The BeadXpress System: An Array of Applications for the Molecular Lab

Gianluca Roma
Product Manager
Illumina’s First FDA Cleared In-Vitro Diagnostic Device

- The BeadXpress System is an FDA 510(k) cleared In-Vitro Diagnostic Device

- FDA Cleared BeadXpress System includes:
  - BeadXpress Reader
  - VeraScan Software

- The Intended Use Statement:
  - The BeadXpress® System is an In-Vitro Diagnostic Device intended for the simultaneous detection of multiple analytes in a DNA sample utilizing VeraCode holographic microbead technology. The BeadXpress System consists of the BeadXpress Reader and VeraScan software.
  - It is cleared for use only with FDA cleared VeraCode tests.
Illumina’s Solution for Molecular Diagnostic Development

VeraCode® Technology

- Cylindrical glass microbeads
- 240 μm length x 28 μm diameter
VeraCode Technology

- High Density Codes Easily Imprinted (24 bit)
- Virtually Unlimited Unique Bead Codes Available – 626 unique codes used in launched products
- Glass Surface of Beads Ideal for Bioassays
- Specific panels created easily with addition or removal of specific bead types

CODE GENERATED BY CREATING EMBEDDED HOLOGRAPHIC DIFFRACTIVE ELEMENTS

BEAD

“READING” BEAM

CODE IMAGE

CONVENTIONAL CCD CAMERA

BINARY CODE

1 0 1 1 0 1 0 1 0 0 0 0 1 0 1

DECIMAL CODE

= 41133
# BeadXpress™ Reader: Specifications

<table>
<thead>
<tr>
<th>Specification</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Delivery Format</td>
<td>Standard 96-well plate &amp; 8-well strip plates</td>
</tr>
<tr>
<td>Multiplexing Per Single Well</td>
<td>1 to 384</td>
</tr>
<tr>
<td>Detection</td>
<td>Optional 1 or 2 color detection</td>
</tr>
<tr>
<td>Throughput</td>
<td>120 samples/hr at 10-plex</td>
</tr>
<tr>
<td></td>
<td>80 samples/hr at 96-plex</td>
</tr>
</tbody>
</table>
VeraCode Bead Loading & Alignment

- Capillary force attracts beads into grooves.
- Beads fall into groove plate.
- Beads align tightly for optimal scanning efficiency.

GROOVE PLATE CROSS-SECTION
Code Detection

Fluor Beam  Code Beam

“READING” BEAM

BEAD

CCD LINE ARRAY

ADC Output

Pixel

ADC Output

Pixel

Array
VeraScan 2.0 – System Operation to Report

Authentication

Test selection & Setup

Analysis & Report

Scan

Optional off-line analysis and review
Molecular Diagnostic Market Segments

- Blood Screening, 31%
- Infectious Diseases, 51%
- Inherited Diseases, 4%
- Oncology, 5%
- Pharmacodiagnostics, 2%
- Tissue Typing, 2%
- Prenatal, 5%
Analyzer for Multiple Applications

GENE REGULATION

PROTEIN EXPRESSION

GENOTYPING
VeraCode Product Portfolio (RUO)

- VeraCode Carboxyl Bead Sets
- VeraCode Universal Capture Bead Sets
- VeraCode ADME Core Panel
- Custom GoldenGate Genotyping, 48, 96, 144 & 384-plex
- DASL Custom Gene Expression, 32 to 384-plex
- Custom GoldenGate Methylation, 48 to 384-plex
VeraCode Product Portfolio (Regulated Products)

- VeraCode GPR Carboxyl Bead Sets
- VeraCode GPR Universal Capture Bead Sets
- VeraCode Pharmacogenetic Panel (in development)
- VeraCode Infectious Disease Panel (in development)
Available Products

CARBOXYL BEAD SETS (PROTEIN BASED ASSAYS)

