SEPTEMBER 2019

RECOMMENDATIONS AND GUIDELINES

/Summary

POST-PRECANCEROUS CERVICAL LESION TREATMENT MONITORING

e-cancer.fr

INSTITUT NATIONAL DU CANCER

The French National Cancer Institute (INCa) is the health and scientific expertise agency in the field of cancer care responsible for coordinating cancer control in France.

The scientific coordination of these guidelines was conducted by the French National Cancer Institute.

The following collaborators contributed to this project: Société française de colposcopie et de pathologie cervico-vaginale (SFCPCV), le Collège national des gynécologues et obstétriciens français (CNGOF), la Fédération nationale des collèges de gynécologie médicale (FNCGM), la Société française de gynécologie (SFG), la Société française d'oncologie gynécologique (SFOG), la Société française de cytologie clinique (SFCC), la Société française de pathologie (SFP), la Société française de gynécopathologie (SFGP), la Société française de microbiologie (SFM), le Centre national de référence des papillomavirus humains (CNR HPV), la Société de pathologie infectieuse de langue française (SPILF), le Collège de la médecine générale (CMG), regional cancer screening coordination centres and regional oncology networks. A few patients also expressed their point of view as independent expert reviewers.

It is recalled that the guidelines cannot envisage all clinical scenarios and cannot therefore be seen as a substitute for the physician's judgement and responsibility to their patient.

It has received financial support from Unicancer within the framework of the guideline programme.

TABLE OF CONTENTS

DECISION TREES

ABBREVIATIONS

ANAES: Agence nationale d'accréditation et d'évaluation en santé [French National Agency for Health Accreditation and Evaluation]
CMG: Collège de la médecine générale [French College of General Medicine]
CNGOF: Collège national des gynécologues et obstétriciens français [French National College of Gynaecologists and Obstetricians]
CNR HPV: French national reference centre for human papillomavirus
FNCGM: Fédération nationale des collèges de gynécologie médicale [French National Federation of Medical Gynaecology Colleges]
HPV: Human papillomavirus
INCa: French National Cancer Institute
SFCC: Société française de cytologie clinique [French Society for Clinical Cytology]
SFCPCV: Société française de colposcopie et de pathologie cervico-vagniale [French Society for Colposcopy and Cervico-Vaginal Diseases]
SFG: Société française de gynécologie [French Gynaecology Society]
SFGP: Société française de gynécopathologie [French Society for Gynaecological Diseases]
SFM: Société française de microbiologie [French Microbiology Society)
SFOG: Société française d'oncologie gynécologique [French Society for Gynaecological Oncology]
SFP: Société française de pathologie [French Pathology Society)
SPILF: Société de pathologie infectieuse de langue française [French-language Society for Infectious Diseases]

INTRODUCTION

The incidence and mortality of invasive cervical cancers (2,835 new cases and 1,084 estimated deaths in 2017) have been falling in France for more than 30 years thanks, in particular, to screening. Until recently, the only test recommended was cervico-uterine cytology, enabling the detection of precancerous lesions or early-stage cancers. Primary screening arrangements have now evolved: the performance of a cervico-uterine cytology test is recommended for women between 25 and 30 years of age, followed by an HPV test between the ages of 30 and 65.

One of the objectives of the 2014–2019 Cancer Plan is to combat inequalities in terms of access to and referral for cervical cancer screening, based on a national organised screening programme.

In order to support the widespread implementation of organised screening and take into account the literature accumulated since 2002, evolving practices and current medical demographics, in 2016 the French National Cancer Institute (INCa) published an update of the 2002 ANAES guidelines concerning the management of women with abnormal cervical cytology.

However, these 2016 recommendations, drawn up with the aim of preventing unnecessary cone biopsies and minimising over-treatment, stopped at the definition of diagnostic strategies in the event of abnormal cytology and treatment strategies in the event of a precancerous lesion confirmed by histology. Therefore, the post-treatment monitoring strategy for precancerous histological lesions that continued to be applied was that of 2002, despite the recommended treatments and their indications having changed. However, appropriate monitoring is necessary because, although the data in the literature does not enable estimation of the cervical cancer risk following the treatment of a low-grade squamous intraepithelial lesion, a recent study demonstrated an increased risk of cervical cancer following the treatment of a high-grade lesion compared to the general population (from 1.4 to 2.6 times higher depending on the histological type of the initial lesion), as well as after conservative treatment for adenocarcinoma in situ (around 8 times higher).

