NHS Lothian

Lothian NHS Board

COLORECTAL CANCER GENE PANEL TESTING PRO FORMA

Patient details *(printed label preferred)*			
Forename(s):		***Sex:***	
Surname:		***Patient ID:***	
DOB:		***Pedigree no.***	
CHI:		***Referrer:***	

Clinical Summary:

Clinical information ***(type of cancer, age of onset, family history)***	***Tumour information***	
	☐	MSI high
	☐	MMR loss of staining (please detail):
	☐	IHC uninformative
	☐	*BRAF* variant detected
	☐	*MLH1* promoter hypermethylation
	☐	Tumour unavailable

Testing requested (please see test directory for specific referral criteria)

Sequence analysis of the colorectal gene cancer panel is undertaken for ALL patients (see genes below):

APC, *BMPR1A*, *MBD4*[‡], *MLH1*, *MSH2*, *MSH3*[‡], *MSH6*, *MUTYH*, *NTHL1*, *PMS2*[§], *POLD1* (exons 4-12), *POLE* (exons 3-13), *PTEN*, *RNF43*, *SMAD4*, *STK11*

[‡]biallelic truncating variants only

[§]*PMS2* analysis includes 1-10; exons 11-15 cannot be reliably investigated by this method due to the presence of the *PMS2CL* pseudogene. These exons are analysed using long range PCR when PMS2 testing is indicated i.e., isolated loss of PMS2 staining in tumour tissue.

Dosage analysis is conducted according to clinical indication as outlined below.

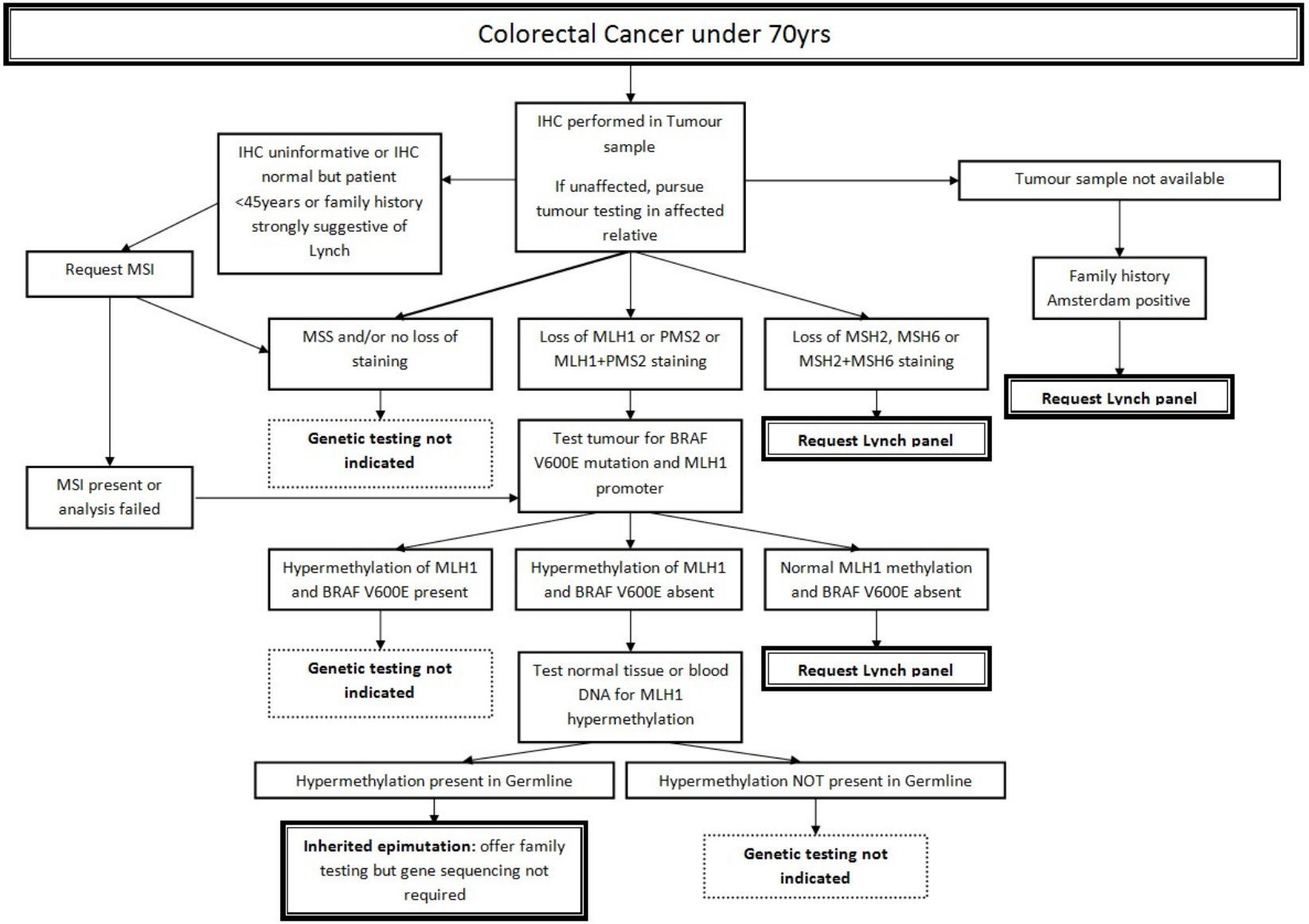
☐ **Please tick (or double click)** to select