PRODUCT
Unique Bead Code Types in Tubes

GUIDELINES
Assay Design Guidelines (RUO)

CUSTOMER DEVELOPED ASSAY
Customer controls level of multiplexing and number of samples

For Research Use Only
Carboxyl Beads: Chemistry of Attachment

PROTEIN ATTACHMENT: TWO-STEP PROCESS

Activate Surface → EDC/Sulfo-NHS → Covalently Bind

Antibodies
Antigens
Peptides
Streptavidin

NUCLEIC ACID ATTACHMENT: ONE-STEP PROCESS

EDC/Sulfo-NHS plus NH₂-Oligo → Nucleic Acids
Cytokine Sandwich Assay Overview

Streptavidin Phycoerythrin

Antibodies immobilized via COOH surface and EDC linker chemistry

Biotinylated Secondary Antibody

Cytokine Antigens

VeraCode Bead

For Research Use Only
Available Products

UNIVERSAL CAPTURE BEAD SETS

PRODUCT

Unique Bead Code Types in Tubes

GUIDELINES

Assay Design Guidelines (RUO)
VeraCode Assay Design Software

CUSTOMER DEVELOPED ASSAY

Customer controls level of multiplexing and number of samples

For Research Use Only
Allele-Specific Primer Extension (ASPE)

For Research Use Only
Low Plex ASPE Genotyping Results

► ≥ 99.99% reproducibility
► 100% concordant genotypes
The VeraCode Assay Designer Software

- Access user-specific accounts
- Input SNP targets
- Choose workflow option
- Customize design parameters
- Select among possible assay designs
- Download detailed ordering information
VeraCode ADME Core Panel
VeraCode ADME* Core Panel

Investigate genetic associations to a drug
► Response
► Dosing
► Safety

Pharmacogenetic studies can be:
► Completed Quickly
► More Efficiently
► More Precisely

Bring Personalized Medicine closer to reality

*Absorption, Distribution, Metabolism, and Excretion
More Core Coverage

Objective: Standardize content for pharmacogenetic drug studies

PharmaADME working group contributed content
- Abbott, Bristol-Myers Squibb, GSK, Johnson & Johnson, Eli Lilly, Merck, Pfizer, Roche, Sanofi Aventis and Wyeth. Genome Quebec also participated

VeraCode ADME include 184 polymorphisms (34 genes)
- >95% Pharma ADME Core List www.pharmaadme.org

<table>
<thead>
<tr>
<th>ADME Core (34 genes, 184 markers)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABCB1</td>
</tr>
<tr>
<td>ABCC2</td>
</tr>
<tr>
<td>ABCG2</td>
</tr>
<tr>
<td>CYP1A1</td>
</tr>
<tr>
<td>CYP1A2</td>
</tr>
<tr>
<td>CYP2A6</td>
</tr>
<tr>
<td>CYP2B6</td>
</tr>
<tr>
<td>CYP2C19</td>
</tr>
<tr>
<td>CYP2C8</td>
</tr>
</tbody>
</table>
Validated Core Content that Matters

Validated Biomarkers and the Drugs they Metabolize

► CYP2D6
  – Metabolizes codine to active drug morphine
  – Metabolizes Stratera® (atomoxetine), used for Attention Deficit Disorder
  – Associated with tamoxifen metabolism

► CYP2C9
  – Referenced in the labeling for blood thinner warfarin

► CYP2C19
  – Referenced in label for anti-platelet Plavix® (clopidogrel)

Experimental Biomarkers and the Drugs they Metabolize

► CYP2A6
  – Associated with Nicotine metabolism
Provides Highly Specific Assay

PRECISELY ADDRESSING HOMOLOGOUS REGIONS

CYP2C9*2
(Conventional)

CYP2C9*2
(VeraCode ADME Core)

Verified
*2 HETs

Intensity (B)

Intensity (A)

Verified
*2 HETs

Intensity (B)

