

# What's New with the Pesticide Residue Program in the FDA?

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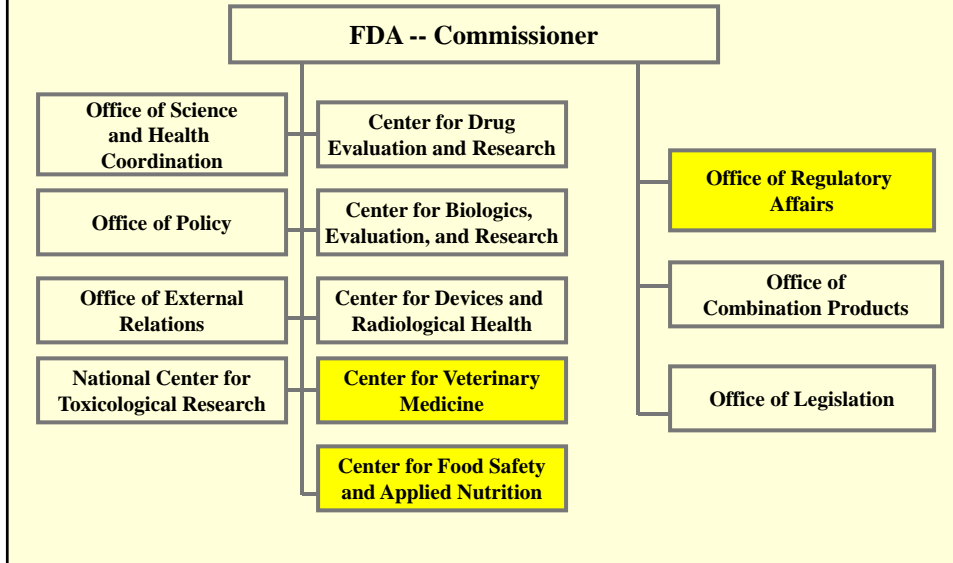
What's New with the Pesticide Residue Program in the FDA?

## Introduction

- Overview
- Program administration
- New LCMS Procedure
- GCMS methods updated
- Methodology
- Future

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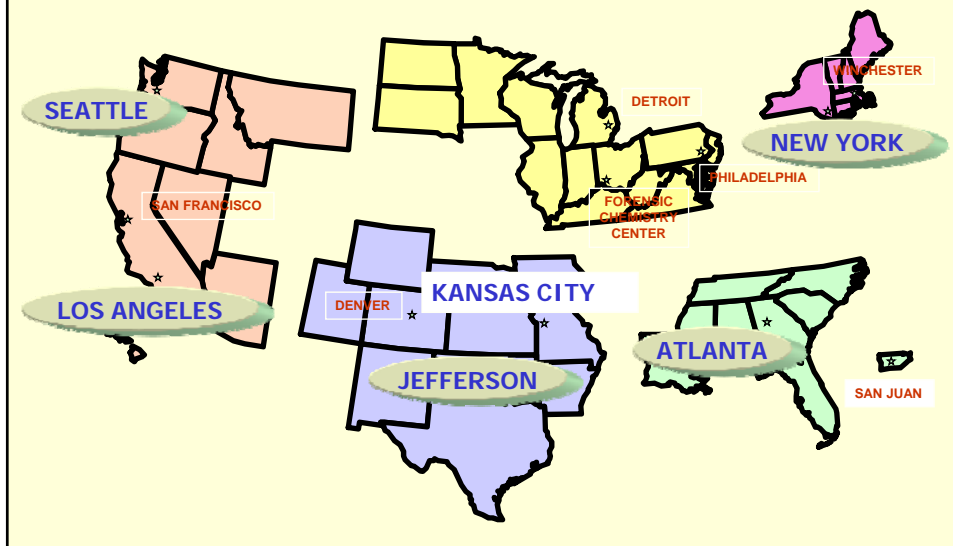
## Overview



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## Overview

### ORA 13 LABORATORIES



## Overview

- Pesticide Programs
  - Regulatory Monitoring
    - ~ 5000 import samples/year
    - ~ 2000 domestic samples/year
  - Total Diet Study
    - Analysis of “table ready” food items
    - 280 items/basket x 4 baskets/year
    - Each item is a composite of 3 cities
    - Total items collected: > 3300

## Overview - Challenges

- Foods
  - Imports: 8-9 M/year
  - Domestic: ???
  - Matrices: unlimited
- Pesticides and industrial chemical contaminants
  - 1000s that are known
  - 10 ppb limit

## Overview - Challenges

- Analyses
  - 20 to 50 samples/day/lab
  - @ 400 analytes/sample = 8-20K determinations/day
- Limited budget: 0.07 % of federal spending
- Congressional review

