## Report Contents

1. **Coriell Personalized Medicine Collaborative Research Study Report. This report includes all data included in the clinical report as well as supplemental interpretations and educational material. This research report is based on Questionnaires Finalized on 08/01/2010**

2. **Clinical Report. This report was generated and approved by Coriell's CLIA certified genotyping laboratory.**

**Sample Results**

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# CPMC Research Study Report

| | | | |
|---|---|---|---|
| **Name:** | NATALIE DEMO | **Gender:** | Female |
| **Date of Birth:** | | **Date Collected:** | 11-30-2016 |
| **Coriell ID:** | DEMONAT | **Date Received:** | 11-30-2016 |
| **Lab Accessioning Number:** | DEMONAT | **Date of Report:** | 05-13-2014 |
| **Ordering Physician:** | Dr. Edward Viner | | |

**Risk of Developing Osteoarthritis Based on:**

- **CPMC Osteoarthritis Variant 1 (rs3815148)**
- **Body Mass Index**
- **Gender**

The CPMC is a research study investigating the utility of personalized genomic information on health and health behavior. Most common health conditions are caused by an interaction between multiple genetic variants and non-genetic risk factors such as lifestyle and environment. The genetic variant risk in this report is based on one genetic variant, but does not represent your complete genetic risk for osteoarthritis. These results were generated as part of this research study in a CLIA-approved laboratory.

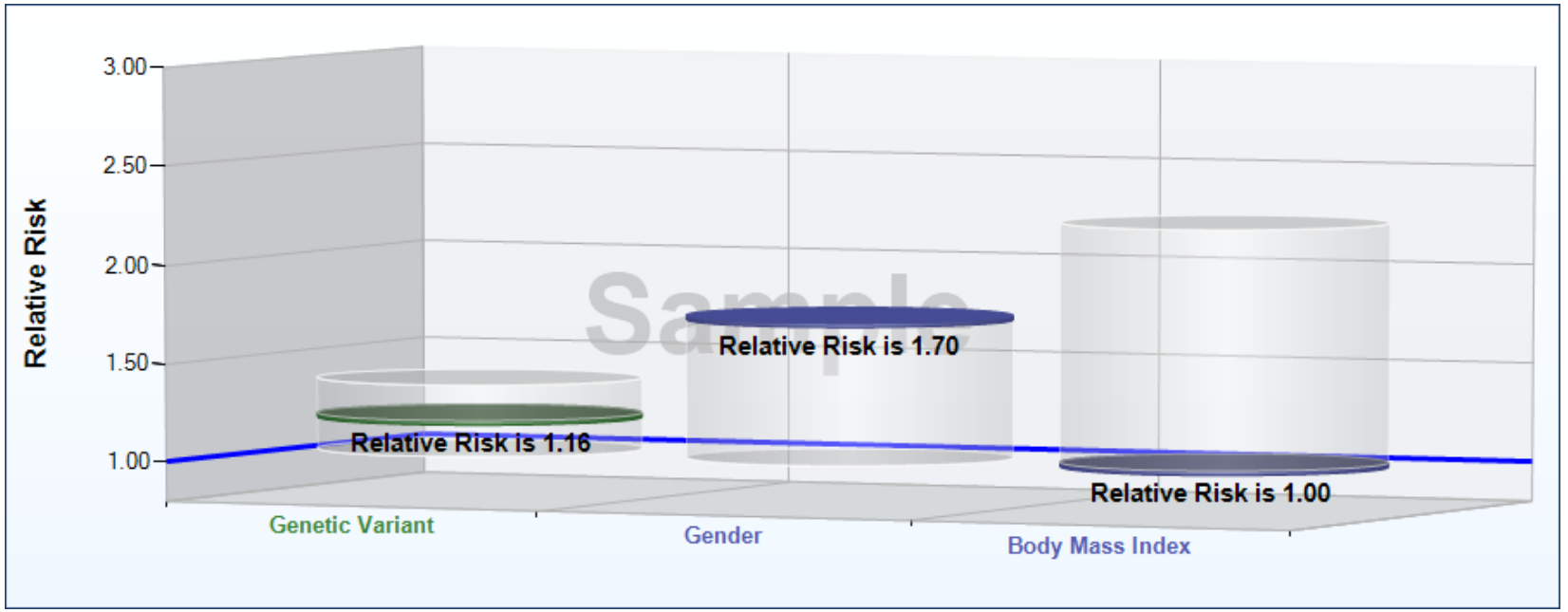
More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website http://cpmc.coriell.org or by contacting our genetic counselor. Participants may schedule an appointment with our board-certified genetic counselor through the web portal by clicking on “request an appointment”. Our genetic counselor also can be reached by email at cpmcgc@coriell.org or by phone at 888-580-8028.