Intensity (A)
Innovative Genotyping Approach

- Make Target
- Add Oligos
- Extend/Ligate
- PCR
- Make ssDNA
- Hyb VBS

For Research Use Only
Faster and Simplified Assay Workflow

For Research Use Only

Assay 32 samples per shift, < 2.5 hours hands on time
# ADME Core: Convenient Visualization Tools

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>5</td>
<td>B1</td>
<td>98.4%</td>
<td>G/G</td>
<td>CYP2C19</td>
<td>*2</td>
<td>G/A</td>
<td>GT Call</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
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<td>CYP2C19</td>
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<td>100%</td>
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<td></td>
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<td>98.4%</td>
<td>G/G</td>
<td>CYP2C19</td>
<td>*4</td>
<td>G/A</td>
<td>GT Call</td>
<td>100%</td>
<td>100%</td>
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<td>100%</td>
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<td>GT Call</td>
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<td>100%</td>
<td>100%</td>
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<tr>
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<td>99.47%</td>
<td>G/G</td>
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<td>*6</td>
<td>G/A</td>
<td>GT Call</td>
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<td>100%</td>
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<td>GT Call</td>
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<td>100%</td>
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<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>No Call</td>
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</table>

![Image](image.png)
# Reports with Automatic Translation

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<tr>
<th>Sample ID</th>
<th>Well</th>
<th>Call Rate</th>
<th>Controls</th>
<th>CYP2C9</th>
<th>CYP2D6</th>
<th>CYP2E1</th>
<th>CYP3A4</th>
<th>CYP3A5</th>
<th>DPYD</th>
<th>GSTM1</th>
<th>GSTT1</th>
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<tbody>
<tr>
<td>7</td>
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<td>AFEDEDB8</td>
<td>*3 HET</td>
<td>*1A/*1A</td>
<td>*1A/*1A</td>
<td>*3 VAR</td>
<td>*1A/*1A</td>
<td>0 copy</td>
<td>*A VAR</td>
<td>1 copy</td>
</tr>
<tr>
<td>6</td>
<td>B4</td>
<td>99.93%</td>
<td>DFDE6DF</td>
<td>*1A/*1A</td>
<td>*2A VAR</td>
<td>*1A/*1A</td>
<td>*3 HET</td>
<td>*6 HET</td>
<td>*1A/*1A</td>
<td>0 copy</td>
<td>*A/*B</td>
</tr>
<tr>
<td>9</td>
<td>C1</td>
<td>99.47%</td>
<td>AFEDEDB8</td>
<td>*3 HET</td>
<td>*3 HET</td>
<td>*1A/*1A</td>
<td>*3 VAR</td>
<td>*1A/*1A</td>
<td>0 copy</td>
<td>*A VAR</td>
<td>1 copy</td>
</tr>
<tr>
<td>10</td>
<td>C2</td>
<td>99.47%</td>
<td>DFDE6DF</td>
<td>*1A/*1A</td>
<td>*1A/*1A</td>
<td>*1A/*1A</td>
<td>*3 HET</td>
<td>*6 HET</td>
<td>*1A/*1A</td>
<td>0 copy</td>
<td>*A/*B</td>
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<tr>
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<td>B6E5EBF</td>
<td>*1A/*1A</td>
<td>*1A/*1A</td>
<td>*1A/*1A</td>
<td>*3 HET</td>
<td>*1A/*1A</td>
<td>*B HET</td>
<td>*A/*B</td>
<td>0 copy</td>
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<tr>
<td>12</td>
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<td>99.47%</td>
<td>DD6E5F7</td>
<td>*1A/*1A</td>
<td>*9 HET</td>
<td>*1A/*1A</td>
<td>*3 VAR</td>
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<td>*A VAR</td>
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<tr>
<td>13</td>
<td>D1</td>
<td>98.4%</td>
<td>B6E5EBF</td>
<td>*1A/*1A</td>
<td>*2A(-1584C&gt;G) No Call</td>
<td>*1A/*1A</td>
<td>*3 HET</td>
<td>*1A/*1A</td>
<td>*B HET</td>
<td>*A/*B</td>
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</tbody>
</table>
## Quality Performance Specifications

