



# U.S. ARMY COMBAT CAPABILITIES DEVELOPMENT COMMAND CHEMICAL BIOLOGICAL CENTER

Technical Considerations for Building Predictive Toxicological Tools  
in Support of the Chem/Bio Defense Mission

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# ABOUT CCDC CHEMICAL BIOLOGICAL CENTER



## OUR MISSION & VISION



**MISSION:** Provide innovative chemical, biological, radiological, nuclear and explosive (CBRNE) defense capabilities to enable the Joint Warfighters' dominance on the battlefield and interagency defense of the homeland.

**VISION:** Be the premier provider of innovative CBRNE solutions for the Army, DOD, the Nation, and our allies.



# MEETING SOLDIER NEEDS



DETECTION

PROTECTION

OBSCURATION

DECONTAMINATION





## UNIQUE INFRASTRUCTURE



**1.22 M SQUARE FEET  
OF LABORATORY AND  
CHAMBER SPACE**

**BSL-2 AND BSL-3  
LABORATORIES  
CAPABLE OF HANDLING  
EXPLOSIVE/TOXIC MATERIAL**

**MAJORITY OF THE  
NATION'S CHEMICAL  
SURETY HOODS**

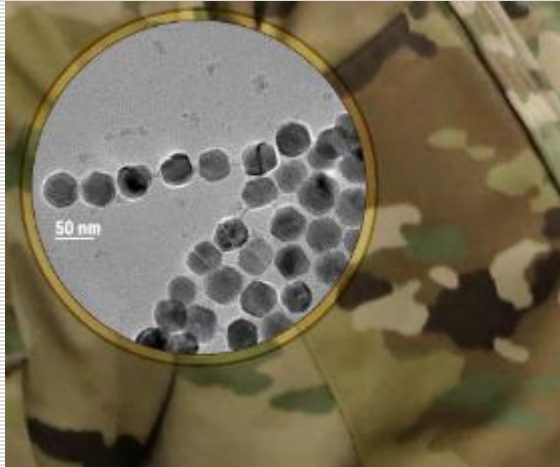




# NOVEL APPROACHES TO CBRN DEFENSE



*HOW CCDC IS RESEARCHING EMERGING CBRN THREATS TO UNDERSTAND THEIR EFFECTS*