Select	Clinical Indication	Additional test details including dosage analysis (MLPA)
☐	**Polyposis** ☐ Desmoid tumour * ☐ CHRPEs **	*APC*, *MUTYH* (selected exons), and *GREM1* (upstream region) * only *APC* and *MUTYH* variants reported ** only *APC* variants reported
☐	**Lynch Syndrome** *(see overleaf for guidelines)*	*MLH1*, *MSH2*, *MSH6* and *EPCAM* (selected exons) *PMS2* only if indicated i.e., isolated loss of PMS2 staining in tumour tissue
☐	**Colorectal Cancer** ☐ patient dx <45yrs	**None as standard** Lynch dosage (see above) will be undertaken for patients dx <45yrs
☐	**Peutz-Jeghers Syndrome**	*STK11*
☐	**Juvenile Polyposis Syndrome**	*SMAD4* and *BMPR1A*
☐	**Hereditary Diffuse Gastric Cancer**	Patients will ONLY be analysed for *CDH1* gene (sequencing and dosage analysis)

Additional sequencing analysis for the following gene panels can be included if clinically indicated:

Breast	☐	*BRCA1*[¤], *BRCA2*[¤], *PALB2*, *PTEN*, *STK11*, *TP53*, *ATM*[#], *CHEK2*[#], *RAD51C*, *RAD51D* [#]Reporting truncating variants only and the ATM variant c.7271T>G p.(Val2424Gly). Please note CHEK2 analysis is restricted to exons 1 to 9 plus the common c.1100delC variant due to the presence of a pseudogene
Ovarian	☐	*BRCA1*[¤], *BRCA2*[¤], *BRIP1*, *MLH1*, *MSH2*, *MSH6*, *RAD51C*, *RAD51D*

[¤]Dosage analysis will be conducted separately by the Aberdeen laboratory


Colorectal Cancer under 70yrs
IHC performed in Tumour sample
If unaffected, pursue tumour testing in affected relative
IHC uninformative or IHC normal but patient <45years or family history strongly suggestive of Lynch
Request MSI
Tumour sample not available
Family history Amsterdam positive
Request Lynch panel
MSS and/or no loss of staining
Loss of MLH1 or PMS2 or MLH1+PMS2 staining
Loss of MSH2, MSH6 or MSH2+MSH6 staining
Genetic testing not indicated
Test tumour for BRAF V600E mutation and MLH1 promoter
Request Lynch panel
MSI present or analysis failed
Hypermethylation of MLH1 and BRAF V600E present
Hypermethylation of MLH1 and BRAF V600E absent
Normal MLH1 methylation and BRAF V600E absent
Genetic testing not indicated
Test normal tissue or blood DNA for MLH1 hypermethylation
Request Lynch panel
Hypermethylation present in Germline
Hypermethylation NOT present in Germline
Inherited epimutation: offer family testing but gene sequencing not required
Genetic testing not indicated