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Performance Specification</th>
<th>ILMN Verification (465 samples, 3 users, 3 systems)</th>
<th>Beta Data (3 sites, 4 users, 24 in house samples and more than 143 beta site samples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locus Success</td>
<td>≥ 95%</td>
<td>95.7%</td>
<td>95.7%</td>
</tr>
<tr>
<td>Assay Time, 32 samples</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DNA to data</td>
<td>≤8 hr</td>
<td>7 hr 38 min</td>
<td>≤8 hr</td>
</tr>
<tr>
<td>Hands on time</td>
<td>≤2.5 hr</td>
<td>1 hr 37 min</td>
<td>≤2.5 hr</td>
</tr>
<tr>
<td>Sample Throughput</td>
<td></td>
<td>1 user, 1 run, 1 plate: 32</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 user, 1 run, 2 plates: 64</td>
<td></td>
</tr>
<tr>
<td>Average Call Rate</td>
<td>≥98%</td>
<td>99.5%</td>
<td>99.2%</td>
</tr>
<tr>
<td>Concordance with Reference</td>
<td>≥99.5%</td>
<td>99.8%</td>
<td>99.8%</td>
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<tr>
<td>Infinium, GA, Sanger sequencing, DMET</td>
<td>≥99.5%</td>
<td>99.8%</td>
<td>99.7%</td>
</tr>
<tr>
<td>Reproducibility</td>
<td>≥99.5%</td>
<td>99.8%</td>
<td></td>
</tr>
</tbody>
</table>
VeraCode ADME Core Panel

More of What’s Important
- 34 genes, 184 polymorphisms
- Covers >95% core content

Quality Counts
- >99.5% Concordance
- >99.5% Reproducibility
- >98% Call Rate

Speed Matters
- Single day sample processing
- <2.5 hrs hands-on
- Simplified workflow
- Useful reports

Follow-on VeraCode Pharmacogenetic Test (In Development)

- CYP2C19 *2,*3,*4,*5,*6,*7,*8,*17

- CYP2C9 *2,*3, VKORC1 -1639G>A

Amp → Label → Hybe → Scan

4hrs
Enabling Clinical Early Adopter

**FDA cleared BeadXpress System**
Regulated device ensures quality and performance meet the standards for a clinical laboratories

**General Purpose Reagent Beads**
Enables customers to develop their own assays using royalty-free beads

**Path to FDA Submissions**
BeadXpress clearance and GMP reagents create a platform for follow-on diagnostic development
Enabling Diagnostic Partners

Signed agreements with EraGen:

**Expanded Menu**

*EraGen can port content to BeadXpress*

EraGen potential transfer menu includes:

- CFTR, Factor II/V, MTHFR
- Respiratory Viral Panel

**Improved Workflow**

*Faster chemistry on BeadXpress*

- Reduced labor costs
- Faster turnaround
- Enables further menu expansion in infectious disease

---

**BeadXpress 510(k) Clearance Removes a Significant Hurdle for development of diagnostic tests by Partners**
EraGen Workflow on BeadXpress

MultiCode®-PLx System
*Single Well - Three Step – Three Hour Process*

1. PCR
   - Target Specific Extension
   - Specific MultiCode Labeling
   - MultiCode Tags for Capture

2. TSE

3. Capture

Applications
- Mutation Detection
- Infectious Disease Testing
- Genotyping

Advantages
- Highly Multiplexed
- No Washes or Transfers
- Single Well Multiplexing
- 3 Hours Run Time
Multiplex Assay Workflow Comparison

