Panels of tests, allowing for the simultaneous multi-analyte detection of a wide range of analytes, from a single undivided sample.
Development of Biochip Array

- Over 185 Scientists involved
- $140,000,000.00 Investment
- 45 new patents
- Three main stages in Biochip development
  - Synthetic Chemistry
  - Nano Dispense
  - Detection technology

The Biochip

- The crux of the technology is the Biochip itself
- Coated in a proprietary silanation process
  - Activation of the Biochip surface
    - Ensures uniformity and reproducibility
  - Modification of surface chemistry
    - Controlled anti-body binding in optimal orientation
Biochip Array Technology

Biochip Surface Chemistry

Non-activated Surface

Activated Surface
Biochip Array Technology

Biochip Manufacturing

- All manufactured by Randox at our HQ in the U.K.
- 20 million chip per year capability
- Fully automated clean-room facility

Quality Control

- Quality control is at the heart of all that Randox does.
- Quality is ensured at every level of product
  - Pre process
    - Quality components
    - Randox Antibodies
  - In process
    - Manufactured to ISO 13485
    - Ensures reproducibility
  - Post Process
    - Internal QC to ensure Functionality, integrity and stability

Nano Dispense of Antibody solution

Quality Control

- Quality control is at the heart of all that Randox does.
- Quality is ensured at every level of product
  - Pre process
    - Quality components
    - Randox Antibodies
  - In process
    - Manufactured to ISO 13485
    - Ensures reproducibility
  - Post Process
    - Internal QC to ensure Functionality, integrity and stability
**Biochip Array Technology**

**Immunoassay Formats**

- Tried and trusted EIA
- Sandwich immunoassay
  - Cytokine and Growth Factor Array
- Competitive immunoassay
  - Drugs of Abuse Array
- Horse Radish Peroxidase Label

**Signal Analysis**

- Chemiluminescence
- L.O.D. compared
  - Fluorescence (ELISA) 2,000,000 zeptomoles
  - Radio Immunoassay 1,000,000 zeptomoles
  - Chemiluminescence 25,000 zeptomoles
- Imaged with super cooled CCD camera
- Quantified by custom software

» Tietz ‘Clinical Chemistry’
### Available Arrays

- Drugs of Abuse Array 1
- Cytokine and Growth Factor Array 1
- Free Thyroid Array
- Total Thyroid Array
- Fertility Array
- Tumour Monitoring Array
- Tumour PSA Array
- Adhesion Molecule Array
- Cardiac Array
- Growth Promoter Array
- Anti-Microbial Array 1
- Cardiovascular DNA Array
- Colorectal Cancer DNA Array
- Anti-Microbial Array 2*
- Anti-Microbial Array 3*
- SyntheticSteroidsArray*
- Drugs of Abuse Array 2*
- Anti-Microbial Array 1
- Anti-Microbial Array 2
- Anti-Microbial Array 3
- SyntheticSteroidsArray
- Drugs of Abuse Array 2

### Drugs of Abuse Array 1

- Amphetamine
- Methamphetamine
- Barbiturates
- Benzodiazepine I
- Benzodiazepine II
- Cocaine Metabolite
- Methadone
- Opiates
- Phencyclidine
- Cannabinoids
- Creatinine (urine application only)

### Drugs of Abuse Array II

- Buprenorphine
- Fentanyl
- Ketamine
- LSD
- MDMA
- Hydromorphone
- Methaqualone
- Oxycodone I
- Oxycodone II
- Propoxyphene
- Creatinine*

### Drugs of Abuse Arrays

- Specific matrix optimised kits for
  - Urine (FDA cleared)
  - Urine Semi-Quant
  - Whole Blood Quant
  - Oral Fluid Quant
**Biochip Array Technology**