This research report includes all data included in the clinical report as well as supplemental interpretations and educational material. Please see the report that follows for the official clinical report.

## Genetic Variant Result, Details and Population Data

# Osteoarthritis

**Risk factors may be related to each other and risk estimates cannot be combined.**
**This graph provides a summary of the relative risks for the genetic variant, body mass index (BMI), and gender.**




You reported that you are a woman with a BMI of <30 kg/m2 (non-obese), between 35 and 44 years old; an estimated 2 in 100 non-obese women in your age group have osteoarthritis.

| Chart Color | Relative Risk Due To: | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|---|---|---|---|---|---|
| | **Genetic Variant** | **1.16** | 1.00 | 1.34 | **You have 1 copy of the non-risk variant and 1 copy of the risk variant. Based on this result, you are 16% more likely (or 1.16 times as likely) to develop osteoarthritis as someone with no copies of this variant.**<br><br>***Having this risk variant contributes to your risk of osteoarthritis.*** |
| | **Gender** | **1.70** | 1.00 | 1.70 | **Because you are female, you are 70% more likely (or 1.7 times as likely) to develop osteoarthritis as a male. Being female contributes to your risk of osteoarthritis.** |
| | **Body Mass Index** | **1.00** | 1.00 | 2.21 | **Based on your BMI you are at a lower risk of developing osteoarthritis compared to individuals who have a BMI of 25 or higher (overweight or obese).** |

# Osteoarthritis

## Risk Due To Genetic Variant #1 (rs3815148)

**Your Result: 1 copy of the non-risk variant and 1 copy of the risk variant were detected (AC).**

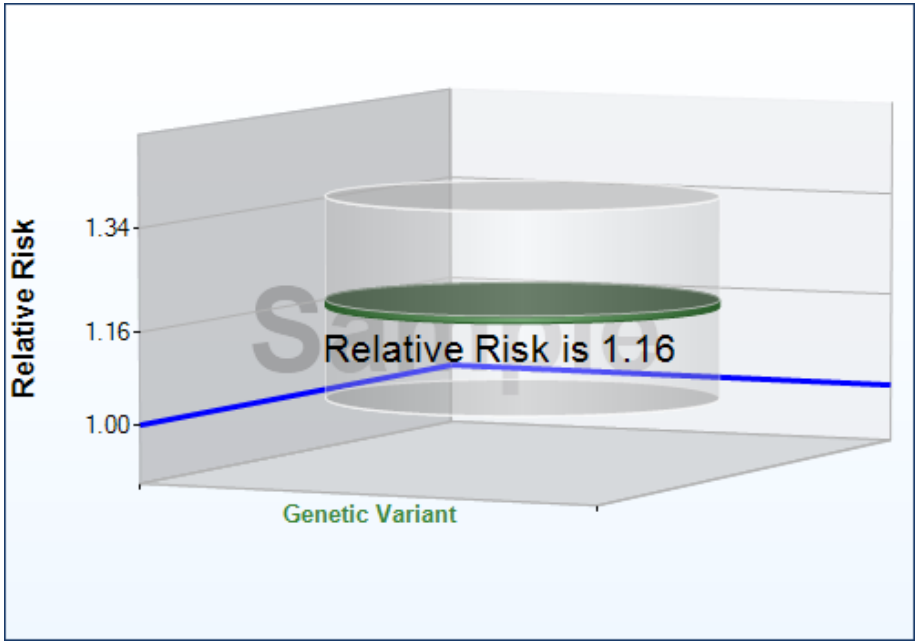
**Non-Risk Variant = A  Risk Variant = C**

| Chart Color | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|---|---|---|---|---|
| | **1.16** | 1.00 | 1.34 | **You have 1 copy of the non-risk variant and 1 copy of the risk variant. Based on this result, you are 16% more likely (or 1.16 times as likely) to develop osteoarthritis as someone with no copies of this variant.**<br><br>***Having this risk variant contributes to your risk of osteoarthritis.*** |