**Synthetic Biology  
Research**



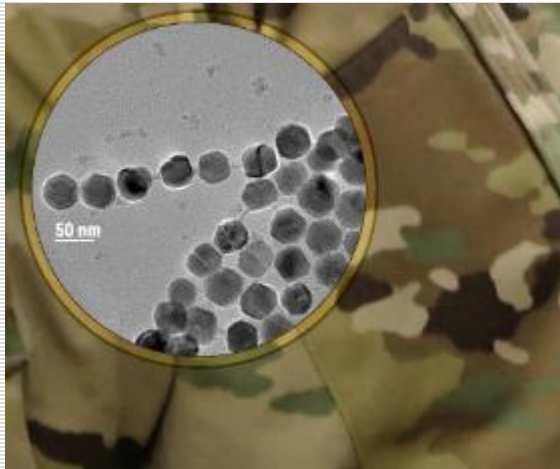
**Cellular  
Toxicology**



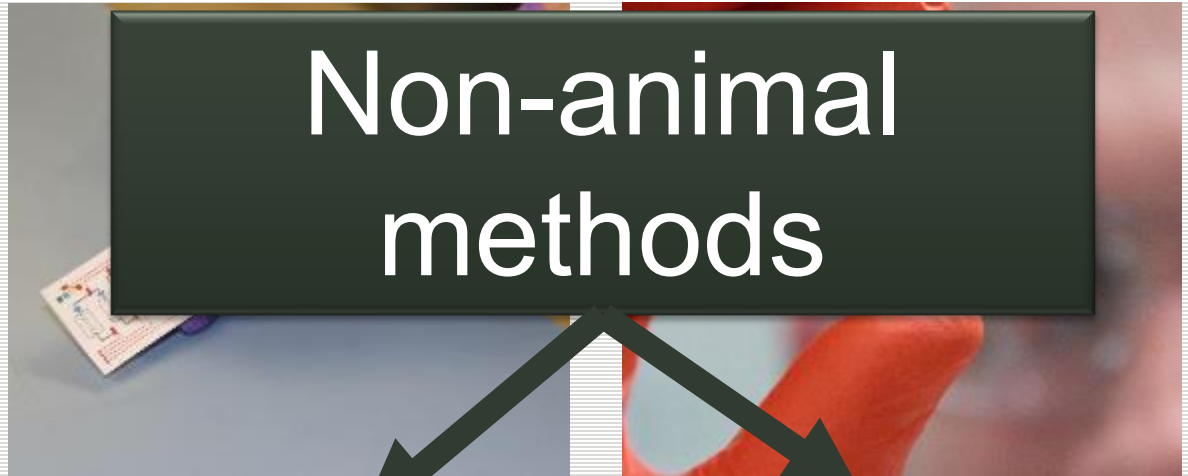
**Threat Agent  
Science**



## HOW CCDC IS RESEARCHING EMERGING CBRN THREATS TO UNDERSTAND THEIR EFFECTS



**Synthetic Biology  
Research**



**Cellular  
Toxicology**

**Threat Agent  
Science**



# SOLUTIONS REQUIRE COLLABORATION



## SMALL BUSINESS

## ACADEMIA



## DOD & FEDERAL PARTNERS

## LOCAL GOVERNMENTS



## INTERNATIONAL

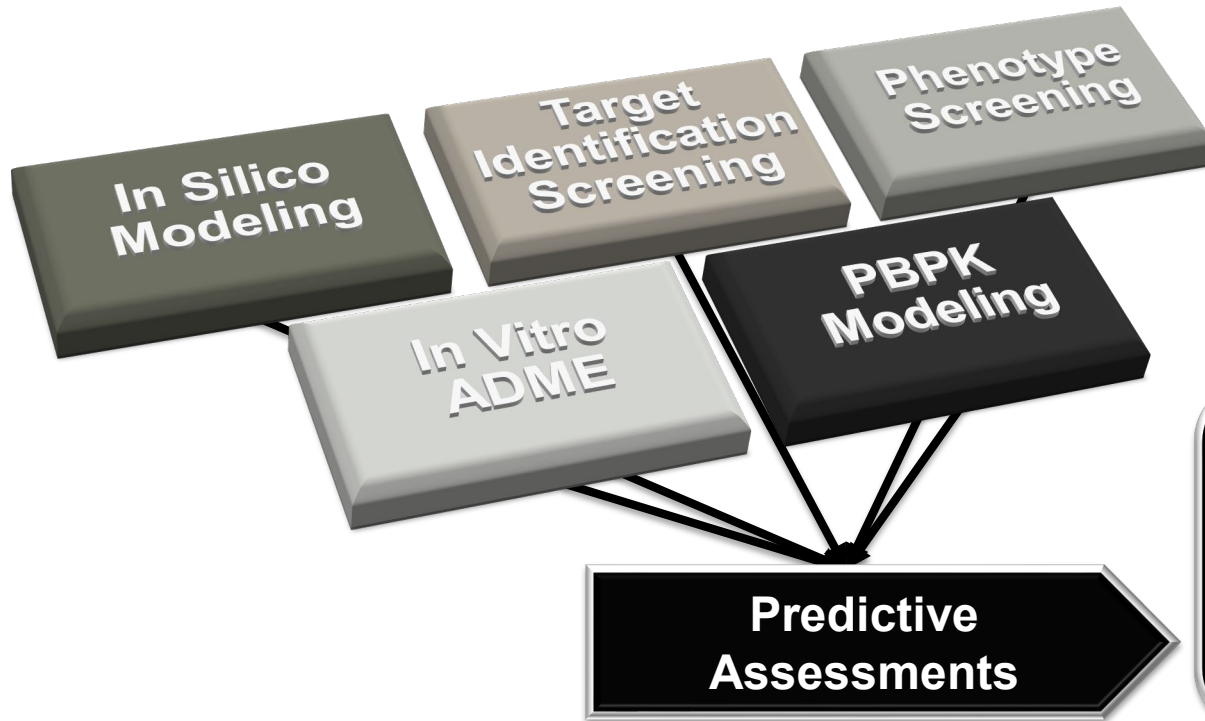
- ✓ Cooperative Research And Development Agreement (CRADA)
- ✓ Educational Partnership Agreements (EPA)
- ✓ Technology Support Agreement (TSA)
- ✓ Patent License Agreement (PLA)
- ✓ Army Small Business Innovation Research (SBIR)
- ✓ Chemical Biological Defense (CBD) SBIR
- ✓ Army Small Business Technology Transfer (STTR)
- ✓ CDC CBC Broad Agency Announcement (BAA)
- ✓ Rapid Innovation Fund BAA
- ✓ Memorandum of Understanding (MOU)
- ✓ Memorandum of Agreement (MOA)
- ✓ Material Transfer Agreement (MTA)
- ✓ Non-DoD Interagency Agreement (IAA)



