Sampling and Detection of Chemical & Radiological Contaminants

James R. Coughlin, Ph.D.
Coughlin & Associates
Laguna Niguel, California
jrcoughlin@cox.net
www.jrcoughlin-associates.com

Food Defense Pertaining to Potential Intentional Contamination

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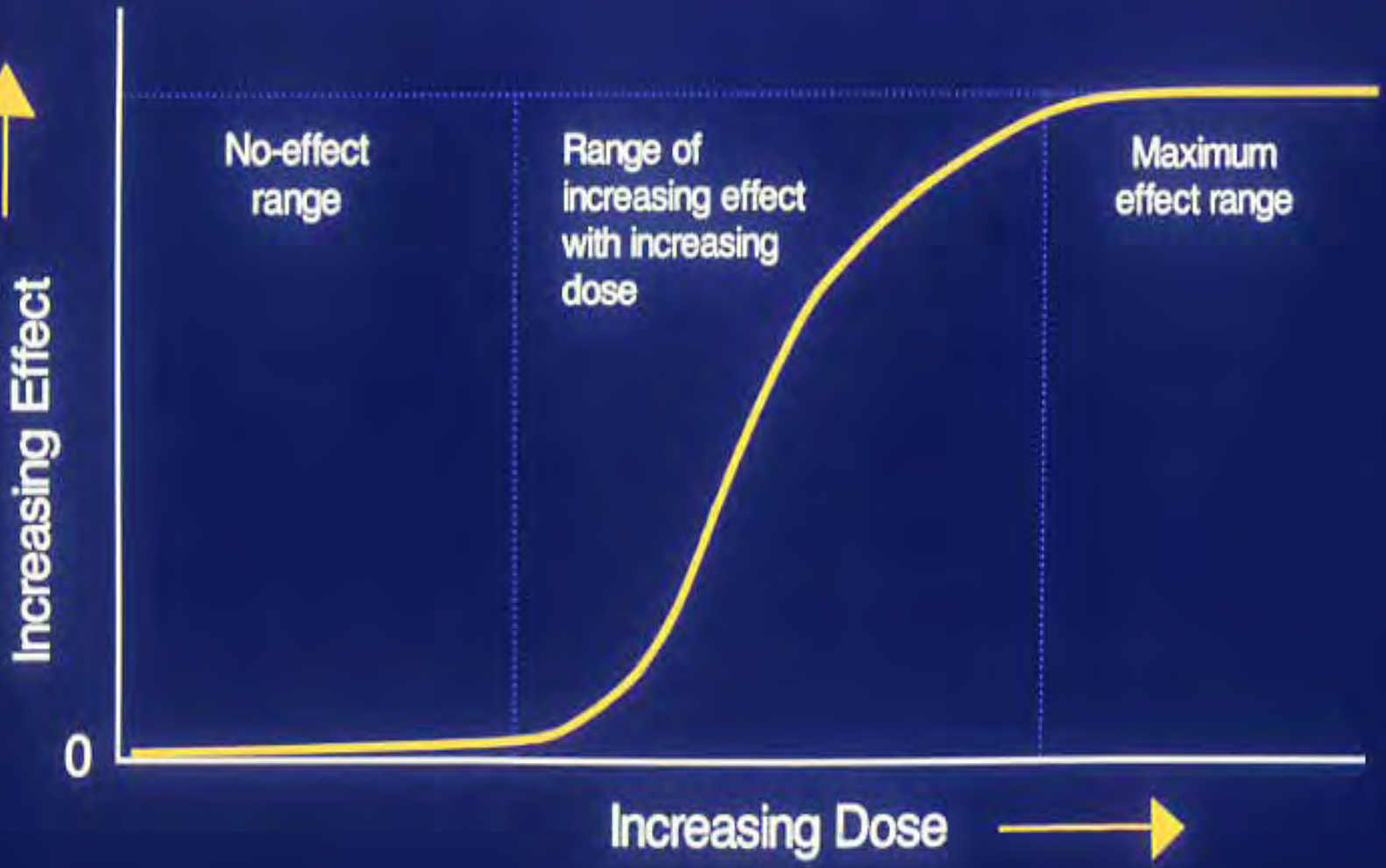
The Dose Makes the Poison!