**Genetic Variant Risk is based on the number of copies of this genetic risk variant.**

**People with one or two copies of the risk variant are compared to people with no copies of the risk variant to determine relative risk.**

**A relative risk greater than 1.00 indicates an increased risk.**




**These results are based on multiple studies.**

# Osteoarthritis

## Risk Based on Gender

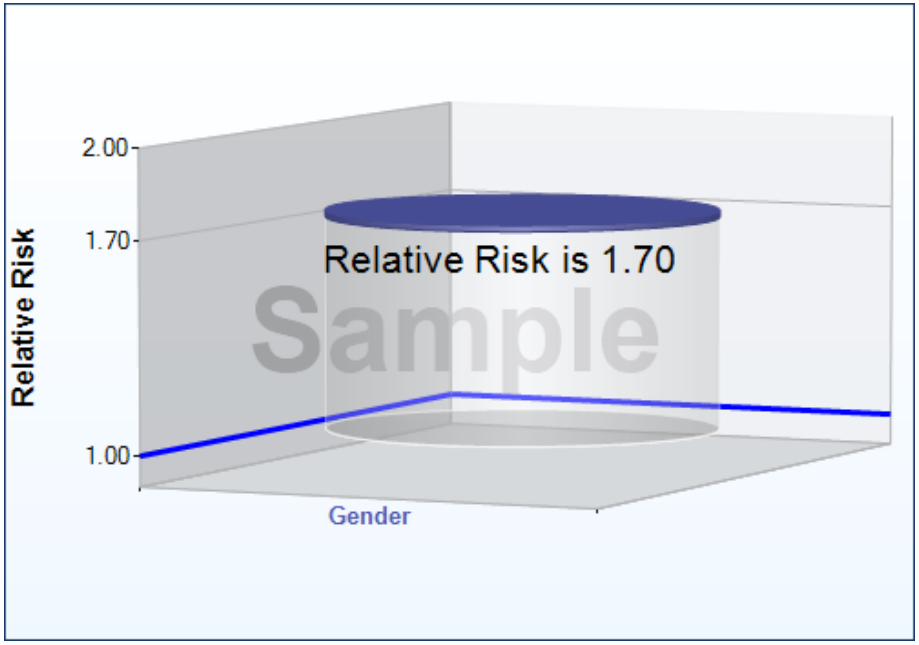
**You reported that you are female.**

| Chart Color | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|---|---|---|---|---|
| | **1.70** | 1.00 | 1.70 | **Because you are female, you are 70% more likely (or 1.7 times as likely) to develop osteoarthritis as a male. Being female contributes to your risk of osteoarthritis.** |

**Risk is compared based on gender.**

**Females, when compared to males, are more likely to develop osteoarthritis.**

**A relative risk greater than 1.00 indicates an increased risk.**




**These results are based on multiple studies.**

# Osteoarthritis

## Risk Due To Body Mass Index

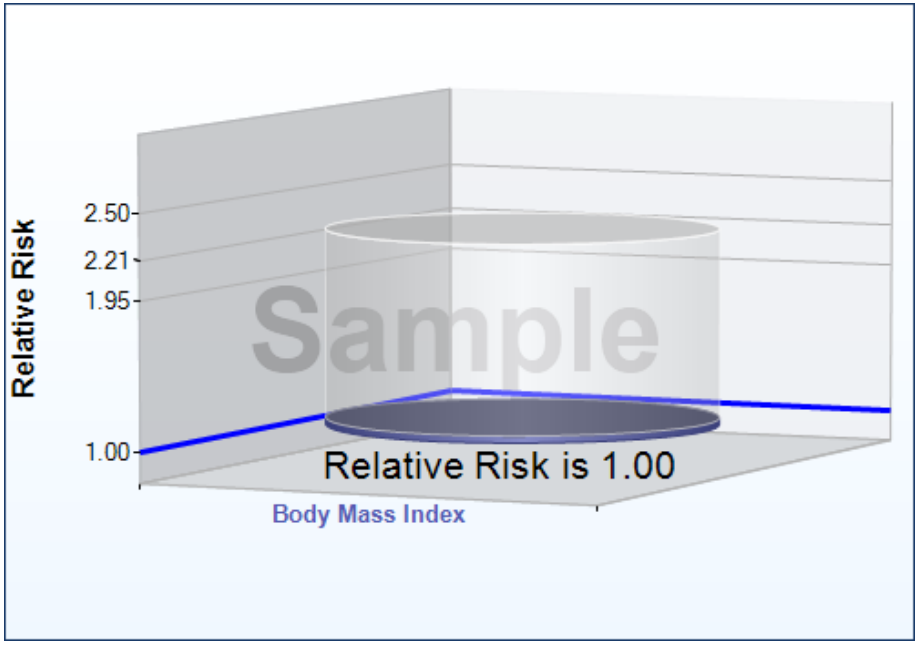
**According to the height and weight you reported, you are not overweight or obese (BMI <25.0).**