Furthermore, while in 2002 monitoring was primarily based on colposcopy combined with cytology, a large number of publications since then have concerned the benefit of using the HPV test in these situations. Several international guidelines have also incorporated the HPV test in the post-treatment monitoring of precancerous lesions. It thus appeared to be necessary to reassess the positions of the various options compared to those recommended in 2002.

The French National Cancer Institute is therefore providing healthcare professionals with updated guidelines relative to the monitoring of patients treated for precancerous histological lesions of the cervix, in line with the guidelines published in 2016.

This document reiterates the main elements detailed in the thesaurus, which can be downloaded from the INCa website (e-cancer.fr).

OBJECTIVES AND TARGETS

These national guidelines are aimed at professionals involved in the care pathway of women confronted with this situation (in particular, gynaecologists, general practitioners, colposcopists, cytopathologists, virologists and biologists).

The patients concerned by these guidelines are those eligible for cervical cancer screening[1] and who are immunocompetent. As knowledge currently stands, the management will be the same for vaccinated and non-vaccinated women. However, these guidelines do not concern immunocompromised patients since the diversity of situations covered by this population is too great and there is little or no associated literature; moreover, these patients were not concerned by the 2016 guidelines.

It is recalled that the guidelines cannot envisage all clinical scenarios and cannot therefore be seen as a substitute for the physician's judgement and responsibility to their patient.

Participation in clinical trials should be encouraged, particularly in the absence of a reference clinical strategy. The implementation of studies addressing questions for which the literature is still fragmented should also be encouraged.

GUIDELINES

GENERAL MESSAGES

The various managements, depending on the initial lesion treated, are presented schematically in the decision trees. However, a few general messages may be highlighted.

The term "high-risk HPV test" refers to the use of a test that can detect the presence of a high-risk HPV, i.e. HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68 +/-66 (whether or not the test used enables specification of the high-risk HPV genotypes detected).

It is recalled that a high-risk HPV test must be performed in a facility involved in an accreditation process and with a validated cell collection medium and HPV test.

In general, for all the lesions taken into consideration in these guidelines, post-treatment monitoring will begin with the performance of a high-risk HPV test 6 months post-treatment:

