NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of Diagnostics Guidance DG11; Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel

Final recommendation post consultation
Transfer the guidance to the 'static guidance list' with a post publication update to reflect the publication of the updated NICE guideline on suspected cancer.

1. Background

This guidance was issued in October 2013.

At the GE meeting of 24 January 2017 it was agreed that we would consult on the recommendations made in the GE proposal paper. A four week consultation has been conducted and the responses are presented below.

2. Proposal put to stakeholders

Transfer the guidance to the 'static guidance list' with a post publication update to reflect the publication of the updated NICE guideline on suspected cancer.

3. Rationale for selecting this proposal

Changes in clinical practice, technology costs or evidence that would lead to a change in the recommendations of the original guidance have not been identified. It is therefore proposed that the guidance is placed on the static list.

4. Summary of consultation comments

Comments received during consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the comments received, and are not endorsed by NICE, its officers or advisory committees.

Respondent: NHS Professional **Response to proposal:** Agree No comments. Accept all the updated evidence and recommend that the guidance remains in place.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE.

Respondent: Royal College of Pathologists **Response to proposal:** Agree I would agree with the conclusion. The DO-IT programme pathway is still in consultation and the cut-off values remain undefined. It's likely a set of values will be proposed but it will also retain scope for flexibility around the statement from the BSG that 'It is recommended that threshold values regarded to be raised significantly are determined on the basis of local audit data, and assay used.'	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE.

Respondent: Royal College of Pathologists **Response to proposal:** No comment One other point to consider might be the introduction of an upper age limit when using calprotectin to rule out IBD in a patient with symptoms of IBD – the DO-IT pathway is proposing a limit of 40	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. NICE may review guidance before the expected review date when there is significant new evidence that it considers is likely to change the recommendations. NICE is keen to hear about any new evidence that becomes available before the review date (please send information to diagnostics@nice.org.uk). NICE will assess the likely impact of the new evidence on the recommendations and will propose an update to the published guidance if required.

Respondent: Royal College of Pathologists **Response to proposal:** Agree I am not aware of any new evidence to suggest anything other than transferring the guidance to the 'static guidance list'.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE.

Respondent: British Society of Gastroenterology **Response to proposal:** Agree We agree with the conclusion that no substantive new evidence has altered the conclusions of DG11	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE.

Respondent: Royal College of Physicians **Response to proposal:** Agree We would like to endorse the response submitted by the British Society of Gastroenterology.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE.

Respondent: Calpro **Response to proposal:** No comment “Phical Calprotectin ELISA has been renamed as IDK Calprotectin ELISA” must be changed to: - renamed to Calpro Calprotectin ELISA”	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing clarification on this point. A table has been added to the end of this document (appendix 1) that lists any changes made to the names of faecal calprotectin tests included in DG11 since its publication.

Respondent: Calpro **Response to proposal:** No comment “Calpro, formerly known as the Phical Test CALP017”. Must be removed. The product CALP0170 was launced in 2011 under the name “Calprolab” (Calpro is the company name). Is a second-generation product of our ELISA assays.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing clarification on this point. A table has been added to the end of this document (appendix 1) that lists any changes made to the names of faecal calprotectin tests included in DG11 since its publication.

Respondent: Calpro **Response to proposal:** No comment Calprosmart Office, name of manufacturer is “Calpro”. The product is CE-marked and available in UK	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing this additional information.

Respondent: Calpro **Response to proposal:** No comment Calpro has launced Calprosmart Self-Test for home monitoring. The product is CE-marked, approved by Notified Body (Llloyds/LRQA) in UK and available in UK. Scientific publication where this system has been used, see “Fecal Calprotectin Measured By Patients at Home Using Smartphones -*A new Clinical Tool in Monitoring Patients with Inflammatory Bowel Disease”*, Kristoffer Kofod Vinding, MD, Henriette Elsbjerg, MB, Erika Belard, MD, Natalia Pedersen, MD, Margarita Elkjaer, MD, PhD, Dorte Marker, Katrine Carlsen, MD, Johan Burish, MD, and Pia Munkholm, MD, DSc, *Inflamm Bowel Dis, v. 0, No. 0, 2015*	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. It was noted in the review proposal document for DG11 that other faecal calprotectin tests that are intended for home-use are available (page 5). However, the use of faecal calprotectin tests in this setting is outside the scope of DG11 - which is concerned with the use of the test in primary care and secondary care (as set out in section 4.2 of the final scope for the assessment). NICE wishes to encourage manufacturers to notify the NICE medical technologies evaluation programme of tests that could be considered for further NICE guidance. Details of how to notify medical technologies (including diagnostics) can be found on the medical technologies evaluation programme webpage.

Respondent: Immundiagnostik AG **Response to proposal:** No comment The observation “PhiCal Calprotectin ELISA has been renamed as IDK Calprotectin ELISA.” belongs to ELISA (K6927) (Immundiagnostik), who was also formerly known as “PhiCal”. It does not belong to CALPRO CALPROTECTIN ELISA TEST (ALP) CAL0100 (Calpro, formerly known as the Phical test CAL0100).	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing clarification on this point. A table has been added to the end of this document (appendix 1) that lists any changes made to the names of faecal calprotectin tests included in DG11 since its publication.

Respondent: Immundiagnostik AG **Response to proposal:** No comment Please replace the 3 rapid test by Preventis with: 1. PreventID® Cal Detect® (KST11005) (Preventis) 2. PreventID® Cal Detect® 50 / 200 (KST11003) (Preventis) 3. PreventID® Cal Screen® (KST11004) (Preventis)	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing clarification on this point. A table has been added to the end of this document (appendix 1) that lists any changes made to the names of faecal calprotectin tests included in DG11 since its publication.