"All things are poison and there is none which is not a poison. Solely the dose differentiates a poison from a remedy."

Paracelsus

(1493-1541)

DOSE-RESPONSE CURVE




ON SECOND THOUGHT... MAKE MINE HOT CHOCOLATE.
COFFEE
UNITED FEATURE SYN— ©1986 DAYTON DAILY NEWS JOURNAL HERALD

Presentation Outline

- **Why, what and how were we analyzing foods, beverages and ingredients prior to 9-11?**
- **What are the new requirements in the "Bioterrorism Act" with regard to sampling and testing?**
- **Physical and chemical characteristics of toxic chemical and radiological agents that help determine methods development**
- **What are the key chemical and radiological agents of concern?**
- **What are the desired characteristics of an analytical method for rapid detection?**
- **FDA's research activities –**
  - **Methods development**
  - **Collaborations (e.g., FDA-FSIS's FERN, CDC's LRN)**
- **Some specific method development examples**

Why, What and How Were We Analyzing Foods before September 11?

- Our analyses in the food industry were focused on both ingredient and finished food quality and safety, but not on food protection and defense (as we heard last night)
  - HACCP plans, mainly for microbiological agents of past and current concern, not much use to date for chemicals
  - Standardized micro, physical and chemical tests

- Government testing was focused on safety of ingredients and finished foods for the whole population and for susceptible subpopulations, like children, the elderly, diseased people:
  - Imports especially (pesticides, heavy metals, mycotoxins)
  - FDA Total Diet Studies for assessing a large number of dietary contaminants.

- University methods development was serving both industry and government needs as well as academic curiosity.

Public Health Security and Bioterrorism Preparedness and Response Act of 2002 ("Bioterrorism Act") (Public Law 107–188, June 12, 2002)

- **Title III includes a number of provisions designed to improve the food safety efforts of the FDA, including new authority to protect the food supply against terrorist acts and other threats.**

- **Many of the Title III provisions are aimed at ensuring the safety of food imports. The ability to intercept adulterated food before it enters domestic commerce is a high priority and is reflected in the provisions that provide FDA increased authority to receive advance information on imports, examine imports and temporarily hold food imports at a port of entry.**

- **Rapid detection of adulterated food was a particular emphasis. Congress addressed the importance of research related to rapid detection of adulterated food with the inclusion of section 302(d).**

Physical/chemical characteristics of toxic chemical and radiological agents drive detection methods development

- **Physical state (solid, liquid or gas)**
- **Chemical class (inorganic, protein, alkaloid, glycoside, heterocyclic, halogenated hydrocarbons, etc.)**
- **Water or lipid solubility**
- **Low vs. high molecular weight**
- **Heat and acid (sensitivity to pH) stability/lability**
- **Color, odor or taste**
- **Sensitivity to light**
- **In addition, knowing the concentration ranges at which potential agents can inflict morbidity or mortality helps to target the most appropriate methods for the limits of detection needed.**

Class of Agent	Examples
Biotoxins (plants/animals)	abrin, ricin, colchicine, digitalis, nicotine, saxitoxin, tetrodotoxin
Blister/Vesicants	mustard gases, Lewisites, phosgene oxime
Blood	arsine, CO, cyanides, Na monofluoroacetate
Caustics (Acids)	hydrofluoric acid
Choking/Lung/Pulmonary	NH3, Br, Cl, MeBr, phosgene, phosphine, sulfuryl fluoride
Incapacitating	BZ, fentanyls & other opioids
Long-acting Anticoagulants	super warfarin
Metals	As, Ba, Hg, thallium
Nerve Agents	sarin, soman, tabun, VX
Organic Solvents	benzene
Riot Control/Tear Gas	bromobenzylcyanide, chloropicrin
Toxic Alcohols	ethylene glycol
Vomiting Agents	adamsite

CDC - Emergency Preparedness and Response: Case Definitions for Chemical Poisonings

- Lists nearly 75 toxic chemical agents both alphabetically and by category

- Each agent is captured on a one-page sheet (pdf's are available) as a "Case Definition"-
  - Clinical description – toxicity symptoms
  - Laboratory criteria for diagnosis – biologic and environmental
  - Case classification – suspected, probable, confirmed
  - Additional resources – literature references

- These agent sheets are continuously being updated:
  - http://www.bt.cdc.gov/agent/agentlistchem.asp
  - *MMWR*, January 14, 2005 / Vol 54 / No. RR-1

Desired Characteristics of Analytical Methods for Rapid Detection

- Fast (duh!)
- Robust; field-tested, portable?
- Reliable (specificity, sensitivity)
- Quantitative for the food product
- Able to handle as many types and forms of food products as possible
- Provides an indication that the food process is operating within specs, if you are in preventative mode.

