

ASSESSMENT PROCESS

- **Any application to modify or add to the Index must be sent by the applicant to the MSSS**

- **Upon receipt of the application, the MSSS ensures everything is in order and determines the steps to take. Where relevant, department authorities send the application to INESSS for assessment.**

- **Assessment by INESSS's scientific staff – scientific litterature**

ASSESSMENT CRITERIA

Dimension	Definition	Components
Clinical benefit	The degree to which the results positively or negatively affect the patient.	• Availability of interventions and their impact • Health benefits and risks
Clinical validity (diagnostic performance)	A measure of how accurate a test is in identifying or predicting a clinical disorder.	• Clinical sensitivity • Clinical specificity • Positive predictive value • Negative predictive value
Analytical validity (technical ability)	An indicator of a test's ability to measure the desired property or characteristic.	• Analytical sensitivity • Analytical specificity • Reliability (precision, accuracy) • Robustness of the test (i.e., resistance to small changes in the analytical variables)

ASSESSMENT CRITERIA (upcoming)

Dimension	Definition	Components
Economic issues	The costs of using medical biology testing in the context of the Québec health system.	• Budget impact analysis • Cost /efficiency
Organizational, ethical, professional, legal and social issues	Issues related to testing that can affect health care organizations, people, their families or society	• Terms of test implementation • Change in care processes

ASSESSMENT PROCESS

- **Assessment by the scientific committee on medical biology tests (most committee members are physicians who are experts in different areas of laboratory medicine ; external experts are also called in – their clinical/medical expertise are recognize among their colleagues)**
- **Composition of the Committee:**
  - **Biochemistry**
  - **Hematology**
  - **Microbiology-infectious diseases**
  - **Genetics**
  - **Pathology**
  - **Pediatrics**

ASSESSMENT PROCESS

- **The committee submits its report to the INESSS Chief Executive Officer, who ratifies the recommendations to be sent to the Minister of Health and Social Services. Depending on the assessment made, one of the following four recommendations may be applied :**
  - **Entry to the *Index* without specific conditions**
  - **Conditional entry under certain conditions**
  - **Refused entry**
  - **Reassessment**

ASSESSMENT PROCESS

- **The Minister approves or rejects the recommendations of INESSS regarding updates to the index**

- **Once the update is made, the *Répertoire québécois et système de mesure des procédures de biologie médicale* is published by the MSSS**

- **INESSS publishes the Notices to the Minister on its website, which set out the recommendations made and their rationale (60 days after sending them to the Minister)**

CURRENT ASSESSMENTS

April 2013 (12 tests)

- The assessment mechanism for new medical biology tests is being implemented gradually

- Phase I involved assessing the 12 tests that were submitted to the MSSS for possible addition to the 2013–2014 Index

- This phase ended on January 31, 2013, with a notice sent by INESSS to the Minister. The Notice was made public on March 31, 2013

CURRENT ASSESSMENTS

April 2013 (12 tests)

The following 12 tests were assessed by INESSS :

- **Quantification of acylcarnitines and amino acids in dried blood spots using MS/MS;**
- **Screening (and diagnosis) of 15 respiratory viruses using NAAT;**
- **Genotyping of HPV viruses using Linear Array;**
- **MGMT promoter methylation using conventional CRP;**
- **Amplification of the EGFR/CEP7 gene using FISH on a paraffin-embedded section;**
- **Codeletion of chromosomes 1p and 19q using FISH on a paraffin-embedded section;**
- **Carbohydrate-deficient transferrin;**
- **Myopathies of unknown etiology (Western blot);**
- **Histomorphometric analysis of a non-decalcified bone sample (complex diseases);**
- **Histomorphometric analysis of a non-decalcified bone sample (non-complex diseases);**
- **Measurement of ADAMTS-13 activity using fluorescence resonance energy transfer (FRET);**
- **Anti-Sa analysis using ELISA.**

CURRENT ASSESSMENTS

June 2013 (19 tests)

- **Phase II consists in a notice to the MSSS concerning the 19 highly specialized medical biology tests already listed in the 2013–2014 Répertoire. Phase II ended on March 31, 2013.**
- **The following are the 19 tests assessed by INESSS :**
- **Mutational analysis of the protein C gene using nucleic acid sequencing;**
- **TNF (measurement after TLR-2 and TLR-4 activation) (ELISA);**
- **Megakaryocyte staining;**
- **Anti-GAD (serous);**
- **Genotyping of influenza using nucleic acid pyrosequencing (NAAT);**
- **Genotyping of influenza using nucleic acid sequencing (NAAT);**
- **Genotyping of cytomegalovirus (CMV) for ganciclovir and/or foscarnet resistance;**

