FRAGILE X MOLECULAR DIAGNOSTICS

Brochure not for distribution in the USA.

FragilEase™

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ORDERING INFORMATION

<table>
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<tr>
<th>Product Description</th>
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<tr>
<td>LabChip MultiDX</td>
<td>CLS136531</td>
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<td>LabChip MultiDX 5K (for 400 samples)</td>
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<td>LabChip MultiDX 5K (for 4800 samples)</td>
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FRAGILEASE™ ASSAY CHARACTERISTICS

- Accurate amplification and detection of repeat sizes with > 500 repeats
- Precise repeat quantification of normal, premutation and full mutation samples
- Accurate detection of both alleles in female samples reducing the need for Southern blot reflexing
- High and low throughput options for cost- and time-efficient analyses
- 96 or 1152 reactions per kit
- Turnaround time from DNA to report approximately 6 hours
- CE marked for IVD use

WORKFLOW

1. FragilEase™ PCR
2. PCR Purification
3. LabChip MultiDX

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1599-9772-02, October 2014
Fragile X Syndrome is one of the most commonly inherited forms of intellectual disability and is caused by trinucleotide repeat expansions in the promoter region of the FMR1 gene on chromosome X. When the CGG motif expands above 200 repeats, the FMR1 gene is silenced by methylation causing Fragile X Syndrome with its typical characteristics including elongated face, large or protruding ears and intellectual disability.

FMR1 alleles are typically categorized into normal, premutation and full mutation alleles based on the number of CGG repeats. While Fragile X syndrome is the most severe form of the disease, individuals with repeat expansions in the premutation range of 55 – 200 repeats can be affected by Fragile X-associated tremor/ataxia syndrome (FXTAS), or Fragile X-associated primary ovarian insufficiency (FXPOI).

Traditionally, Fragile X testing is performed by use of a laboratory developed FMR1-specific PCR often followed by capillary electrophoresis. However, amplifying the entire CGG-rich template beyond about 100 – 130 repeats is challenging. In addition, differentiating full mutations from homozygous normal female samples has historically required a Southern blot reflex test.

**FragilEase™**

FragilEase™ is a PCR assay designed to amplify the entire CGG repeat sequence in the FMR1 promoter region. By use of proprietary PCR reagents that allow an accurate amplification of the trinucleotide repeats, FragilEase™ can reliably detect full mutations with over 300 repeats, significantly reducing the amount of Southern blot reflexing. In addition, together with the LabChip MultiDX electrophoresis instrument and FraXsoft™ for data analysis and interpretation, PerkinElmer offers a streamlined workflow solution for quick and easy sample analysis with a reporting time of less than a day.

**LabChip MultiDX**

By using PerkinElmer’s patented microfluidic technology to perform reproducible, high-resolution electrophoretic separations the LabChip MultiDX provides a rapid, accurate and cost-effective way of analyzing FragilEase™ derived PCR products. In addition, differentiating full mutations from homozygous normal female samples has historically required a Southern blot reflex test.

**FraXsoft™**

FraXsoft™ provides easy-to-use analysis and interpretation option for our FragilEase™ products. FraXsoft™ allows the analysis of data derived from various microfluidic capillary electrophoresis systems and, based on the number of repeats in user-defined standard samples, calculates the number of CGG trinucleotide repeats in the samples tested. The mutation status of each sample can be classified according to ESHG, ACMG, or user-defined guidelines. FraXsoft™ provides intuitive data visualization for streamlined, quick and clear data interpretation of FragilEase™ data.
Fragile X Syndrome is one of the most commonly inherited forms of intellectual disability and is caused by trinucleotide repeat expansions in the promoter region of the FMR1 gene on chromosome X. When the CGG motif expands above 200 repeats, the FMR1 gene is silenced by methylation causing Fragile X Syndrome with its typical characteristics including elongated face, large or protruding ears and intellectual disability. FMR1 alleles are typically categorized into normal, premutation and full mutation alleles based on the number of CGG repeats. While Fragile X syndrome is the most severe form of the disease, individuals with repeat expansions in the premutation range of 55 – 200 repeats can be affected by Fragile X-associated tremor/ataxia syndrome (FXTAS), or Fragile X-associated primary ovarian insufficiency (FXPOI). Traditionally, Fragile X testing is performed by use of a laboratory developed FMR1-specific PCR often followed by capillary electrophoresis.  However, amplifying the entire CGG-rich template beyond about 100 – 130 repeats is challenging. In addition, differentiating full mutations from homozygous normal female samples has historically required a Southern blot reflex test.

LabChip MultiDX By using PerkinElmer’s patented microfluidic technology to perform reproducible, high-resolution electrophoretic separations the LabChip MultiDX provides a rapid, accurate and cost-effective way of analyzing FragilEaseTM derived PCR products. The LabChip MultiDX microfluidics platform is supported by the 5K Chip and 5K Reagents Kit that are designed to provide the user with everything needed to analyze the FragilEaseTM PCR products. LabChip MultiDX lab chip MultiDX

FRAXSOFT™ CHARACTERISTICS • Repeat size calculation based on user-defined standard samples • Graphical as well as numerical display of data based on ESHG, ACMG, or user-defined guidelines • Mutation status classification • Report creation in multiple languages

FraXsoftTM provides an easy-to-use analysis and interpretation option for our FragilEaseTM products. FraXsoftTM allows the analysis of data derived from various microfluidic capillary electrophoresis systems and, based on the number of repeats in user-defined standard samples, calculates the number of CGG trinucleotide repeats in the samples tested. The mutation status of each sample can be classified according to ESHG, ACMG or user-defined guidelines. FraXsoftTM provides intuitive data visualization for streamlined, quick and clear data interpretation of FragilEaseTM data.