FDA Report to Congress

TESTING FOR RAPID DETECTION OF ADULTERATION OF FOOD

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REPORT TO CONGRESS
SUBMITTED TO
THE COMMITTEE ON ENERGY AND COMMERCE OF THE HOUSE OF REPRESENTATIVES
AND
THE COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS OF THE SENATE

OCTOBER 2003

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
U. S. FOOD AND DRUG ADMINISTRATION

http://www.fda.gov/oc/bioterrorism/report_congress.html#appendixa

Appendix A
Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Section 302

(d) TESTING FOR RAPID DETECTION OF ADULTERATION OF FOOD.—Section 801 of the Federal Food, Drug, and Cosmetic Act, as amended by subsection (a) of this section, is amended by adding at the end the following:

(i)(1) For use in inspections of food under this section, the Secretary shall provide for research on the development of tests and sampling methodologies—

(A) whose purpose is to test food in order to rapidly detect the adulteration of the food, with the greatest priority given to detect the intentional adulteration of food; and

(B) whose results offer significant improvements over the available technology in terms of accuracy, timing, or costs.

Appendix A, Section 302 (cont'd)

(2) In providing for research under paragraph (1), the Secretary shall give priority to conducting research on the development of tests that are suitable for inspections of food at ports of entry into the United States.

(3) In providing for research under paragraph (1), the Secretary shall as appropriate coordinate with the Director of the Centers for Disease Control and Prevention, the Director of the National Institutes of Health, the Administrator of the Environmental Protection Agency, and the Secretary of Agriculture.

(4) The Secretary shall annually submit to the Committee on Energy and Commerce of the House of Representatives, and the Committee on Health, Education, Labor, and Pensions of the Senate, a report describing the progress made in research under paragraph (1), including progress regarding paragraph (2).

Summary of FDA Report to Congress (October 2003)

- **FDA reported on over 90 active research projects on the development of tests and sampling methodologies intended to increase the detection of adulteration of food.**

- **Commercially available test kits are currently being analyzed for various food matrices to evaluate their suitability for field use at ports of entry**
  - **One project was the development of a sample pretreatment procedure using a commercial test paper to detect a highly toxic substance in various food matrices, but the procedure needs additional development to be deployed for field use.**

- **FDA has significantly improved its capability to rapidly analyze a large number of samples and quickly and accurately identify toxic chemicals intentionally added to foods. The various research projects detailed in Appendix B are at varying stages of development.**

- **Some projects focus primarily on the tools that will be valuable in developing the final assays and methodologies used in detection. These techniques not only detect adulteration, but they can identify common traits in adulterated foods which can aid in the investigation to track and identify a perpetrator of intentional adulteration.**

Appendix B: Research Projects for Tests and Sampling Methodologies to Rapidly Detect Adulteration

- **Monofluoric acid using LC-MS: original detection method was cumbersome and did not have adequate sensitivity; develop procedure offering a straightforward, rapid method for extraction/detection.**
- **Immunoassay kits for tetrodotoxin: using antibodies from a proprietary hybridoma, Hawaii Biotech Group Inc. will supply immunoassay kits.**
- **Optical biosensor technology: develop novel optical affinity biosensor technology that will enable fast, sensitive and specific detection and identification of foodborne pathogens and toxins.**
- **Detection of abrin: determine feasibility of using commercially available diagnostic assays for ricin; if not feasible, develop new ELISA, HPLC and LC/MS.**
- **Evaluation of z-nose technology: evaluate this instrument for selectivity and sensitivity; then develop detection methods for specific chemicals; this method may offer the selectivity and sensitivity of a lab GC, but with much shorter analysis times.**
- **Evaluation of quadrupole time-of-flight MS: this relatively new equipment will be used to investigate detection of highly toxic proteins.**

