INFORMED CONSENT FOR 3B-EXOME

3billion, Inc. ("**3billion**") requires a completed Informed Consent Form ("**ICF**") to be received before the Whole Exome Sequencing Test ("**3B-EXOME**") can begin. The ICF must be completed by the patient, patient's parent (in case the patient is a minor or not capable of consenting) or a legally authorized representative of the patient ("**you/your child**").

What Is Whole Exome Sequencing?

Whole Exome Sequencing (WES) is a method of genomic sequencing that simultaneously reads the protein-coding regions (i.e., exons) of all ~20,000 genes, the entirety of which is called an exome. The exome accounts for less than 2% of the human genome but because ~85% of the variants reported to cause rare genetic disorders are known to reside in this region, 3B-EXOME is an effective single-test method for identifying genetic changes causing rare genetic disorders.

What Is the Purpose of This Test?

Your Authorised Health Professional ("**AHP**") or your child's AHP is recommending that you or your child receive 3B-EXOME to find a genetic change (i.e., variant) that could explain the medical condition you or your child may have. The test is voluntary.

What Is Needed for This Test?

If you consent to 3B-EXOME, your AHP will take a sample (e.g., whole blood or buccal swab) from you. The sample will be sent to 3billion's laboratories located in South Korea. Under some circumstances, an additional sample may be requested. Should you decide to withdraw from receiving the test, 3billion will destroy the sample and the data upon test cancellation.

What Type of Results Are Reported from This Test?

1. Primary Findings

Positive results: pathogenic or likely pathogenic variants are reported. These variants are clinically significant genetic change(s) that are very likely to cause the medical condition you or your child has.

Inconclusive results: variants of uncertain significance are reported. These variants are genetic change(s) that may cause the medical condition you or your child has but with insufficient evidence. Additional phenotyping and/or family testing may be recommended to help determine the significance of the results.

Negative results: no variants are reported. This means that at the time of testing, there were no variants that can explain the medical condition you or your child has. However, this does not mean that you or your child do not have a genetic condition or are free from genetic disorders or other medical conditions. It is still possible that the causal variant cannot be identified by 3B-EXOME due to (i) certain limitations set forth under the "Test Limitations and Risks" section below and/or (ii) the underlying genetic disorder not being known at the time of testing.

2. Secondary Findings

3B-EXOME may reveal genetic changes that are not directly related to the reason for ordering this test. If "Secondary Findings" are requested, pathogenic or likely pathogenic variants in genes that are considered 'medically actionable' will be reported as set forth in the "Secondary Findings" section below.

3. For Family Members

If you are a family member being simultaneously tested as part of a duo or trio testing to aid in the interpretation of 3B-EXOME, your clinical information may also be requested. However, even if you share the same variant reported for your child (i.e., proband), **the information will only appear in the proband's report**. You will receive a separate report for the secondary findings if you opted-in to receive such information in accordance with the "Secondary Findings" section below.

Test Limitations and Risks

1. 3B-EXOME can detect single nucleotide variants, small insertions/deletions (<50 bp) and large (>=3 consecutive exons) copy number variants with high accuracy in most of the genomic regions. If low level mosaicism variants on autosomes and sex chromosomes, small (<3 consecutive exons) copy number variants (CNVs), structural variants (SVs) including inversions and translocations, or low heteroplasmic level mitochondrial genome variants are suspected, it is recommended to perform other tests specifically designed to detect these types of variants.
2. There are certain exonic regions that cannot be sequenced due to technical difficulties with amplification, sequencing and/or alignment. If variants within these regions are suspected, it is recommended to perform alternate testing that are designed to sequence those regions/genes adequately. Intronic variants, epigenetic factors, or variants in regulatory regions called by being near coding exons may not be interpretable.
3. The results are based on currently available scientific and medical information and therefore a negative test result does not rule out a diagnosis of a certain disorder. Advanced medical and scientific knowledge may change the test results at a future date and therefore your AHP may decide to request a reanalysis of the sequencing data. If you opt-in for reanalysis, 3billion will perform automated reanalysis, and should any clinically significant change be identified, send an updated report to your AHP (see the "**Data Retention**" section below). Reanalysis service expires 10 years from the date of the initial result as your consent for reanalysis is renewed on a 10-year cycle. The physician will have the option to renew the patient's confirmation of consent for reanalysis to extend the service for another 10 years.
4. 3B-EXOME was validated to be highly accurate. However, inaccurate results may still occur. The reasons include, but are not limited to, mislabeled samples, low-quality samples, inaccurate order information, inaccurate medical/scientific information in public databases and/or technical errors.
5. 3B-EXOME can identify genetic change(s) that are not directly related to the medical condition 3B-EXOME is being performed for but are considered medically actionable (see the "**Secondary Findings**" section). However, 3B-EXOME should not be considered a screening test for all medical conditions or medical risks that you may experience later.
6. When family members are simultaneously tested as part of a duo or trio testing, there is a risk that other genetic information not related to the medical condition may be revealed. Such information includes medical risk in the family member, non-paternity or non-maternity (i.e., father or mother is not the biological parent). As these types of information can be critical in correctly interpreting the test results, it may have to be shared with your AHP and documented on the report. Alternative testing options, such as proband-only testing, single gene or gene panel testing, are available that will not uncover these types of findings. Consult with your AHP if you are concerned.

