Supplemental Table 1. **Criteria used for ascertaining provider suspicion of pathogenicity**

	Evidence of Suspicion of Pathogenicity	No Evidence of Suspicion of Pathogenicity
General	• Mention of other labs' classifications as pathogenic or likely pathogenic • Molecular diagnosis mentions that variant is possibly pathogenic or likely pathogenic • Option for "genetic testing recommended for deleterious mutation" marked (if no additional known deleterious P/LP variant is identified) • Molecular diagnosis describes variant as "suspicious" • Clinical or molecular diagnosis mentions possible influence of variant	• Molecular diagnosis of "[gene name] VUS" without evidence of suspicion • No additional screening beyond general population guidelines recommended for associated cancers • No genetic testing recommended for family members • Molecular diagnosis of "[gene name] mutation" when a known pathogenic variant was also identified, without mention of other variant • When a known pathogenic variant was also identified, genetic testing recommended only for known pathogenic variant
CDKN2A	• Pancreatic cancer screening recommended without personal or family history of pancreatic cancer • Dermatology exam recommended without personal or family history of skin cancer	• Clinical diagnosis of "sporadic melanoma" or "sporadic pancreatic cancer" • Dermatology exam and VUS tracking studies recommended in context of family history of melanoma, without evidence of suspicion • Dermatology exam recommended in context of personal history of melanoma, without evidence of suspicion
CHEK2	• Molecular diagnosis describes variant as "moderate risk" • Earlier or more frequent colonoscopies compared to general population in absence of personal or family history of colon cancer	• General population colonoscopy guidelines recommended • Clinical diagnosis of "familial breast cancer" without evidence of suspicion • Clinical diagnosis of "sporadic colon cancer" without evidence of suspicion
MLH1	• Earlier or more frequent colonoscopies compared to general population in absence of personal or family history of colon cancer	• Clinical diagnosis of "unexplained pancreatic cancer" • General population colonoscopy guidelines recommended
MUTYH	• Earlier or more frequent colonoscopies compared to general population in absence of personal or family history of colon cancer	• General population colonoscopy guidelines recommended

RAD51C	• Ovarian cancer screening and/or oophorectomy discussed or recommended	• Ovarian cancer screening and/or oophorectomy not discussed or recommended
TP53	• Whole body MRI recommended without a clinical diagnosis of LFS	• Clinical diagnosis of "sporadic breast cancer"

Supplemental Table 2. **Distribution of laboratory classifications of variants with conflicts when patient result was reported in 2014-2016**

Variant	Date	Count	Testing Lab	Lab 1	Lab 2	Lab 3	Lab 4	Lab 5	Lab 6	Lab 7	Lab 8	Expert Panel
APC												
c.3920T>A	11/2014	1	LPV	P	RF	LB						
	12/2015	3	LPV	P	RF	RF	RF	VUS				
	3/2016	1	LPV	P	RF	RF	RF	VUS	VUS			
	4/2016	1	LPV	P	RF	RF	RF	VUS	VUS			
	6/2016	1	LPV	P	RF	RF	RF	VUS	VUS			
	8/2016	1	LPV	P	RF	RF	RF	VUS	VUS			
	11/2016	2	LPV	P	RF	RF	RF	VUS	VUS		LP	
CDKN2A												
c.146T>C	11/2014	1	VUS	LP	VUS	VUS						
	7/2015	1	VUS	LP	VUS	VUS						
	8/2015	1	VUS	LP	VUS	VUS						
	11/2015	2	VUS	LP	VUS	LB						
	1/2016	1	VUS	LP	VUS	LB						
	3/2016	1	VUS	LP	VUS	LB						
	4/2016	1	VUS	LP	VUS	LB						
CHEK2												
c.1283C>T	12/2014	1	VUS	P	P							
	1/2015	1	VUS	P	P							
	10/2016	1	VUS	P	P	P	P			P		
	11/2016	1	VUS	P	P	P	P			P		
CHEK2												
c.1427C>T	5/2015	1	VUS	LP	P							
	3/2016	2	VUS	LP	P	VUS	VUS					
CHEK2												
c.349A>G	8/2014	1	VUS	LP	LP							
	9/2015	1	VUS	LP	LP							
CHEK2												
c.470T>C	9/2014	1	VUS	P	LP							
	3/2015	1	VUS	P	LP					P		
	5/2015	1	VUS	P	LP					P		
	7/2015	1	VUS	P	LP					P		
	3/2016	1	VUS	P	LP	P	LP			P	LP	
	8/2016	1	VUS	P	LP	P	LP	VUS		P	LP	
	11/2016	1	VUS	P	LP	P	LP	VUS	LP	P	LP	
CHEK2												
c.917G>C	11/2015	1	VUS	VUS	LP							
MLH1												
c.191A>G	7/2016	1	VUS	LP	VUS	VUS						LP
MSH2												
c.1046C>G	1/2015	1	VUS									LP
MUTYH												
c.857G>A	12/2014	1	VUS		P							
MUTYH												
c.934-2A>G	5/2015	2	LP	VUS	P	LP						
	6/2015	1	LP	VUS	P	LP						
	7/2015	2	LP	VUS	P	LP						
	8/2015	1	LP	VUS	P	LP						