| Chart Color | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|---|---|---|---|---|
| | **1.00** | 1.00 | 2.21 | **Based on your BMI you are at a lower risk of developing osteoarthritis compared to individuals who have a BMI of 25 or higher (overweight or obese).** |

**Risk is compared based on Body Mass Index (BMI).**
**BMI is used to determine if someone is overweight or obese.**

**People who were overweight (BMI 25.0-29.9) or obese (BMI ≥ 30.0) were compared to people who were not overweight (BMI < 25.0) to determine relative risk.**

**A relative risk greater than 1.00 indicates an increased risk.**




**These results are based on multiple studies.**

# Osteoarthritis - Variant #1 (rs3815148)

We all have 2 copies of every gene, one from each of our parents.
Each copy may have small changes called genetic variants.
Some genetic variants are associated with an increased risk of disease.
Some genetic variants are associated with a decreased risk of disease.

Having one or two copies of this variant **increases** your risk of osteoarthritis.

## How Common Is This Variant?

**Non-Risk Variant = A** **Risk Variant = C**

**AA - 64 in 100 people have 2 copies of the non-risk variant**

**CA - 29 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant**

**CC - 7 in 100 people have 2 copies of the risk variant**

**This frequency is based on data from African American populations.**

**Gene: COG5** **Chromosome: 7q22**

**Causes**

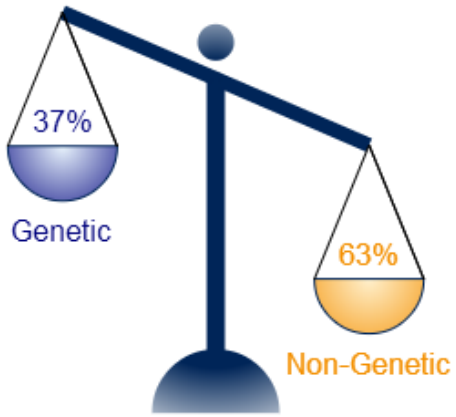
# Genetic vs. Non-Genetic Risk Factors

Osteoarthritis can be caused by both genetic factors and non-genetic (or environmental) risk factors.

It is estimated that **non-genetic** factors (like body mass index (BMI)) account for about **63%** of the risk of osteoarthritis.

It is estimated that **37%** of the risk for osteoarthritis is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