# BUILDING FOR FUTURE CB NEEDS



## Primary Thrust Areas for Molecular Toxicology



- Potency
- Molecular Target(s)
- Mechanism of Toxicity
- Similarity Assessment
- Species Differences
- Human Risk Assessment





# IN SILICO MODELING



Need:

- Predicted safe, hazardous and lethal exposure concentrations (no safety margins)
- Relative potency within a chemical class
- Potential physical hazards
- Potential molecular targets and MOA
- Differences in target affinity of similar analogs
- MIXTURE effects

Hazard classifications are NOT a primary concern, or issues related to regulatory safety testing of new chemicals



# IN SILICO MODELING



## Criteria for Successful Integration:

- Software considerations (can it be integrated into Army IT infrastructure?)
- Ease of updating with proprietary data
- Ease of integration with other modeling tools
- Built on data sets relevant to the CBD mission



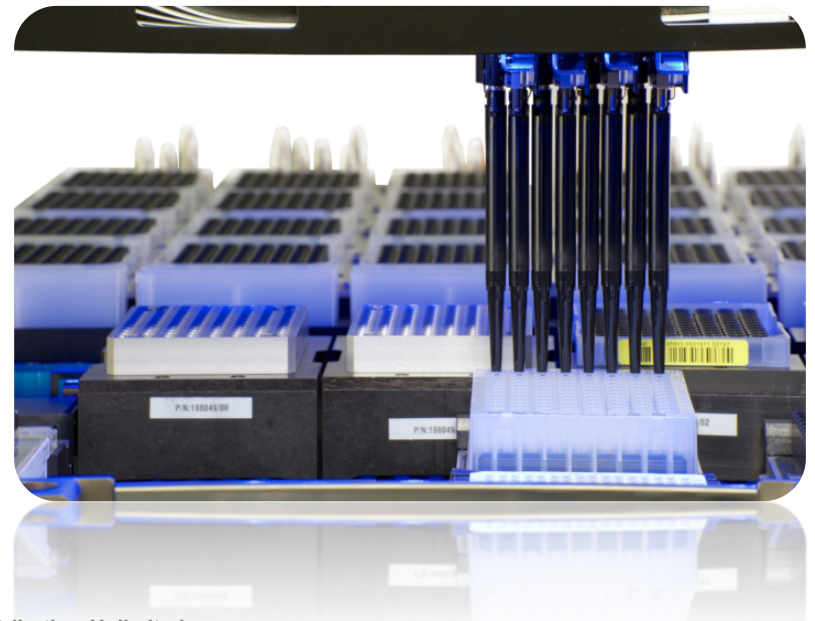
# TARGET IDENTIFICATION



Need: High-content tools that can identify potential primary and secondary molecular targets of possible threat compounds.