	10/2015	1	LP	VUS	P	LP	
	6/2016	1	LP	VUS		LP	
	11/2016	1	LP	VUS	P	LP	
RAD51C **c.965+5G>A**	9/2016	1	VUS	LP		VUS	
TP53 **c.1040C>A**	9/2015	1	VUS	LP			
TP53 **c.374C>T**	2/2016	1	VUS	LP			LP

Count equals the number of individuals found to have the variant in which their report was issued in the particular month. Total count equals 50. Testing Lab is the laboratory at which the patient was tested. Labs 1 through 8 are other major commercial laboratories that had classifications submitted to ClinVar reflecting the classification at the time of the patient's report, and Expert Panel is a ClinVar-defined expert panel that had a classification submitted to ClinVar reflecting the classification at the time of the patient's report. P refers to a pathogenic/deleterious classification. LP refers to a likely pathogenic/suspected deleterious classification. LB refers to a likely benign/favor polymorphism classification. RF refers to a classification of "risk factor," and LPV refers to a classification of "low penetrance variant." Both terms are used to describe low penetrance pathogenic variants.

Supplemental Table 3. Complete HGVS Nomenclature for Variants with Conflicts

Gene	HGVS cDNA	HGVS gDNA (GRCh38)	HGVS protein
APC	NM_000038.6:c.3920T>A	NC_000005.10:g.112839514T>A	NP_000029.2:p.(Ile1307Lys)
CDKN2A	NM_000077.5:c.146T>C	NC_000009.12:g.21974682A>G	NP_000068.1:p.(Ile49Thr)
CHEK2	NM_007194.4:c.1283C>T	NC_000022.11:g.28695219G>A	NP_009125.1:p.(Ser428Phe)
CHEK2	NM_007194.4:c.1427C>T	NC_000022.11:g.28694066G>A	NP_009125.1:p.(Thr476Met)
CHEK2	NM_007194.4:c.349A>G	NC_000022.11:g.28725338T>C	NP_009125.1:p.(Arg117Gly)
CHEK2	NM_007194.4:c.470T>C	NC_000022.11:g.28725099A>G	NP_009125.1:p.(Ile157Thr)
CHEK2	NM_007194.4:c.917G>C	NC_000022.11:g.28699929C>G	NP_009125.1:p.(Gly306Ala)
MLH1	NM_000249.4:c.191A>G	NC_000003.12:g.36996693A>G	NP_000240.1:p.(Asn64Ser)
MSH2	NM_000251.3:c.1046C>G	NC_000002.12:g.47416399C>G	NP_000242.1:p.(Pro349Arg)
MUTYH[a]	NM_001128425.2:c.857G>A	NC_000001.11:g.45332242C>T	NP_001121897.1:p.(Gly286Glu)
MUTYH[b]	NM_001128425.2:c.934-2A>G	NC_000001.11:g.45332088T>C	NP_001121897.1:p.?
MUTYH[a]	NM_001048174.2:c.773G>A	NC_000001.11:g.45332242C>T	NP_001041639.1:p.(Gly258Glu)
MUTYH[b]	NM_001048174.2:c.850-2A>G	NC_000001.11:g.45332088T>C	NP_001041639.1:p.?
RAD51C	NM_058216.3:c.965+5G>A	NC_000017.11:g.58724105G>A	NP_478123.1:p.?
TP53	NM_000546.6:c.1040C>A	NC_000017.11:g.7670669G>T	NP_000537.3:p.(Ala347Asp)
TP53	NM_000546.6:c.374C>T	NC_000017.11:g.7675995G>A	NP_000537.3:p.(Thr125Met)

[a]These two variants are the same variant described using different transcripts. [b]These two variants are the same variant described using different transcripts. [a,b]NM_001128425.2 was utilized by the testing laboratory, and NM_001048174.2 is the MANE transcript.