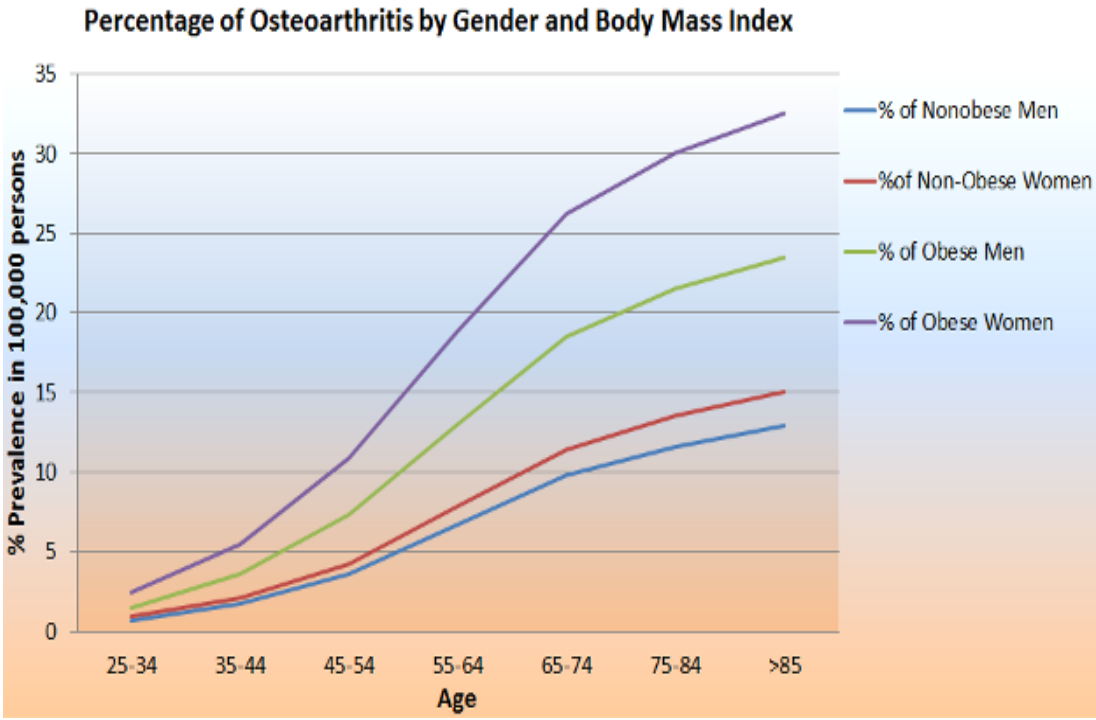
**There are many different genetic and non-genetic risk factors that contribute to the risk of osteoarthritis. We are only able to tell you about your risk due to your gender, 1 genetic and 1 non-genetic risk factor at this time.**



**How Common**

Your age, race and gender contribute to your risk of osteoarthritis.

**You reported that you are a woman with a BMI of <30 kg/m2 (non-obese), between 35 and 44 years old; an estimated 2 in 100 non-obese women in your age group have osteoarthritis.**



## Limitations

# Osteoarthritis

- This result alone does NOT diagnose osteoarthritis. Osteoarthritis must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop osteoarthritis.
- This result does NOT mean that you will not develop osteoarthritis in the future.
- This result ONLY assesses your risk for developing osteoarthritis due to the factors presented in this report and does not mean that other genetic variants or risk factors for osteoarthritis are present or absent.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on your risk to develop osteoarthritis than any individual genetic variant.
- Risk estimates are based on current available literature.
- Although rare, it is possible that you may receive an incorrect result; 100% accuracy of reported results cannot be guaranteed.
- Occasionally there may be a specific variant on a gene chip that is not able to be read or interpreted. In this case you will not receive a result for that variant. It is expected that you will receive results for about 95% of variants approved by the ICOB.
- Relative risks used to estimate risk of disease for CPMC participants are based on groups of people with the same risk or protective factor as the individual CPMC participant. In some cases, the relative risk is estimated based upon an odds ratio and known or assumed disease prevalence.
- Separate risk estimates for each risk or protective factor have been given. Risk or protective factors may be related to each other and risk estimates cannot be combined.
- Risk information for non-genetic factors is based on information you provided in your medical, family, lifestyle questionnaire. If you did not provide answers or if you answered “do not know”, risk estimates for some factors may not be available.
- Risk information for non-genetic factors is based on information you provided in your medical, family, lifestyle questionnaire and may not be reflective of your current risk if any of these factors have changed. You will be given the opportunity to update your medical, family and lifestyle questionnaire responses periodically.
- Every effort will be made to provide you with risk information based on your reported race/ethnicity. However, data may not be available for all races/ethnicities for all risk factors. Please see your individual results to determine which race/ethnicity the data given is based on.
- For some risk factors data may be provided by gender. Every effort will be made to provide you with risk information based on your reported gender. However, when risk data is not available for both genders, risk results for the available gender will be provided.

## Methods

# Osteoarthritis

**This condition and genetic variant(s) were approved by the Informed Cohort Oversight Board (ICOB)**

**Test Methodology**
Saliva samples were collected using Oragene DNA Collection Kits (DNA Genotek) and DNA was extracted manually according to the manufacturer's instructions. Purified DNA was quantified using UV absorbance at 260 nm. Five hundred nanograms of the resulting DNA from each sample were used as template in the Affymetrix Genome-Wide Human SNP Nsp/Sty 6.0 GeneChip assay. Data analysis was performed using Affymetrix Genotyping Console software.