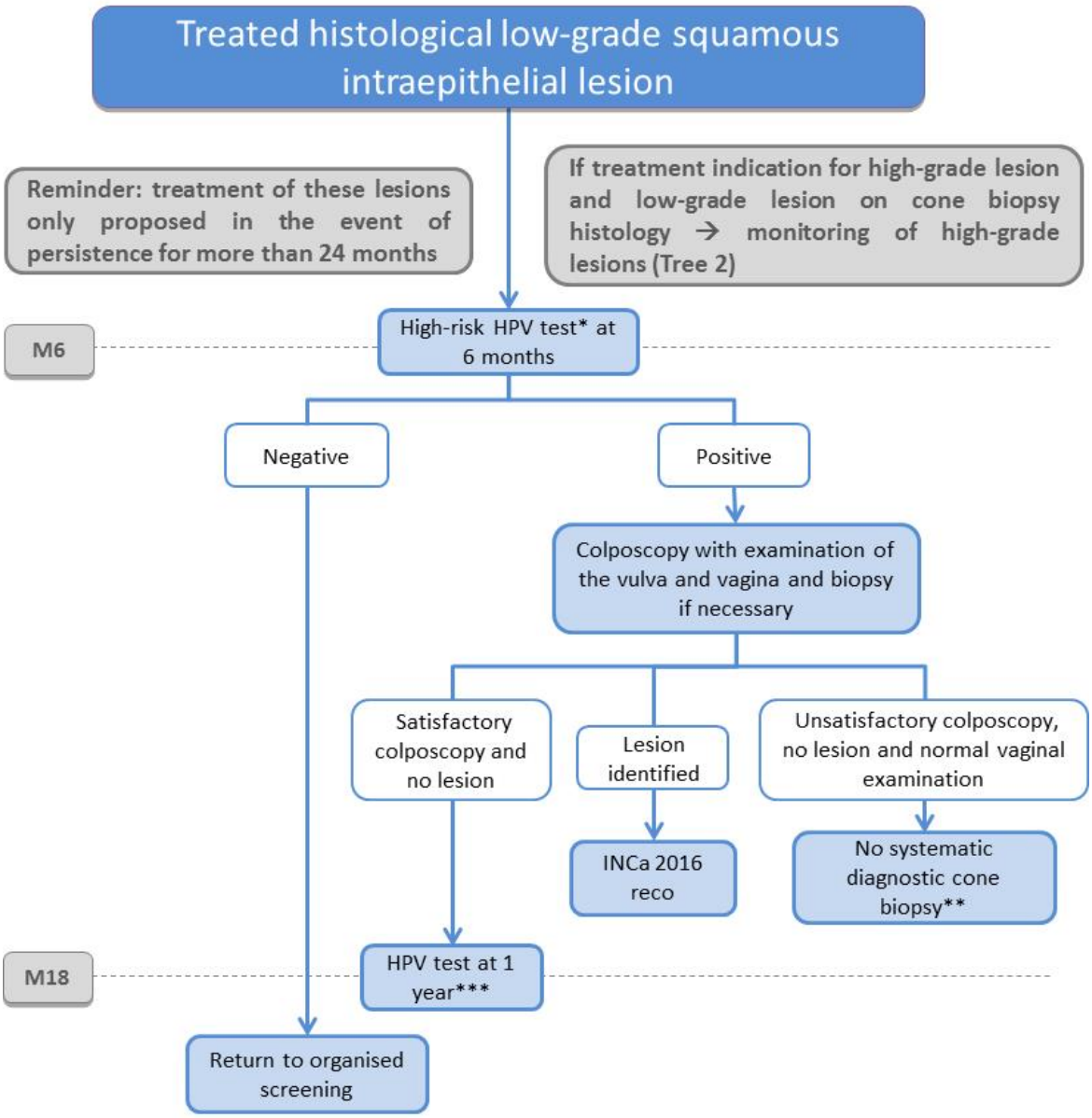
- if the result of this test is positive, the subsequent management will be the same for all scenarios;
- if the result of this test is negative, subsequent monitoring will differ depending on the patient's risk of developing a further cervical or vaginal lesion.

The grades of the guidelines are not indicated in the trees presented in this document but are associated with the text of the guidelines in the thesaurus, which can be downloaded online.

[1] Women aged 25 to 65 years.

