Radiation Diagnostic Tools In Development at
The Biomedical Advanced Research and Development Authority

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HHS\ASPR\BARDA

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HHS Organization

ASPR

OS

Biomedical Advanced Research & Development Authority

Acq. Management Contracts & Grants

Preparedness & Emergency Operations

OFPA

COO

Policy and Planning

CBRN Division

Mfg., Facilities & Engineering Division

Clinical Studies Division

SSTD Division

RQA Division

Pan Flu Division

Modeling Division
BARDA Mission

Support development and availability of countermeasures for CBRN threats, pandemic influenza, and emerging infectious diseases through advanced product development, stockpile acquisition/building, manufacturing infrastructure building, and product innovation.

Washington Office Center

Patriots Plaza II
Medical Countermeasures

Medical Devices  Antimicrobials  Diagnostics  Vaccines  Therapeutics

• **Diagnostics is a Medical Countermeasure** when it informs care of individual casualties/patients with other countermeasures

• **Countermeasures empower local response**
Man-made and Natural Threats

- CBRN Threats
  - Chemical nerve agents & cyanide
  - Radiological and nuclear agents
  - Biothreats (anthrax, smallpox, plaque, tularemia, VHF, and others)

- Pandemic influenza

- Emerging infectious diseases
BARDA Diagnostics Intended Users

- Primary Focus for Dx
  - Enhance Local Surge Capability
    - Sentinel Labs
    - Physicians Office Labs (POL)
    - Point of Care (POC)
- Clinical Samples Only
  - Dx results that provide information on the health condition of an individual casualty.
Diagnostics Instrument Strategy (All Threats)

• **Laboratory**
  — Leverage platforms widely placed in clinical labs (at the time of the incident) to inform routine healthcare. Only develop additional platforms if essential assay technologies not compatible with existing platforms.
  — Fund adaptation, if required, to allow utilization of existing products.

• **Point of Care / Physician’s Office Lab**
  — Develop new platforms where existing platforms do not meet needs of ConOps.
  — Improve performance of existing platforms
BARDA/CBRN Biodosimetry Program
## Post Event Radiation Injury Diagnostics
### Currently Available Technologies

<table>
<thead>
<tr>
<th>Type</th>
<th>POC</th>
<th>Centralized Laboratory</th>
<th>Biodosimetry or Bioassay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosomal Aberration</td>
<td>None</td>
<td>Dicentric Chromosome Assay&lt;br&gt;• Domestic Labs - 2&lt;br&gt;• Oak Ridge / Radiation Assistance Center (REAC)&lt;br&gt;• 100’s of samples / day&lt;br&gt;• DoD / Armed Forces Radiation Research Institute (AFRRI)&lt;br&gt;• 100’s of samples / day&lt;br&gt;• Additional International Capacity&lt;br&gt;Micronuclei Assay&lt;br&gt;• Additional international Capacity - Health Canada &amp; Others</td>
<td>Biodosimetry</td>
</tr>
<tr>
<td>Lymphocyte Depletion Kinetics&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Limited</td>
<td>Extensive Capacity – Blood Cell Counters</td>
<td>Biodosimetry</td>
</tr>
<tr>
<td>Time to Emesis</td>
<td>Extensive – Accuracy low</td>
<td>N/A</td>
<td>Biodosimetry</td>
</tr>
<tr>
<td>Bioassay</td>
<td>None</td>
<td>CDC&lt;br&gt;• Screen&lt;br&gt;• Gama emitters – 3000 samples/day&lt;br&gt;• Alpha or beta emitters - 300 samples/day&lt;br&gt;• ID &amp; Quantify Specific Radionuclides ~300/day</td>
<td>Bioassay</td>
</tr>
</tbody>
</table>
### Radiation Diagnostics Tool
#### Effectiveness vs. Type of Incident

<table>
<thead>
<tr>
<th>Type of Incident</th>
<th>Exposure (Biodosimetry)</th>
<th>Contamination (Bioassay)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improvised Nuclear Device (IND)</td>
<td>Effective (shine)</td>
<td>Effective (fallout)</td>
</tr>
<tr>
<td>Nuclear Power Plant (NPP)</td>
<td>Limited</td>
<td>Effective (fallout)</td>
</tr>
<tr>
<td>Radiation Dispersal Device (RDD)</td>
<td>Limited</td>
<td>Effective</td>
</tr>
<tr>
<td>Radiation Exposure Device (RED)</td>
<td>Effective</td>
<td>Not useful</td>
</tr>
</tbody>
</table>

**Biodosimetry** determines a “past” radiation dose from an “exposure” incident.

**Bioassay** determines “past, current and future” radiation doses from a “contamination” incident.

*ASPR: Resilient People. Healthy Communities. A Nation Prepared.*
10 KT IND Scenario Planning

A mass casualty event such as an IND may bring 1,000,000 people or more for evaluation for radiation exposure and/or contamination.