Criteria for successful model integration:

- Technology transfer doesn't require unique infrastructure or equipment
- Sensitivity/Specificity for CBD relevant threat compounds
- Subcytotoxic responses
- Human targets





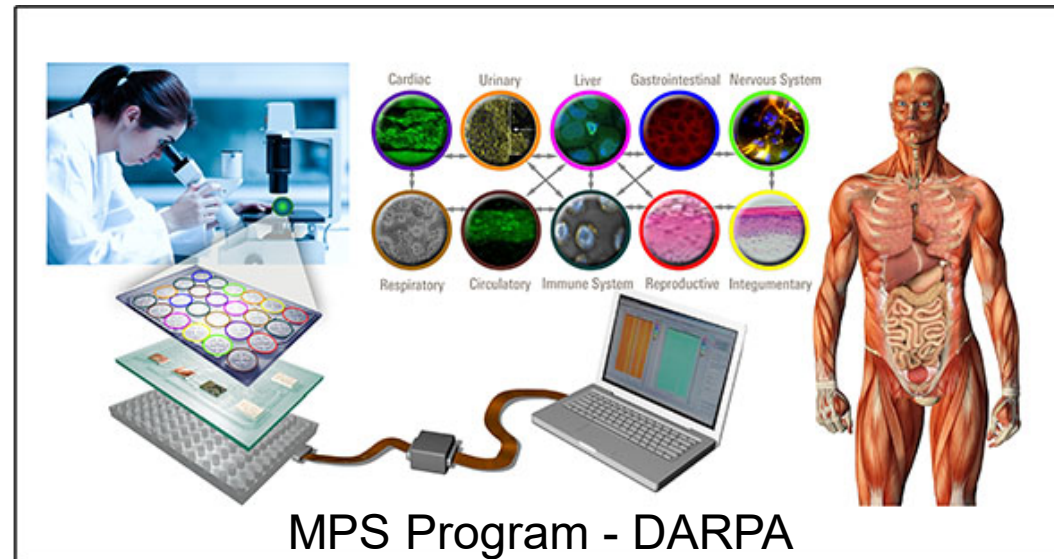
# PHENOTYPIC SCREENING



Need: Target agnostic systems that measure organ specific function

Criteria for Successful Model Integration:

- Organ systems of interest: hepatic, CNS, cardiac, respiratory, dermal
- Consider ADME and organ-organ interactions
- As simple as possible!
- Avoid unnecessary Complexity
- Give indication of MOA





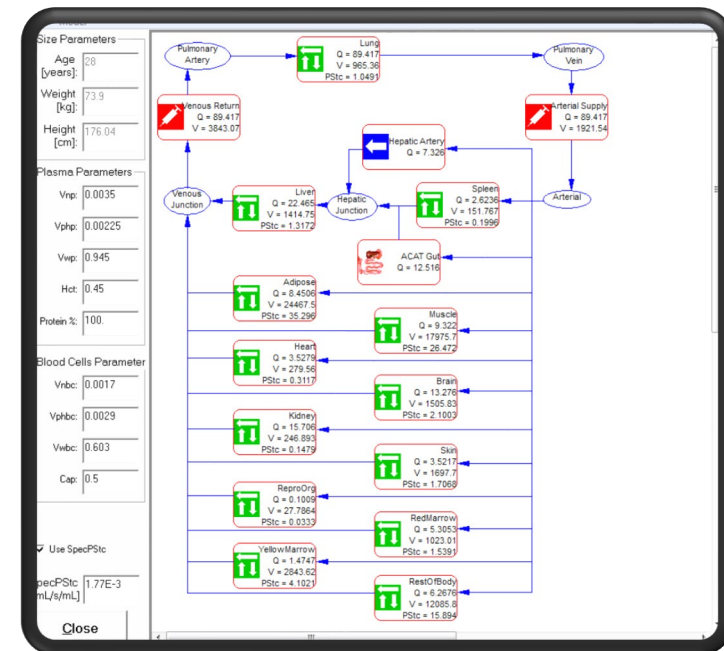
# ADME AND PBPK MODELING



Need: Extrapolation from existing data, batch processing and high-throughput toxicokinetics (HTTK), in vitro to in vivo extrapolations (IVIVE)

## Criteria for Successful Integration:

- Ability to integrate with other tools
- Consider respiratory and dermal routes of exposure







# OTHER MAJOR CONSIDERATIONS FOR CBRN SOLUTIONS



- Consumable over reusable materials/platforms that come into contact with test substance.
- Ease of decontamination
- Ease of operation within engineering controls
- On-site service!! Equipment does not leave the lab.



Thank you!



## CONTACT US



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