CURRENT ASSESSMENTS

June 2013 (19 tests)

- Human papilloma virus (HPV) (sequencing using a cytobrush);
- Methylmalonic acid (MMAA, MMAB, MCEE, TCb1R, MUTASE genes) Individual mutation (NAAT);
- Colon cancer—PMS2 (TPT);
- Colon cancer—MSH6 (TPT);
- Chromosome X and Y (NAAT);
- Measurement of arginosuccinate synthetase activity;
- Measurement of carbanyl phosphate synthetase activity;
- Renal cell carcinoma (Alpha-TFEB in t(6;11)) (NAAT) on tissues;
- Renal cell carcinoma (PRCC-TFE3 in t(X;1)) (NAAT) on tissues;
- Dermatofibrosarcoma protuberans (COL1A1-PDGFB in t(17;22)) (NAAT) on tissues;
- Fibrous dysplasia (codon 201 and 227 mutations in GNAS1) (NAAT) on tissues;
- Angiomatoid fibrous histiocytoma (FUS-ATF1 in t(12;16), EWSR1-CREB1 in t(2,22)) (NAAT) on tissues.

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Review and recommendation process (an example)

ADAMTS-13 activity testing by FRET

(Fluorescence Resonance Energy Transfer)

ADAMTS-13 activity testing by FRET

(Fluorescence Resonance Energy Transfer)

ADAMTS-13:

- **metalloprotease**
- **role: to limit the formation of platelet aggregation through the cleavage of von Willebrand Factor**
- **severe deficiency of ADAMTS-13 is responsible for thrombotic thrombocytopenic purpura (TTP)**

ADAMTS-13 activity testing by FRET

(Fluorescence Resonance Energy Transfer)

FRET (Fluorescence Resonance Energy Transfer)

- **A synthetic fragment of the protein von Willebrand factor is used as substrate.**

- **The substrate is in form lyophilized and reconstituted liquid added to the wells of a plate containing different samples (blood) that will be placed in a fluorometer.**

- **In the presence of protease ADAMTS-13, the substrate for synthesis will be cleaved releasing a fluorophore which, after excitement between 340 and 350 nm, fluoresces.**

ADAMTS-13 activity testing by FRET

(*Fluorescence Resonance Energy Transfer*)

Assessment (clinical validity) – only one study available

- **Sensitivity: 89%**
- **Specificity: 100%**
- **Positive predictive value: No results**
- **Negative predictive value: No results**
- **ROC Curve: No results**

ADAMTS-13 activity testing by FRET

(*Fluorescence Resonance Energy Transfer*)

Assessment (analytical validity) – Few studies available (< 10)

- **Analytical sensitivity: No results**
- **Analytical specificity: No results**
- **Reliability (precision, accuracy): Very few results**
- **Robustness of the test: Very few results**

ADAMTS-13 activity testing by FRET

(Fluorescence Resonance Energy Transfer)

Assessment (clinical benefit)

- **Annual volume anticipated: 200 tests /year**
- **Without treatment: mortality 85% to 100%**
- **Health benefits: High**
- **Risks: low**

ADAMTS-13 activity testing by FRET

(Fluorescence Resonance Energy Transfer)

Assessment (other issues)

- **Economic issues: No results**
- **Literature concerning organizational issues: No results**

ADAMTS-13 activity testing by FRET

(Fluorescence Resonance Energy Transfer)

Recommendation process (1)

- **The assessment is discussed by the members of the Scientific Committee**
- **Since data were lacking, a combination of clinical experience and expert consensus was used**
- **Questions concerning organizational, ethical, professional, legal and social issues were addressed to the clinical expert of the Committee (Haematologist)**

ADAMTS-13 activity testing by FRET

(*Fluorescence Resonance Energy Transfer*)

Recommendation process (2)

- **The Scientific Committee made the recommendation**
  - **Entry to the *Index* under certain conditions (periodic assessment of the test)**
  - **It is the most sensitive analysis that exists; there's no better test.**
  - **The clinical need is so important that it is appropriate to introduce it even if the clinical validity is not fully proven.**

- **The Scientific Committee send the recommendation to INESSS's CEO**

ADAMTS-13 activity testing by FRET

(Fluorescence Resonance Energy Transfer)

Recommendation process (3)

- **INESSS's CEO accept the recommendation and send it to the Minister of health and Social Services**
- **The Minister approves or rejects the recommendations**
- **INESSS publishes the Notices to the Minister on its website, which set out the recommendations made and their rationale (60 days after sending them to the Minister)**

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