### Amphetamine Class

<table>
<thead>
<tr>
<th>Target</th>
<th>Urine</th>
<th>Blood</th>
<th>Oral Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>d-Amphetamine / + Methamphetamine</td>
<td>50 ng/mL / 1000 ng/mL</td>
<td>25 ng/mL / 50 ng/mL</td>
<td>50 ng/mL / 50 ng/mL</td>
</tr>
<tr>
<td>Cut-off</td>
<td>1000 ng/mL / 1000 ng/mL</td>
<td>25 ng/mL / 50 ng/mL</td>
<td>50 ng/mL / 50 ng/mL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>d-Amphetamine assay</th>
<th>Methamphetamine assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;0.2%</td>
<td>&gt;0.2%</td>
</tr>
<tr>
<td>100%</td>
<td>0.4%</td>
</tr>
<tr>
<td>544%</td>
<td>0.4%</td>
</tr>
<tr>
<td>0.4%</td>
<td>36%</td>
</tr>
</tbody>
</table>

### Barbiturates

<table>
<thead>
<tr>
<th>Target</th>
<th>Urine</th>
<th>Blood</th>
<th>Oral Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>200 ng/mL</td>
<td>50 ng/mL</td>
<td>5 ng/mL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cross reactivity (urine)</th>
<th>Barbiturates assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>100%</td>
</tr>
<tr>
<td>Secobarbital</td>
<td>512%</td>
</tr>
<tr>
<td>Pentobarbital</td>
<td>183%</td>
</tr>
<tr>
<td>Amobarbital</td>
<td>84%</td>
</tr>
<tr>
<td>Barbital</td>
<td>40%</td>
</tr>
<tr>
<td>Butalbital</td>
<td>172%</td>
</tr>
</tbody>
</table>

### Benzodiazepines

<table>
<thead>
<tr>
<th>Target</th>
<th>Urine</th>
<th>Blood</th>
<th>Oral Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxazepam / Lorazepam</td>
<td>1 ng/mL / 200 ng/mL</td>
<td>50 ng/mL / 50 ng/mL</td>
<td>1 ng/mL / 1 ng/mL</td>
</tr>
<tr>
<td>Cut-off</td>
<td>200 ng/mL / 200 ng/mL</td>
<td>50 ng/mL / 50 ng/mL</td>
<td>1 ng/mL / 1 ng/mL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cross reactivity (urine)</th>
<th>Benzodiazepines assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxazepam</td>
<td>100%</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>7%</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>181%</td>
</tr>
<tr>
<td>Diazepam</td>
<td>512%</td>
</tr>
<tr>
<td>Temazepam</td>
<td>444%</td>
</tr>
<tr>
<td>Nordiazepam</td>
<td>250%</td>
</tr>
<tr>
<td>Nitrazepam</td>
<td>241%</td>
</tr>
<tr>
<td>Flunitrazepam</td>
<td>100%</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>8.4%</td>
</tr>
<tr>
<td>Lorazepam glucuronide</td>
<td>&lt;0.1%</td>
</tr>
</tbody>
</table>

**RANDOX clinical diagnostic solutions**
### Cannabinoids

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Oral Fluid</th>
<th>Blood</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 ng/mL</td>
<td>10 ng/mL</td>
<td>50 ng/mL</td>
<td>11 nor-9-THC-COOH</td>
</tr>
<tr>
<td>50 ng/mL</td>
<td>10 ng/mL</td>
<td>4 ng/mL</td>
<td>11 nor-9-THC</td>
</tr>
</tbody>
</table>

**Target**
- Oral Fluid: 11 nor-9-THC-COOH
- Blood: 11 nor-9-THC-COOH
- Urine: 11 nor-9-THC

**Cross reactivity (urine)**
- 11 nor-9-THC-COOH: 100%
- 11 nor-9-THC-COOH: 49%
- 11 hydroxy-9-THC: 3%
- 11 hydroxy-9-THC: <5%
- Cannabinol: <0.5%
- Cannabidiol: <0.5%

### Methadone

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Oral Fluid</th>
<th>Blood</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 ng/mL</td>
<td>25 ng/mL</td>
<td>5 ng/mL</td>
<td>Methadone</td>
</tr>
<tr>
<td>25 ng/mL</td>
<td>25 ng/mL</td>
<td>5 ng/mL</td>
<td>Methadone</td>
</tr>
<tr>
<td>5 ng/mL</td>
<td>5 ng/mL</td>
<td>5 ng/mL</td>
<td>Methadone</td>
</tr>
</tbody>
</table>