LabChip MultiDX and FraXsoftTM together offer a streamlined workflow solution for quick and easy sample analysis with a reporting time of less than a day.

DNA

FragilEase PCR (~3 h)
Purification (~1 h)
Capillary Electrophoresis (~1 h)
Analysis and Reporting (~0.5 h)

PerkinElmer’s FragilEase™ PCR assay is designed to amplify the entire CGG repeat sequence in the FMR1 promoter region. By use of proprietary PCR reagents that allow an accurate amplification of the trinucleotide repeats, FragilEase™ can reliably detect full mutations with over 300 repeats twice significantly reducing the amount of Southern blot reflexing. In addition, together with the LabChip MultiDX electrophoresis instrument and FraXsoft™ for data analysis and interpretation, PerkinElmer offers a streamlined workflow solution for quick and easy sample analysis with a reporting time of less than a day.

Features
• Compact Benchtop Footprint
• High throughput analysis using 96- and 384-well plates
• CE marked for IVD use

Microfluidic capillary electrophoresis analysis of a Coriell female normal sample (NA07538), and a Coriell male Fragile X sample (NA06852) with >200 repeats, together with the PerkinElmer’s microfluidics and CE interpretation and classification.

Microfluidic capillary electrophoresis analysis of a Coriell female normal sample (NA07538), and a Coriell male Fragile X sample (NA06852) with >200 repeats, together with the PerkinElmer’s microfluidics and CE interpretation and classification.
Fragile X Syndrome is one of the most commonly inherited forms of intellectual disability and is caused by trinucleotide repeat expansions in the promoter region of the FMR1 gene on chromosome X. When the CGG motif expands above 200 repeats, the FMR1 gene is silenced by methylation causing Fragile X Syndrome with its typical characteristics including elongated face, large or protruding ears and intellectual disability.

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FragilEase™

Microfluidic capillary electrophoresis analysis of a Coriell female normal sample (NA07538).

Figure 1

LabChip MultiDX

By using PerkinElmer’s patented microfluidic technology to perform reproducible, high-resolution electrophoretic separations the LabChip MultiDX provides a rapid, accurate and cost-effective way of analyzing FragilEase™ derived PCR products. The LabChip MultiDX microfluidics platform is supported by the 5K Chip and 5K Reagents Kit that are designed to provide the user with everything needed to analyze the FragilEase™ PCR products.

LabChip MultiDX MULTIX SPECIFICATIONS

• Height 18.75 in. (48 cm)
• Width 19.25 in. (49 cm)
• Depth 25.375 in. (64 cm)
• Weight 88 lbs. (40 kg)
• Plate formats: 96-well or 384-well microplates
• Weight 40 kg (88 lbs)
• Operating Temperature 65° to 78°F (18° to 26°C)
• Operating Humidity 20% to 70% relative humidity, noncondensing
• Power Input: 3.0A max at 100-127V ac, 50-60Hz (±10%); 1.5A max at 200-240Vac, 50-60Hz (±10%)

FraXsoft™

FraXsoft™ provides an easy-to-use analysis and interpretation option for our FragilEase™ products. FraXsoft™ allows the analysis of data derived from various microfluidic capillary electrophoresis systems and, based on the number of repeats in user-defined standard samples, calculates the number of CGG trinucleotide repeats in the samples tested. The mutation status of each sample can be classified according to ESHG, ACMG, or user-defined guidelines. FraXsoft™ provides intuitive data visualization for streamlined, quick and clear data interpretation of FragilEase™ data.

FraXsoft™ CHARACTERISTICS

• Repeat size calculation based on user-defined standard samples
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In other countries please check availability with your PerkinElmer sales representative.

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<td>FragilEase™ PCR kit</td>
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FRAGILEASE™ ASSAY CHARACTERISTICS

- Accurate amplification and detection of repeat sizes with > 500 repeats
- Precise repeat quantification of normal, premutation and full mutation sample
- Accurate detection of both alleles in female samples reducing the need for Southern blot reflexing
- High and low throughput options for cost- and time-efficient analyses
- 16 or 1152 reactions per kit
- Turnaround time from DNA to report approximately 6 hours
- CE marked for IVD use

WORKFLOW

1. FragilEase™ PCR
2. PCR Purification
3. LabChip MultiDX

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FRAGILEASE™ ASSAY CHARACTERISTICS

• Accurate amplification and detection of repeat sizes with > 900 repeats
• Precise repeat quantification of normal, premutation and full mutation samples
• Accurate detection of both alleles in female samples reducing the need for Southern blot reflexing
• High and low throughput options for cost- and time-efficient analyses
• 50 or 1152 reactions per kit
• Turnaround time from DNA to report approximately 24 hours
• CE marked for IVD use

High and low throughput options for cost- and time-efficient analyses

96 or 1152 reactions per kit

Turnaround time from DNA to report approximately 24 hours

CE marked for IVD use

FragilEase™ PCR

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