POST-LOW-GRADE SQUAMOUS INTRAEPITHELIAL LESION TREATMENT MONITORING

TREE 1. MONITORING OF PATIENTS TREATED FOR A HISTOLOGICAL LOW-GRADE SQUAMOUS INTRAEPITHELIAL LESION



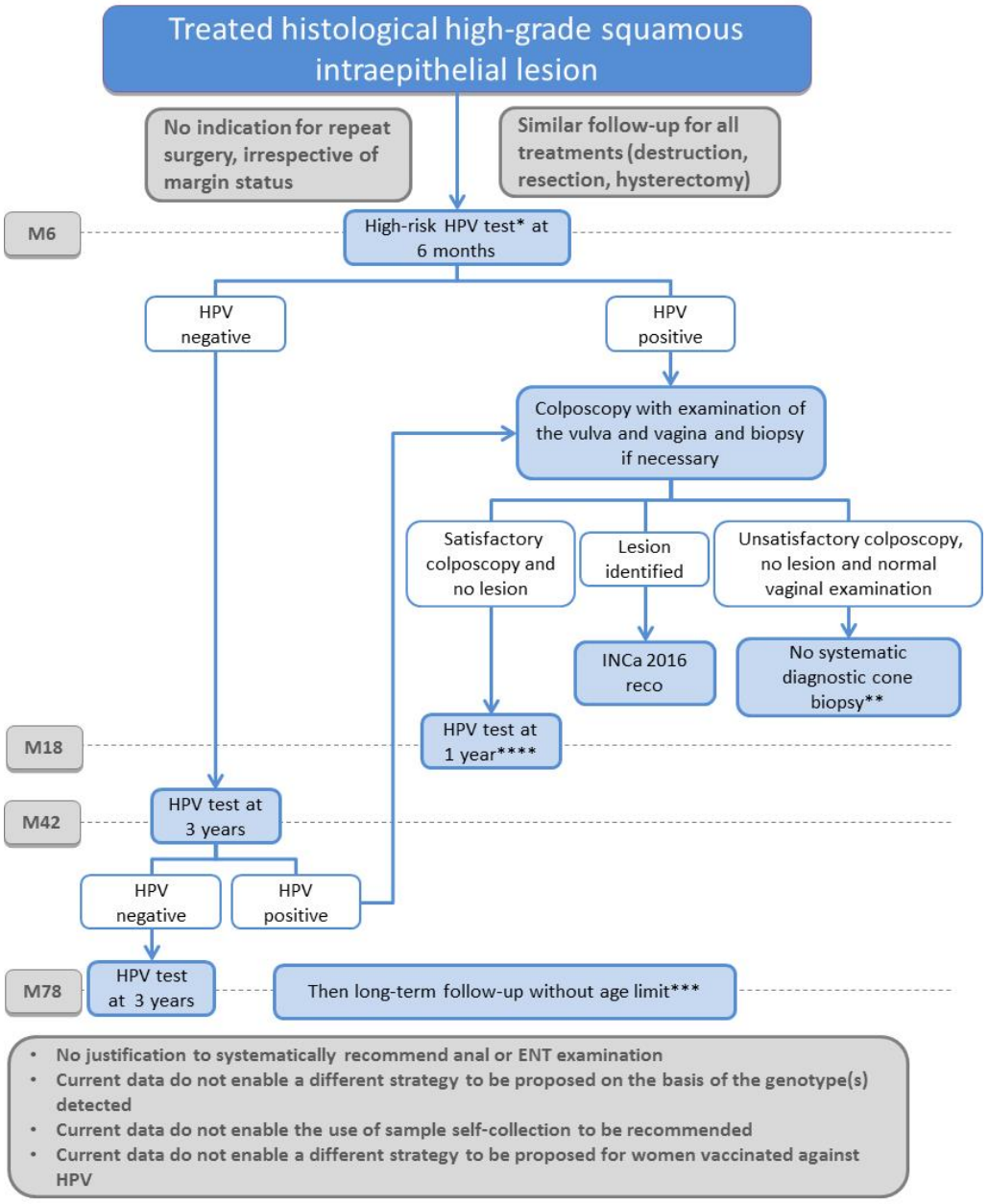
* High-risk HPV test performed in a facility involved in an accreditation process and with a validated cell collection medium and HPV test.

** The data in the literature do not enable a particular strategy to be recommended, particularly diagnostic cone biopsy. Existing tools (new colposcopy in optimal conditions, cytology, endocervical curettage, HPV test) may be used to decide the management.

*** If positive: colposcopy with examination of the vulva and vagina +/- biopsies. If negative: HPV test at 3 years.

POST-HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESION TREATMENT MONITORING

TREE 2. MONITORING OF PATIENTS TREATED FOR A HISTOLOGICAL HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESION



* High-risk HPV test performed in a facility involved in an accreditation process and with a validated cell collection medium and HPV test.