Respondent: Immundiagnostik AG **Response to proposal:** No comment Please add: “Preventis QuantOn Cal® Calprotectin home test, CE-marked”. QuantOn Cal® is a test system for the quantitative determination of faecal calprotectin, intended for self-testing by the patient using a rapid test and the patient’s smartphone, which transmits anonymysed results securely to the doctor’s patient management portal. It is available in the UK and it is CE-marked.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. It was noted in the review proposal document for DG11 that other faecal calprotectin tests that are intended for home-use are available (page 5). However, the use of faecal calprotectin tests in this setting is outside the scope of DG11 - which is concerned with the use of the test in primary care and secondary care (as set out in section 4.2 of the final scope for the assessment). NICE wishes to encourage manufacturers to notify the NICE medical technologies evaluation programme of tests that could be considered for further NICE guidance. Details of how to notify medical technologies (including diagnostics) can be found on the medical technologies evaluation programme webpage.

Respondent: Immundiagnostik AG **Response to proposal:** No comment “using the PhiCal ELISA-based test” on page 6: Holtman et al. had several publications in 2016, and I think you mean to cite the review (Pediatrics. 2016;137(1):e20152126) here, but no specific Calprotectin test is mentioned in it. Also, the reference isn’t included in the reference list. In section 6.3.2 Primary care you correctly cite the publication Ann Fam Med 2016;14:437-445. doi: 10.1370/afm.1949, which is included in the reference list.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing clarification on this point. The Holtman et al. (2016) study referenced on page 6 of the review proposal does refer to the Pediatrics, 137 (1) paper – which is included in the reference list of the review proposal. No specific faecal calprotectin test is mentioned in this study. The Holtman et al. (2016) study referred to on page 7 of the review proposal (which was omitted from the reference list) is referenced below: Holtman GA, Leeuwen YLB, Kollen BJ et al. (2016) Diagnostic Accuracy of Fecal Calprotectin for Pediatric Inflammatory Bowel Disease in Primary Care: A Prospective Cohort Study. Ann Fam Med., 14(5): 437-45.

Respondent: Immundiagnostik AG **Response to proposal:** No comment Please replace “using the PhiCal ELISA-based test” with “using the PhiCal Calpro ALP ELISA-based test”.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing clarification on this point. All data in the review proposal is presented along with an accompanying literature reference, from which the faecal calprotectin test used in the study and details on the test methodology used can be found.

Respondent: Immundiagnostik AG **Response to proposal:** No comment Please change “Immunodiagnostik” to “Immundiagnostik”.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing clarification on this point.

Respondent: Immundiagnostik AG **Response to proposal:** No comment Please replace “measured using the PhiCal ELISA-based test” with “using the PhiCal Calpro ALP ELISA-based test”.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing clarification on this point. All data in the review proposal is presented along with an accompanying literature reference, from which the faecal calprotectin test used in the study and details on the test methodology used can be found.

Respondent: Immundiagnostik AG **Response to proposal:** No comment Dhaliwal et al. (2015): Please replace “PhiCal v1” or “PhiCal v2” with “Immundiagnostik PhiCal v1” or “Immundiagnostik PhiCal v2”.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing clarification on this point. All data in the review proposal is presented along with an accompanying literature reference, from which the faecal calprotectin test used in the study and details on the test methodology used can be found.

Respondent: Immundiagnostik AG **Response to proposal:** No comment Okuyama et al. (2016): Please replace “PhiCal Calprotectin” with “Immundiagnostik PhiCal Calprotectin”.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for providing clarification on this point. All data in the review proposal is presented along with an accompanying literature reference, from which the faecal calprotectin test used in the study and details on the test methodology used can be found.

Paper signed off by: Sarah Byron, 9th March 2017

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Appendix 1

Since DG11 published, several of the faecal calprotectin tests mentioned in the guidance document have been renamed as set out in table 1.

Table 1 Changes to technologies included in guidance

Technology name in DG11	Currently known as
EK-CAL calprotectin ELISA test (Range: 10–600 micrograms/g; Bühlmann)	BÜHLMANN ® fCAL ELISA (different kits are available in this format: EK-CAL is a single ELISA plate kit, EK-CAL2 is a double ELISA plate kit, EK-CAL2-WEX is a double ELISA plate kit for use with the CALEX extraction device. For all these kits the two assay ranges are possible – 10-600 and 30-1800 micrograms/g using two different assay protocols).
EK-CAL calprotectin ELISA test (Range: 30–1800 micrograms/g; Bühlmann)	BÜHLMANN fCAL® ELISA
LF-CAL25 Quantum Blue calprotectin test (Bühlmann) (Range 30 – 300 micrograms/g)	BÜHLMANN Quantum Blue ® fCAL
LF-CHR 25 Quantum Blue calprotectin test (Bühlmann) (Range 100 – 1800 micrograms/g)	BÜHLMANN Quantum Blue® fCAL High Range
ELISA (K6927) (Immundiagnostik)	IDK Calprotectin ELISA (K6927) (Immundiagnostik)

KST11005 CalDetect Calprotectin Rapid test (version 1 – Caldetect; Preventis)	PreventID Cal Detect (KST11005) (Preventis)
Preventis (sister company to Immundiagnostik) CalDetect Calprotectin Rapid test (version 3 – CalScreen)	PreventID Cal Detect 50 / 200 (KST11003) (Preventis)
CalDetect Calprotectin Rapid test (version 3 – CalScreen; Preventis)	PreventID Cal Screen (KST11004) (Preventis)