Appendix B (cont'd)

- **Tetrodotoxin: a mouse bioassay, a commercially produced immunoassay kit, a receptor assay method and LC/MS methods will be evaluated/optimized to provide rapid, practical screening and confirmation.**

- **Colorimetric sensor array for chemicals in water, water/ethanol: ChemSensing has demonstrated/patented use of SmellSeeing™ and TasteSeeing™ dye arrays to quantify a wide range of compounds, including strongly complexing (alcohols, amines) and weakly complexing (halocarbons, ketones) analytes.**

- **Transportable system for radionuclide analysis: develop for measuring gamma-, beta-, and alpha- radiation; SOPs will be written so analyses can be performed by general analytical chemists with only minimal training.**

- **Paralytic shellfish poisons: compare N2A cell bioassay, pre-column oxidation/derivatization HPLC with fluorescence detection, and electrospray LC/MS for rapid analysis.**

- **Nitron portable X-ray fluorescence (XRF) device: to detect and/or quantify metals in foods, dietary supplements, herbal products, food cans in rapid fashion in field setting; key objective is to evaluate effectiveness in detecting a mixture of toxic elements added to a variety of foods at a variety of levels.**

Detection and classification of threat agents via high-content assays of mammalian cells. Tencza SB, Sipe MA. J. Appl. Toxicol. 24:371-377(2004)

- **One property common to all chemical or biological threat agents is damage to mammalian cells.**
- **This threat detection and classification method employed high-content screening (HCS); a commercial image-based cell screening platform was used, comprising fluorescent reagents, automated image acquisition hardware, image analysis algorithms, data management and informatics.**
- **These assays measure a cell's response to a compound, which may include activation or inhibition of signal transduction pathways, morphological changes or cytotoxic effects; data on cell responses to a library of compounds was used as a training set.**
- **Although the assays appeared to perform well, only 4 of the 9 toxic samples were detected, but the system was specific, since no false positives were detected; improvements were later applied, resulting in a higher level of detection.**
- **Thus, an HCS approach was shown to have potential in detecting threat agents, but additional work is necessary to make this a comprehensive detection and classification system.**

Shellfish-Associated Toxins and Poisonings

- **Tens of toxins elaborated by planktonic algae cause shellfish poisoning (SP):**
  - **Paralytic (PSP), diarrheic (DSP), neurotoxic (NSP), amnesic (ASP)**

- **Analytical techniques for detection and quantitation:**
  - **A mouse bioassay has historically been the most universally applied technique for examining shellfish toxins, especially for PSP; unfortunately results for this assay fluctuate considerably, and fatty acids interfere; a newer suckling mouse assay, that has been used for control of DSP, measures fluid accumulation after injection of the shellfish extract**
  - **A good HPLC procedure has replaced the mouse assay to identify individual PSP toxins at a detection limit for saxitoxin = 20 fg/100 g (0.2 ppm)**
  - **An excellent HPLC procedure has a detection limit for okadaic acid = 400 ng/g (400 ppb)**
  - **A commercially available immunoassay has a detection limit for okadaic acid = 1 fg/100 g (10 ppb)**
  - **A satisfactory HPLC procedure for ASP has a detection limit for domoic acid = 750 ng/g (750 ppb).**

Source: FDA/CFSAN's "Foodborne Pathogenic Microorganisms and Natural Toxins Handbook" ["Bad Bug Book"]

LRN, FERN and EPA…

- CDC's Laboratory Response Network (LRN)
  - Set up in 1999 to establish a network of 140 labs that can respond to biological and chemical terrorism, incl. foods

- FDA-FSIS Food Emergency Response Network (FERN)
  - Laboratories capable of analyzing thousands of food samples for threat agents
  - Some focus on rapid test methods, agent sensor technologies

- "EPA's Role in Water Security Research: The Water Security Research and Technical Support Action Plan" (March 2004)
  - Major goal is to determine what approaches, methods and technologies can be used both in "early warning" mode and in "emergency response" mode
  - Contains a lot of focus on threat assessments and methods development.

My Conclusions

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