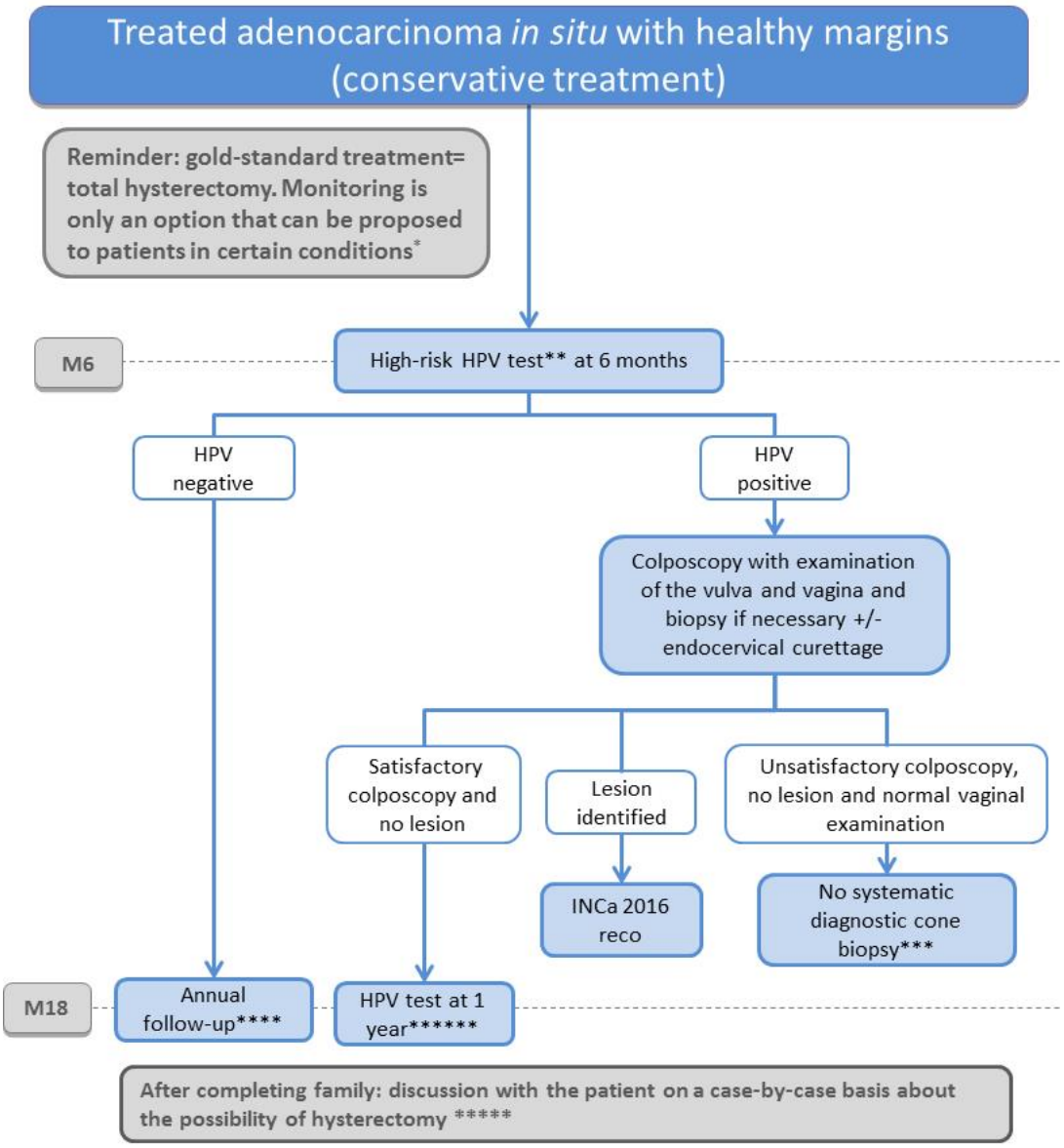
** The data in the literature do not enable a particular strategy to be recommended, particularly diagnostic cone biopsy. Existing tools (new colposcopy in optimal conditions, cytology, endocervical curettage, HPV test) may be used to decide the management.

*** The data in the literature do not enable precise determination of the arrangements and frequencies for long-term monitoring.

**** If positive: colposcopy with examination of the vulva and vagina +/- biopsies. If negative: HPV test at 3 years.

POST-ADENOCARCINOMA *IN SITU* TREATMENT MONITORING

TREE 3. MONITORING OF PATIENTS HAVING UNDERGONE CONSERVATIVE TREATMENT WITH NEGATIVE MARGINS FOR ADENOCARCINOMA *IN SITU*



***** If the patient, having been informed about the risks of recurrence, plans to have children, wishes to favour conservative treatment and agrees to the current monitoring principles.