**Target**
- Oral Fluid: Methadone
- Blood: Methadone
- Urine: Methadone

**Cross reactivity (urine)**
- Methadone: 100%
- EDDP: <0.1%
- EMDP: <0.1%
- LAAM: <1.0%

### Opiates

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Oral Fluid</th>
<th>Blood</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 ng/mL</td>
<td>25 ng/mL</td>
<td>40 ng/mL</td>
<td>Morphine</td>
</tr>
<tr>
<td>25 ng/mL</td>
<td>25 ng/mL</td>
<td>40 ng/mL</td>
<td>Morphine</td>
</tr>
</tbody>
</table>

**Target**
- Oral Fluid: Morphine
- Blood: Morphine
- Urine: Morphine

**Cross reactivity (urine)**
- Morphine: 100%
- Codeine: 115%
- Morphine-3-glucuronide: 67%
- Hydromorphone: 27%
- Hydrocodone: 17%
- Dihydrocodeine: 13%

### Phencyclidine

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Oral Fluid</th>
<th>Blood</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 ng/mL</td>
<td>5 ng/mL</td>
<td>10 ng/mL</td>
<td>Phencyclidine</td>
</tr>
<tr>
<td>5 ng/mL</td>
<td>5 ng/mL</td>
<td>10 ng/mL</td>
<td>Phencyclidine</td>
</tr>
</tbody>
</table>

**Target**
- Oral Fluid: Phencyclidine
- Blood: Phencyclidine
- Urine: Phencyclidine

**Cross reactivity (urine)**
- Phencyclidine: 100%
- TCP: 90%
Biochip Array Technology

Cocaine Metabolite

<table>
<thead>
<tr>
<th>Target</th>
<th>Urine</th>
<th>Blood</th>
<th>Oral Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzoylecgonine</td>
<td>Benzoylecgonine</td>
<td>Benzoylecgonine</td>
<td></td>
</tr>
<tr>
<td>Cut-off</td>
<td>300 ng/mL</td>
<td>50 ng/mL</td>
<td>20 ng/mL</td>
</tr>
</tbody>
</table>

Cross-reactivity (urine):

- Benzoylecgonine: 100%
- Cocaethylene: 4.1%
- Ecgonine: <0.1%
- Ecgonine methyl ester: <3%
- Norcocaine: <0.1%

Sensitivities and Ranges

<table>
<thead>
<tr>
<th>Assay Type</th>
<th>Urine Sensitivity</th>
<th>Urine Assay Range</th>
<th>Whole Blood Sensitivity</th>
<th>Whole Blood Assay Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>8.1 ng/ml</td>
<td>0-2500 ng/ml</td>
<td>0.4 ng/ml</td>
<td>0-125 ng/ml</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>45.2 ng/ml</td>
<td>0-2000 ng/ml</td>
<td>6.25 ng/ml</td>
<td>0-250 ng/ml</td>
</tr>
<tr>
<td>Cocaine Metabolite</td>
<td>2.3 ng/ml</td>
<td>0-800 ng/ml</td>
<td>0.01 ng/ml</td>
<td>0-250 ng/ml</td>
</tr>
<tr>
<td>Methadone</td>
<td>0.6 ng/ml</td>
<td>0-800 ng/ml</td>
<td>0.13 ng/ml</td>
<td>0-125 ng/ml</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>3.6 ng/ml</td>
<td>0-150 ng/ml</td>
<td>0.28 ng/ml</td>
<td>0-50 ng/ml</td>
</tr>
<tr>
<td>Barbiturate</td>
<td>9.4 ng/ml</td>
<td>0-800 ng/ml</td>
<td>0.1 ng/ml</td>
<td>0-250 ng/ml</td>
</tr>
<tr>
<td>Opiates</td>
<td>0.8 ng/ml</td>
<td>0-3500 ng/ml</td>
<td>0.12 ng/ml</td>
<td>0-125 ng/ml</td>
</tr>
<tr>
<td>Benzodiazepine 1</td>
<td>0.6 ng/ml</td>
<td>0-500 ng/ml</td>
<td>0.04 ng/ml</td>
<td>0-250 ng/ml</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>1.1 ng/ml</td>
<td>0-500 ng/ml</td>
<td>0.1 ng/ml</td>
<td>0-250 ng/ml</td>
</tr>
<tr>
<td>Phencyclidine (PCP)</td>
<td>1.9 ng/ml</td>
<td>0-100 ng/ml</td>
<td>0.16 ng/ml</td>
<td>0-50 ng/ml</td>
</tr>
</tbody>
</table>