**See CPMC Technical Paper for genetic variant selection and reporting methodology.**

[Risk interpretation based on Coriell's Osteoarthritis Risk Algorithm Version 1 (May 13, 2014)]


1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. Genet Med. 13(2):131-139.
2. Blagojevic, M. (2010). Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. Osteoarthritis Cartilage. 18(1):24-33.
3. MacGregor, AJ. (2009). The genetic influence on radiograph osteoarthritis is site specific at the hand, hip, and knee. Rheumatology. 48:277-280.
4. Kerkhof, HJ. (2010). A genome-wide association study identifies an osteoarthritis susceptibility locus on chromosome 7q22. Arthritis Rheum. 62(2):499-510.
5. Losina, E. et al (2013). Lifetime risk and age at diagnosis of symptomatic knee osteoarthritis in the US. Arthritis Care Res. 65(5):703-711.
6. McVean G.A. et al (2012). An integrated map of genetic variation from 1,092 human genomes. Nature. 491; 56-65.

**Sample Results**

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## Clinical Report for Osteoarthritis Genetic Variant 1 (rs3815148)

| | | | |
|---|---|---|---|
| **Name:** | NATALIE DEMO | **Sample Type:** | Saliva |
| **Race/Ethnicity:** | Black or African-American | **Gender:** | Female |
| **Date of Birth:** | | **Date Collected:** | 11-30-2016 |
| **Coriell ID:** | DEMONAT | **Date Received:** | 11-30-2016 |
| **Lab Accessioning Number:** | DEMONAT | **Date of Report:** | 05-13-2014 |
| **Ordering Physician:** | Dr. Edward Viner | | |

| **Name of Gene/Region:** COG5 | | **Chromosomal Location:** 7q22 |
|---|---|---|
| **Variants tested** | **Result** | **Reference Genotype** |
| rs3815148 | AC | AA |
| **Interpretation** | **Individuals with this result are 16% more likely (or 1.16 times as likely) to develop osteoarthritis as someone with no copies of this variant.** These risk estimates are based on studies involving multiple populations that include individuals with European ancestry. When race/ethnicity specific risk estimates are not available, risk estimates based on Caucasian populations are provided. | |
| **Other Risks** | Other genetic variants and other risk factors including co-morbidities, lifestyle and family history may contribute to the risk of osteoarthritis. For additional information on other risk factors please see the accompanying CPMC research report. | |

Risk interpretation based on Coriell's Osteoarthritis Risk Algorithm Version 1 (May 13, 2014)

### Test Limitations

DNA-based testing is highly accurate, however there are many sources of potential error including: mis-identification of samples, rare technical errors, trace contamination of PCR reactions, and rare genetic variants that interfere with analysis. There may be other variants, not included in this test, that influence the risk to develop osteoarthritis. This test is not diagnostic for osteoarthritis and cannot rule out the risk of developing osteoarthritis in the future. Risk estimates are based on current available literature (see reference). This test or one or more of its components was developed and its performance characteristics determined by the Coriell Institute for Medical Research. It has not been approved by the Food and Drug Administration (FDA). The FDA has determined that such approval is not necessary. The Coriell Institute is regulated under the Clinical Laboratory Improvement Amendments (CLIA) of 1988 as qualified to perform high-complexity testing.

### Test Methodology

Saliva samples were collected using Oragene DNA Collection Kits (DNA Genotek) and DNA was extracted manually according to the manufacturer's instructions or automatically using a DNAdvance Kit (Agencourt). Purified DNA was quantified using UV absorbance at 260 nm. Five hundred nanograms of the resulting DNA from each sample were used as template in the Affymetrix Genome-Wide Human SNP Nsp/Sty 6.0 GeneChip assay. Data analysis was performed using Affymetrix Genotyping Console software.

electronically signed by
Marie Hoover, PhD, Laboratory Director
This clinical report only includes data generated in the CLIA approved genotyping laboratory, for additional information please see the CPMC research report.

### References

1. Kerkhof HJ, Lories RJ, Meulenbelt I, et al. 2010. A genome-wide association study identifies an osteoarthritis susceptibility locus on chromosome 7q22. Arthritis Rheum. 62(2):499-510.