**EraGen Workflow Analysis**

Sample* to Answer

- **ILMN (EraGen)**
  - Prep Transfers: 0
  - Washes: 0
  - Filtration: 0
  - Labor (hrs): 0.25
  - Total: 2:35

- **Third Wave**
  - Prep Transfers: 1
  - Washes: 1
  - Filtration: 0
  - Labor (hrs): 2
  - Total: 5:30

- **Luminex (TmBio)**
  - Prep Transfers: 1
  - Washes: 1
  - Filtration: 1
  - Labor (hrs): 3
  - Total: 6:30

**Automation Friendly**

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
<th>Time</th>
</tr>
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<tbody>
<tr>
<td>RXN Setup</td>
<td>20 µL Master Mix 10 µL Sample</td>
<td>0:05</td>
</tr>
<tr>
<td>PCR</td>
<td>Amplify and Label</td>
<td>1:30</td>
</tr>
<tr>
<td>Hyb Setup</td>
<td>50 µL Hybridization Buffer 30 µL Reaction</td>
<td>0:05</td>
</tr>
<tr>
<td>Hybridization</td>
<td>Room Temperature @ 850 RPM</td>
<td>0:15</td>
</tr>
<tr>
<td>BeadXpress</td>
<td>Read Full Plate (96 Samples)</td>
<td>0:40</td>
</tr>
</tbody>
</table>

**96 Clinical Specimens**

**Total Assay Time: 2:35**

*Workflows start from extracted DNA
The BeadXpress: For Infectious Disease Testing

Bacterial infections

- Bacterial meningitis
  - Streptococcus pneumoniae
  - Neisseria meningitidis
  - Haemophilus influenzae
  - Streptococcus agalactiae
  - Listeria monocytogenes

- Otitis media
  - Streptococcus pneumoniae

- Pneumonia
  - Community-acquired:
    - Streptococcus pneumoniae
    - Haemophilus influenzae
    - Staphylococcus aureus
  - Atypical:
    - Mycoplasma pneumoniae
    - Chlamydia pneumoniae
    - Legionella pneumophila
  - Tuberculosis
    - Mycobacterium tuberculosis

- Skin infections
  - Staphylococcus aureus
  - Streptococcus pyogenes
  - Pseudomonas aeruginosa

- Eye infections
  - Staphylococcus aureus
  - Neisseria gonorrhoeae
  - Chlamydia trachomatis

- Sinusitis
  - Streptococcus pneumoniae
  - Haemophilus influenzae

- Upper respiratory tract infection
  - Streptococcus pyogenes
  - Haemophilus influenzae

- Gastritis
  - Helicobacter pylori

- Food poisoning
  - Campylobacter jejuni
  - Salmonella
  - Shigella
  - Clostridium
  - Staphylococcus aureus
  - Escherichia coli

- Sexually transmitted diseases
  - Chlamydia trachomatis
  - Neisseria gonorrhoeae
  - Treponema pallidum
  - Ureaplasma urealyticum
  - Haemophilus ducreyi

- Urinary tract infections
  - Escherichia coli
  - Other Enterobacteriaceae
  - Staphylococcus saprophyticus
  - Pseudomonas aeruginosa
Advantages of Multiplexed Panels

- **Increase Productivity**
  - More results in less time

- **Decrease Costs**
  - Lower Reagent costs per analyte detected

RT-PCR Singleplex  
VeraCode Multiplex
An Array of Applications for the Molecular Laboratory

Research Use Only

- VeraCode Universal Capture & Carboxyl Beads
- VeraCode ADME Core Panel
- Custom GoldenGate Genotyping, 48, 96, 144, 192 & 384-plex
- DASL Custom Gene Expression, 32 to 384-plex
- Custom GoldenGate Methylation, 48 to 384-plex

Regulated Products

- VeraCode GPR Carboxyl Beads
- VeraCode GPR Universal Capture Beads
- VeraCode PGx Panel (in development)
- VeraCode IDx Panel (in development)