Drugs of Abuse Array II

<table>
<thead>
<tr>
<th>Assay</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>Buprenorphine</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Norfentanyl &amp; fentanyl</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Hydromorphone</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Norketamine &amp; ketamine</td>
</tr>
<tr>
<td>LSD</td>
<td>Nor-LSD &amp; LSD</td>
</tr>
<tr>
<td>MDMA</td>
<td>MDMA &amp; MDEA</td>
</tr>
<tr>
<td>Methaqualone</td>
<td>Free &amp; 2'-hydroxymethaqualone, 3'-hydroxymethaqualone</td>
</tr>
<tr>
<td>Oxycodone 1</td>
<td>Noroxycodone &amp; oxycodone &amp; hydrocodone</td>
</tr>
<tr>
<td>Oxycodone 2</td>
<td>Oxymorphone &amp; oxycodone</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>Norpropoxyphene &amp; propoxyphene</td>
</tr>
</tbody>
</table>

Whole Blood Trials

- MEO USA trial using pre/post-mortem bloods.
- 33 samples x 10 assays = 330 tests completed.
- 1 x Investigator runs.
- Overall completion time = 1 hr 40 mins.
  - Includes:-
    - Sample preparation (dilution ¼)
    - Calibrator Reconstitution
    - Controls
Biochip Array Technology

Urine Evaluation

- FDA Trials
- To assess the overall performance of drugs of abuse screening on the evidence immunoassay technology
- To compare the evidence performance to an alternate immunoassay system
- To compare the evidence performance to results obtained by GC/MS

More than 1300 clinical urine samples covering the entire range of possible test results for all ten drugs of abuse
Comparison carried out by independent clinical toxicology laboratory in Texas
10% of samples fell within ±25% of the assay cut-off concentrations
### Methamphetamine

- Evidence with CEDIA: 96.7% Agreement
- Evidence with GC/MS: 97.0% Agreement
- CEDIA with GC/MS: 82.2% Agreement

#### % Agreement:
- Evidence with CEDIA: 96.7%
- Evidence with GC/MS: 97.0%
- CEDIA with GC/MS: 82.2%

#### Total number of samples:
- Evidence with CEDIA: 1249
- Evidence with GC/MS: 305
- CEDIA with GC/MS: 219

#### Discrepant samples:
- Evidence with CEDIA: 40
- Evidence with GC/MS: 9
- CEDIA with GC/MS: 39

### Cannabinoids

- Evidence with CEDIA: 97.9% Agreement
- Evidence with GC/MS: 93.9% Agreement
- CEDIA with GC/MS: 81.8% Agreement

#### % Agreement:
- Evidence with CEDIA: 97.9%
- Evidence with GC/MS: 93.9%
- CEDIA with GC/MS: 81.8%

#### Total number of samples:
- Evidence with CEDIA: 1335
- Evidence with GC/MS: 231
- CEDIA with GC/MS: 231

#### Discrepant samples:
- Evidence with CEDIA: 28
- Evidence with GC/MS: 14
- CEDIA with GC/MS: 42

### Opiates

- Evidence with CEDIA: 92.6% Agreement
- Evidence with GC/MS: 89.1% Agreement
- CEDIA with GC/MS: 80.0% Agreement