* High-risk HPV test performed in a facility involved in an accreditation process and with a validated cell collection medium and HPV test.

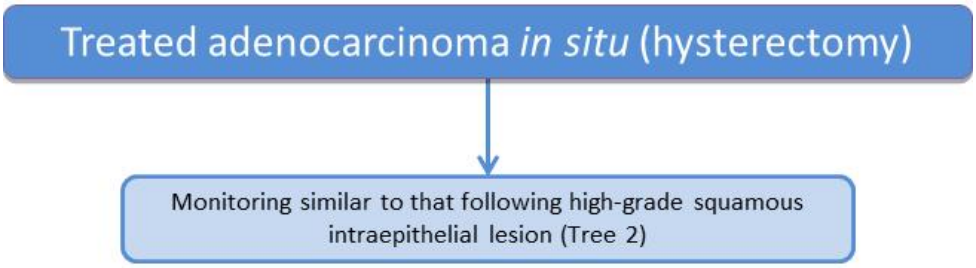
******* The data in the literature do not enable a particular strategy to be recommended, particularly diagnostic cone biopsy. Existing tools (new colposcopy in optimal conditions, cytology, endocervical curettage, HPV test) may be used to decide the management.

******** The data in the literature do not allow for any recommendations regarding the precise conditions of this monitoring, which will therefore be based on existing investigations (cytology, HPV test, colposcopy, endocervical curettage).

********* Given the higher long-term risk of invasive cancer and the monitoring difficulties, particularly colposcopic.

****** If positive: colposcopy with examination of the vulva and vagina +/- biopsies. If negative: HPV test at 3 years.

TREE 4. MONITORING OF PATIENTS HAVING UNDERGONE A HYSTERECTOMY FOR ADENOCARCINOMA *IN SITU*



METHODOLOGY

GUIDELINE FORMULATION

The guidelines formulation methodology is detailed in the thesaurus, available to download from the French National Cancer Institute (INCa) website.

It was based on:

- critical analysis of the best scientific data available used to assign a level of evidence to the findings of the literature;
- and the justified opinion of the experts of the working group.

A systematic bibliographic search was conducted over the period from 1 January 2002 or 1 January 2008 (depending on the chapters and amount of literature available) to 1 April 2019. The bibliographic search, analysis of the literature and summary of the scientific data were performed by the French National Cancer Institute, with the support of the working group. The guidelines were formulated by the multidisciplinary working group, coordinated by INCa. The guidelines were subsequently reviewed by a panel of independent reviewers from the working group by means of quantitative (grading) and qualitative (observations) reviews. The members of the working group finally reviewed the compiled observations with a view to finalising the document at a final meeting.

LEVELS OF EVIDENCE

The level of evidence consists of the ranking of the data of the literature on which the formulated guidelines are based. It is dependent on the type and quality of the studies available. Details of the levels of evidence used are provided in the thesaurus. The findings of the literature were subsequently summarised and assigned a level of evidence according to the scale described in the thesaurus.

GRADING OF GUIDELINES

Each guideline is associated with a grade according to the scale described in the thesaurus and based on the level of evidence of the literature and the expert review by the working group and the reviewers. **In the absence of any literature or when the level of evidence of the data in the literature was judged to be too weak, the working group chose not to formulate a guideline.**

WORKING GROUP SET-UP

These national guidelines were formulated by a multidisciplinary working group representing the specialisations and types of practice concerned by the monitoring of patients treated for a precancerous cervical lesion.

The experts in this working group were appointed by the French National Cancer Institute (INCa) following a call for experts published on its website and relayed by learned societies (SFCPCV, CNGOF, FNCGM, SFG, SFCC, SFP, CNR HPV, SPILF, CMG) and regional screening coordination centres. INCa then selected the experts following an analysis of their declarations of interests and their *curriculum vitae*.

