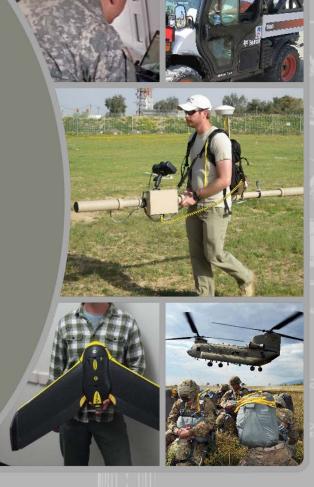# Perspective on the US Army's Uses for Predictive Models of Acute Oral Toxicity

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Opinions expressed are those of the author and do not necessarily reflect US Army policy.

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Army and Chemicals: It's Complicated

Battlefield Warfighter Needs	Military Enterprise Needs
Intelligence Preparation of the Battlefield What chem/bio threats exist Where do chem/bio threats exist What is the risk of incapacitation What are the appropriate countermeasures **Small Unit Needs** Sensors to identify chemical/biological What are the likely acute symptoms Will this lead to incapacitation What is appropriate countermeasure	**Military Materials Design and Production** Kill new chemical entities early in development Move toxicity testing earlier in development Methods that use only structure for tox screening Decrease testing costs Increase testing throughput

OBJECTIVE: DECIDE FASTER

My Role At the US Army

- Objective
    - To get the Army (and our partner Agencies) the best models and tools to DECIDE FASTER
    - Intelligence Preparation of the Battlefield, Emergency Response, and Enterprise Needs (platforms, weapons, materials)

- Approach
    - Technology Development
        - Basic and applied research portfolio in Artificial Intelligence
            - Ethical, Legal, Social Implications of AI
            - AI to predict toxicity using only structural information or read-across
            - Fill model and needs gaps

    - Technology Enabling
        - Work with others outside Army to develop applied research products
        - Acquire open source and freely available tools

    - Technology Transfer
        - Develop predictive AI and model platforms that use existing data and structural information to make predictions that enable the Army to DECIDE FASTER

What Do We Need from QSAR Models?

- Open source and freely available are most useful
- Need the data used to train, test, and validate

- Why?
  - Need to be able to validate that the tool does what it says through code examination
  - AI/Models and Bias
    - Need to identify potential sources of bias and outcomes of any bias to mitigate impact on decisions
  - Operational Security (OpSec)
    - Need to ensure we understand what the software might communicate with, how it communicates, and what it communicates with
  - We seek to build software systems that enable end-users to use these models
    - Typically academic models lack a GUI – our end users expect a GUI experience

Our Challenges with Computational Models

- Army chemistries tend to be unique
  - Energetics and explosives tend to have a large number of C-N bonds
  - Thus, many of our chemistries fall outside the domain of applicability of most models
  - We have unique mixtures as a result

- De novo chemical-biological interactions are generally necessary
  - Docking and 3-D models tend to not perform that great (in general)

Where Are Moving?

- "Industrial" Side
  - Structures to perform early structural screening
  - Identify potential toxicity liabilities (human and environmental) early in development
  - Tradespace analysis
  - Potential for readiness impacts
    - Environmental toxicity in endangered species may close training sites until cleaned up
  - Understanding and forecasting liabilities of legacy contaminants

- Intelligence side
  - Inform about potential toxicity of chemicals that may be encountered on the battlefield
    - Urban warfare significantly increases the list of potential chemicals
  - Inform about potential chemicals that may be used as emerging chemical warfare agents
  - Inform about potential PPE that may be required, or how targeting may impact environmental conditions that may degrade operations
    - Example: Hitting this building may cause release of XYZ chemical that may cause severe respiratory distress in local population
      - Lead to secondary mobility issues due to emergency response workers in the area
      - Warfighters may require PPE to prevent exposure that would degrade readiness

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Things to Remember

- Army develops chemicals and materials for warfighter use

- Army interests in toxicology span multiple fields
  - Public health
  - Occupational health
  - Environmental health
  - Intelligence Preparation of the Battlefield

- Army is interested in acquiring and fielding new computational technologies to meet its varied needs

- Models need to be open source, with all of the data used for training, testing and validation made available
  - To ensure works as advertised
  - To understand potential biases
  - Operational Security

- Army chemistries tend to be different from commerce chemical and pharmaceutical industry

- Army is also interested in being able to identify potential liabilities from ALL chemicals
  - Forecast potential use of chemicals as weapons
  - Forecast potential outcomes from targeting

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