Sample Retention

Your sample may be de-identified and used for test development, validation, improvement or training purposes. 3billion will not return the remaining samples to you or your AHP, unless specific prior arrangements had been made.

Data Retention

Pursuant to laboratory best practices, 3billion will retain your de-identified sequencing data for a minimum of two (2) years and the final report for the required statutory period. Thereafter, 3billion will retain your medical and genetic information indefinitely unless specific requirements have been made. De-identified information may be used for test development, validation and improvement or training purposes.

Scientific Contributions

The de-identified results of this test may be summarized and used anonymously in case studies at meetings, scientific journals, or uploaded on public genetic variant databases such as ClinVar to improve understanding, diagnosis, and treatment of similar clinical conditions.

Confidentiality/Privacy Protections

To maintain confidentiality of your sample and your Protected Health Information (collectively "**PHI**") collected for the test, 3B-EXOME results will only be released to your AHP, to the ordering laboratory, to you, to other AHPs involved in your diagnosis and treatment upon your request, or as otherwise required by law or regulation. Unless required by law, 3billion will not disclose your PHI to any person or entity without obtaining prior written consent from you. However, the report may become part of your medical record, and your health insurance provider or other entities may have legal access to the information. Furthermore, you have the right to request access to your PHI or request corrections of any errors in your PHI. You also have the right to ask that your PHI be erased, subject to the applicable laws or regulations. If requests for access, correction, completion, or erasure cannot be fulfilled, you will be informed and provided with the reasons why it cannot be fulfilled.

Accreditations and Certifications

CAP License #	**CLIA ID #**
8750906, AU-ID# 2052626	99D2274041

CONSENT & SIGNATURE

Unique ID _____ Date of birth YYYY / MM / DD

For Proband

This page must be completed and submitted with the requisition before testing can begin.

Secondary Findings and Reanalysis

The American College of Medical Genetics and Genomics (ACMG) recommends that secondary findings identified in a specific subset of medically actionable genes associated with various inherited disorders be reported for individuals undergoing 3B-EXOME (PMID: 34012068). Accordingly, 3billion will report secondary findings within this gene list if you agree to receive them. Somatic mosaicism or carrier status in these genes will not be reported.
If you do wish to receive secondary findings, please check the box:

Yes ☐

When primary findings do not yield positive results, 3billion can include your data for the daily variant reclassification using new medical and scientific knowledge.
If you do wish to have your data reanalyzed, please check the box:

Yes ☐

By signing this form, I acknowledge that I have read this Informed Consent Form and understand its content. I had the opportunity to ask questions and my questions have been adequately answered. I also understand that I can withdraw my consent with effect for the future in full or in part at any time, and I have the right not to know the results of the test as mentioned in the preceding description. If the undersigning is the legal guardian of the research participant, he/she herewith confirms to provide the above consent declarations not for himself/herself but on behalf of the respective research participant.

Patient

3billion ID E _____ - _____
(e.g. EPE25-ABCD)
To be filled out by a healthcare provider

Date YYYY / MM / DD

Signature _____

if patient is a minor, Relationship _____

Date YYYY / MM / DD

Signature _____

CONSENT & SIGNATURE

Unique ID _____ Date of birth YYYY / MM / DD

For Biological Parent

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Biological Parent

☑ Father ☐ Mother

3billion ID E _____ - _____
(e.g. ETE25-ABCD)

To be filled out by a healthcare provider

Date YYYY / MM / DD

Signature _____

CONSENT & SIGNATURE

Unique ID _____ Date of birth YYYY / MM / DD

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Biological Parent

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(e.g. ETE25-ABCD)

To be filled out by a healthcare provider

Date YYYY / MM / DD

Signature _____