#### % Agreement:
- Evidence with CEDIA: 92.6%
- Evidence with GC/MS: 89.1%
- CEDIA with GC/MS: 80.0%

#### Total number of samples:
- Evidence with CEDIA: 1334
- Evidence with GC/MS: 320
- CEDIA with GC/MS: 320

#### Discrepant samples:
- Evidence with CEDIA: 99
- Evidence with GC/MS: 35
- CEDIA with GC/MS: 128

### Overall Summary

#### % Agreement

- Evidence with CEDIA: 96.9%
- Evidence with GC/MS: 90.5%
- CEDIA with GC/MS: 83.4%

#### Total number of tests: 11,750
**Biochip Array Technology**

User Defined Cut-off selection.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Min</th>
<th>Max</th>
<th>Cut Off</th>
</tr>
</thead>
<tbody>
<tr>
<td>METHAMPHETAMINE</td>
<td>100</td>
<td>1800</td>
<td>0</td>
</tr>
<tr>
<td>BARBITURATE</td>
<td>46</td>
<td>900</td>
<td>0</td>
</tr>
<tr>
<td>BENSODAZEPINE1</td>
<td>50</td>
<td>900</td>
<td>0</td>
</tr>
<tr>
<td>BENSODAZEPINE2</td>
<td>50</td>
<td>900</td>
<td>0</td>
</tr>
<tr>
<td>METHADONE</td>
<td>25</td>
<td>900</td>
<td>0</td>
</tr>
<tr>
<td>OPIATE</td>
<td>50</td>
<td>3000</td>
<td>0</td>
</tr>
<tr>
<td>PCP</td>
<td>10</td>
<td>150</td>
<td>0</td>
</tr>
<tr>
<td>BZD</td>
<td>20</td>
<td>700</td>
<td>0</td>
</tr>
<tr>
<td>CREATININE</td>
<td>2</td>
<td>600</td>
<td>0</td>
</tr>
<tr>
<td>THC</td>
<td>15</td>
<td>200</td>
<td>0</td>
</tr>
<tr>
<td>AMPHETAMINE</td>
<td>75</td>
<td>1800</td>
<td>0</td>
</tr>
</tbody>
</table>

Apply To Samples  | Cancel

**Analysers and Software**

**Features**

- Semi-automated
- Based on Biochip Array Technology
  - Multiple test sites per biochip
- Fast Results
  - 54 biochips ie. 540 Tests in 1 hour
- Small sample volumes
  - Urine – 3.5μl per test
  - Whole Blood – 6μl per test
  - Oral Fluid – 10μl per test
Features

• Quality of results
  – All Randox products are developed to ISO 13485, diagnostic standards
  – Full trace-ability through manufacture
  – Antibody Specificity
  – Self sufficient antibody supply
  – Specific Methamphetamine and Lorazepam assays

• Cut-off selection
  – Cut-offs can be selected and reselected without recalibration
  – Different cut-offs can be selected for the same analyte during the same run, ie. Opiates sample A 25ng/mL, sample B 10ng/mL.

• Fully Quantitative Analysis
  – Identified as positive/negative
  – Concentration of compound also displayed

Features

• Software
  – Windows XP® based
  – Colour coding easy to follow
  – Multiple search formats
  – Easy export of results
  – Fully LIMS connectable
  – Extensive QC facilities
    • Levy Jennings and Multi-point rules.
  – Enhance trouble shooting
Biochip Array Technology

Features

• Fully Automated
  – Walk away system
• High throughput
  – 130 samples per hour x no. of tests per chip
• Chain of custody Features
  – Sample access doors lock once sample is loaded
    • Password Protected

• Retrospective Testing
  – Although only invoiced for tests reported, all assays are carried out simultaneously
  – If certain assays are not reported they can be recalled at a later stage.
References


FitzGerald SP, Lamont JV, McConnell RI, Benchikh EO; Development of a high throughput automated analyser using biochip array technology. Clinical Chemistry; 51 (7) 1165-1176