The professionals in the national review group were proposed by learned societies with an interest in the scope of the guidelines and regional cancer networks (detailed in the thesaurus).

WORKING GROUP, COORDINATION AND EXPERT REVIEWERS

The experts of the working group were consulted *intuitu personae* and not as a representative of an organisation, learned society or group of professionals.

The French National Cancer Institute (INCa) selected the experts following an analysis of their declarations of interests, published on the DPI-SANTE website, and their *curriculum vitae*. The composition of the working group was submitted to the INCa's Expert Review Commission.

WORKING GROUP

Dr AVÉROUS Gerlinde, pathologist, CHU Hautepierre, Strasbourg (scientific coordinator)
Prof. CARCOPINO Xavier, gynaecologist-obstetrician, Hôpital Nord, Marseille (scientific coordinator)
Prof. PRÉTET Jean-Luc, cell biologist, Université de Bourgogne Franche-Comté and CHRU, Besançon (scientific coordinator)
Dr BERGERON Christine, pathologist, Laboratoire Cerba, Cergy-Pontoise
Dr BORNE Hélène, medical gynaecologist, non-hospital practice, Paris and CH des Quatre villes, Saint-Cloud
Prof. BRUN Jean-Luc, gynaecologist-obstetrician, CHU de Bordeaux
Dr CARTIER Isabelle, pathologist, laboratoire Cartier, Paris
Prof. CLAVEL Christine, biologist, CHU/URCA pathology laboratory, Reims
Dr COCHAND-PRIOLLET Béatrix, pathologist, Hôpital Cochin, Paris
Dr DE REILHAC Pia, medical gynaecologist, non-hospital practice, Nantes
Dr DEVAL-SÉCHERRE Véronique, advising physician, Regional cancer screening coordination centre - Charente regional site, Angoulême
Prof. FAURE Karine, infectiologist, CHRU, Lille
Dr GODARD Jean, general practitioner, non-hospital practice, Val-de-Saâne
Prof. GONDRY Jean, gynaecologist-obstetrician, Université Jules Vernes, Inserm and CHU, Amiens
Prof. LEVÊQUE Jean, gynaecologist-obstetrician, CHU/Centre Eugène Marquis, Rennes
Dr MARUANI Julia, medical gynaecologist, AP-HM and non-hospital practice, Marseille
Dr MERGUI Jean-Luc, gynaecologist-obstetrician, Hôpital de la Pitié-Salpêtrière/non-hospital practice, Paris
Dr MOUSTÉOU Françoise, medical gynaecologist, non-hospital practice, Cagnes-sur-Mer
Prof. PAYAN Christopher, virologist, Université de Bretagne Occidentale and CHRU Cavale Blanche, Brest
Dr PÉRÉ Hélène, virologist, Hôpital Européen Georges Pompidou, Paris
Dr RIMAILHO Jacques, general surgeon and medical gynaecologist, Hôpital de Rangueil, University and non-hospital practice, Toulouse
Dr SENGCHANH-VIDAL Somany, coordinating physician, Centre - Val de Loire Regional cancer screening coordination centre, Tours
Dr THOMAS Nadia, coordinating physician, Regional cancer screening coordination centre, Cayenne (French Guiana)

Withdrawal from the working group: Dr BUNGE Lucie, general practitioner, municipal health centre and non-hospital practice, Saint-Denis (withdrawal after the launch meeting but before the start of the scientific work and guidelines formulation)

PROJECT COORDINATION
BY THE FRENCH NATIONAL CANCER INSTITUTE

MOROIS Sophie, project manager in Best Practices Department
DUPERRAY Marianne, head of Best Practices Department
Dr DAHAN Muriel, Director of Guidelines and Medicines Division (up to February 2019)
VERMEL Christine, head of Expert Review Quality and Conformity team

NATIONAL REVIEW

The list of the 99 reviewers is available in the thesaurus, available to download from the INCa website (e-cancer.fr).

Notes

Notes

INSTITUT NATIONAL DU CANCER

52, avenue André Morizet
92100 Boulogne-Billancourt
France

Tel. +33 (1) 41 10 50 00
diffusion@institutcancer.fr

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