Given the large numbers to be processed and the time-sensitive nature of the therapeutic window for MCMs, radiation dose assessment will require a multi-phased, multi-parametric approach.
<table>
<thead>
<tr>
<th></th>
<th><strong>Point of Care Device (POC)</strong></th>
<th><strong>High Throughput Device (HT)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of result:</strong></td>
<td>Qualitative</td>
<td>Quantitative (accuracy ± 0.5Gy)</td>
</tr>
<tr>
<td><strong>CONOPs:</strong></td>
<td>Initial Triage / Sorting</td>
<td>Injury Assessment / Treatment</td>
</tr>
<tr>
<td><strong>Exposure level:</strong></td>
<td>2 Gy (200 rad) (threshold)</td>
<td>Range: 0.5 – 10 Gy</td>
</tr>
<tr>
<td><strong>Ease of operation:</strong></td>
<td>Easy to operate, minimal complexity (requires minimal training; CLIA waived)</td>
<td>Laboratory instrument—more labor intensive, requires training</td>
</tr>
<tr>
<td><strong>Device characteristics:</strong></td>
<td>Integrated components—no separate sample preparation</td>
<td>May include separate components as needed. High automation desired.</td>
</tr>
<tr>
<td><strong>Setting for use:</strong></td>
<td>Tents, shelters, open settings</td>
<td>Labs, hospitals, fixed facilities</td>
</tr>
<tr>
<td><strong># Patients / Event</strong></td>
<td>Up to 1,000,000 in 6 days</td>
<td>Up to 400,000 (may need multiple assessments)</td>
</tr>
<tr>
<td><strong>Time to result:</strong></td>
<td>Rapid but individual sample result (&lt; 30 minutes)</td>
<td>Up to 24 hours</td>
</tr>
</tbody>
</table>
High Technical Risk
Product Development

- Start multiple projects
  - Multiple technologies
  - Multiple contractors
- Many will start but few will finish

- Reduce the number of projects as maturity increases
  - In Process Reviews (IPRs)
  - Keeping the strongest performers
  - Maintain distribution of technologies until strongest for con-ops emerge

<table>
<thead>
<tr>
<th>TRL</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
</table>

Discovery/Research
Proof of Concept
Product Dev.
Integration
Verification
Clinicals, FDA
Operation

BARDA Biodosimetry Projects

BARDA Biodosimetry Program

- POC & Laboratory Diagnostics
  - POC – Qualitative, Dose ≥2Gy
  - Lab – Quantitative 0.5 to 10Gy
- 11 projects awarded to date
  - 10 in FY2010
  - 1 in FY 2011
- 6 projects continuing forward from 2012
  - Biomarker feasibility shown
    • Mouse or human
  - In product development phase
    • Proof of concept complete (TRL4)

Biodosimetry Technologies

- DNA damage
- Ocular screen
- Proteomics
- Gene expression
- Electron paramagnetic resonance
- Cytology
- Volatile organic compounds
## Point Of Care Biodosimetry Tools (In development)

<table>
<thead>
<tr>
<th>Contractor</th>
<th>POC Technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRI International</td>
<td>Protein Expression immunoassay</td>
</tr>
<tr>
<td>Dartmouth Medical School</td>
<td>Election paramagnetic resonance</td>
</tr>
<tr>
<td>MesoScale Diagnostics</td>
<td>Protein expression immunoassay</td>
</tr>
<tr>
<td>Stanford University</td>
<td>Protein expression immunoassay</td>
</tr>
<tr>
<td>University of Rochester</td>
<td>DNA damage Alu fragments</td>
</tr>
<tr>
<td>ChromoLogic, Ocular dosimetry</td>
<td>Non-invasive</td>
</tr>
<tr>
<td>Visca</td>
<td>Gene expression qRT-PCR</td>
</tr>
<tr>
<td>Menssana Research Research</td>
<td>VOCs in Breath</td>
</tr>
</tbody>
</table>

Jan. 2013
## High Throughput Laboratory Biodosimetry Tools (In Development)

<table>
<thead>
<tr>
<th>Contractor</th>
<th>HT Technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duke University</td>
<td>Gene expression <em>Chemical ligation</em></td>
</tr>
<tr>
<td>Arizona State University</td>
<td>Gene expression <em>Chemical ligation</em></td>
</tr>
<tr>
<td>MesoScale Diagnostics, LLC</td>
<td>Protein expression / <em>immunoassay</em></td>
</tr>
<tr>
<td>Northrop Grumman</td>
<td>Cytology <em>micronuclei</em></td>
</tr>
<tr>
<td>Stanford University</td>
<td>Protein expression biomarker <em>immunoassay</em></td>
</tr>
</tbody>
</table>

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Interfacing with BARDA

- [http://www.phe.gov/about/barda/Pages/default.aspx](http://www.phe.gov/about/barda/Pages/default.aspx)
  - Program description, information, news, announcements

- [www.medicalcountermeasures.gov](http://www.medicalcountermeasures.gov)
  - Portal to BARDA
  - Register, request a meeting
  - Tech Watch

- [www.fedbizopps.gov](http://www.fedbizopps.gov)
  - Official announcements and detailed information about all government solicitations
  
  – [Rodney.Wallace@hhs.gov](mailto:Rodney.Wallace@hhs.gov)