***Supplemental Table 4*. Counseling strategy for patients with discrepant classifications of the same variant seen by the same provider**

(A) *CDKN2A* c.146T>C, Provider 1

	VUS (1/2016)	Likely Pathogenic (12/2016)
Gender	Female	Female
Age at Testing	32	59
Personal History	Uterine cancer	Pancreatic cancer
Family History of *CDKN2A*-Related Cancers	First-degree relative with melanoma	First-degree relative with pancreatic cancer
Additional Variants	None	*NBN* VUS
Dermatology Exam	Continue/begin now, repeat yearly	Baseline evaluation now, repeat as indicated
Pancreatic Cancer Screening	None	None[a]
Family Member Testing	VUS tracking studies	Targeted variant testing for first-degree relatives

[a]No screening was recommended while undergoing treatment for metastatic cancer.

(B) *CHEK2* c.470T>C, Provider 2

	Pathogenic (12/2015)	VUS (8/2016)	Pathogenic (1/2017)
Gender	Female	Male	Female
Age at Testing	47	66	58
Personal History	None	Colon cancer	Breast cancer and pancreatic cancer
Family History of *CHEK2*-Related Cancers	Two first-degree relatives with DCIS; three second-degree and one third-degree relative with breast cancer	First-degree relative with colon cancer; second-degree relative with colon cancer; second-degree relative with breast cancer	Third-degree relative with breast cancer; second-, third-, and fourth-degree relatives with thyroid cancer
Additional Variants	None	*APC* VUS	VUSs in *GALNT12, NBN, and TYR*
Mammogram	Continue/begin now, repeat yearly	N/A	None[a]

Breast MRI	Continue/begin now, repeat yearly	N/A	None[a]
Colonoscopy	Continue/begin now, repeat every 5 years	None[a]	None[a]
Family Member Testing	None[b]	None[c]	Targeted variant testing recommended for first-degree relatives

[a]No screening was recommended while undergoing treatment for metastatic cancer.
[b]Other at-risk family members had previously undergone testing; patient's testing was recommended due to this variant being found in family members.
[c]No additional relatives had previously undergone testing.

(C) *CHEK2* c.470T>C, Provider 3

	VUS (11/2016)	**Pathogenic (4/2018)**
Gender	Female	Female
Age at Testing	39	36
Personal History	Breast DCIS	Gastric cancer
Family History of *CHEK2*-Related Cancers	None	One second-degree relative with colon cancer
Additional Variants	*NBN* VUS	*RAD50* and *RECQL4* VUSs
Mammogram	Continue/begin now, repeat yearly	Begin at age 40, repeat yearly
Breast MRI	Not recommended	Begin at age 40, repeat yearly
Colonoscopy	Begin at age 40, repeat every 5 years	Begin at age 40, repeat every 5 years
Family Member Testing	None	Targeted variant testing for first-degree relatives

(D) *MUTYH* c.934-2A>G, Provider 1

	VUS (2/2019)	**Likely Pathogenic (12/2018)**
Gender	Female	Female
Age at Testing	48	51
Personal History	Breast cancer	None
Family History of Colon Cancer and Polyps	None	Second-degree relative with colon cancer

Additional Variants	*DICER1* and *MSH6* VUSs	*BAP1* VUS
Colonoscopy	Not discussed	Continue/begin now, repeat every 5 years
Family Member Testing	None	Targeted variant testing suggested for family members

(E) *MUTYH* c.934-2A>G, Provider 2

	VUS (12/2016)	**Likely Pathogenic (11/2016)**
Gender	Female	Female
Age at Testing	70	47
Personal History	Ovarian cancer	None
Family History of Colon Cancer and Polyps	None	None
Additional Variants	None	*CDKN2A*, *CHEK2*, and *MSH2* VUSs
Colonoscopy	Not discussed	Continue/begin now, repeat every 5 years
Family Member Testing	None	Targeted variant testing for siblings and children; panel for sister with additional cancer history