## Program Administration

- Analyze more samples
  - Increase laboratory efficiency
    - Streamline preparation process
    - Faster methods
    - Modernize data flow
  - Uniformity of protocols and methodology
  - Integrated approach
  - National Sample Distributor

## Program Administration

- Intelligent Sampling
  - Coordination with other federal agencies
    - pesticide usage data (EPA)
    - PDP program (PDP)
  - Foreign offices in China, India, Central and South America, e.g., isocarbophos
  - PREDICT uses FDA historical data to select import samples

## Program Administration

- Coordination with states: FERN
- International coordination/outreach
  - Attendance international workshops
  - IFSTL (JIFSAN)
  - CAFTA

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## Program Administration



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## LC-MS/MS Determination

- Background
  - 2004: “..the pesticides program has not evolved to take full advantage of current science and technology ...LC-MS needs to be incorporated into routine screening procedures” (internal audit)
  - 2008: FDA purchases 8 LC-MS/MS
  - 2009: method developed and collaborated

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## LC-MS/MS Determination

- Scope: 180-200 pesticides in 15 minutes
- Chromatography: reverse phase
- Columns: ODS
  - 100 x 2.1 mm, ~3  $\mu\text{m}$
  - 50 cm x 4.6 mm, 1.9  $\mu\text{m}$
- Mobile Phase: 0.1 % formic acid & 4 mM ammonium formate in water and methanol
- Injection: 2  $\mu\text{L}$

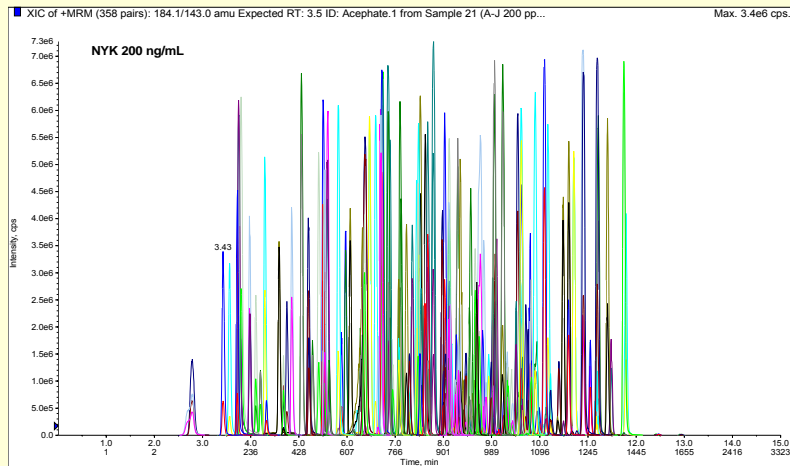
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## LC-MS/MS Determination

- MS Ionization: Positive electrospray
- MS Detection: scheduled MRM (two transitions)

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## LC-MS/MS Determination



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## LC-MS/MS Determination

- Validation Protocol
  - 7 laboratories
  - 173 analytes - 368 transitions evaluated
  - Single level calibration at 200 ng/mL
  - Levels (ng/mL): 2, 5, 10, 20, 50, 100, 200, 500, 1000

## LC-MS/MS Determination

- Results (368 transitions)
  - Accuracy:
    - Overall 105 % (3%)
    - Range: all within 95 – 115 %
  - Linearity: > .99 for 364 transitions
  - IDL: < 10 ng/mL for 363 transitions
  - Extended Range
    - 500 ng/mL: 74 - 125 %
    - 1000 ng/mL: 55 – 122 %

## GC-MS SIM Determination

- Scope: >300 pesticides
- MS Detection: 3-4 ions/analyte
- LOQ: 10-20 ppb
- Three methods (20 min each)
  - Organohalogens (OH): >120 pesticides
  - Organophosphates (OP): >70 pesticides
  - Others (NSO): >120 pesticides
- Two methods (45 min each):
  - OH + NSO (> 250 pesticides)
  - OP (> 70 pesticides)

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## GC-MS Fullscan Screen

- Scope: >900 pesticides in 20 minutes
- Screen: no standards
- ID: spectral matching of AMDIS deconvoluted spectra

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## Methodology

- QuEChERS (Q) LC-MS/MS Collaboration
  - 6 laboratories
  - 174 analytes
  - Single calibration level (200 ng/mL)
  - Standard in solvent
  - Orange, carrot, and spinach
  - Fortification levels (ppm): 20, 100, 400, 1000

## Methodology

- Q x LC-MS/MS Collaboration Results
  - Accuracy: 165 @  $\pm 30\%$ , 169 @  $\pm 50\%$
  - Precision (RSD): 170  $\leq 15\%$ , 167  $\leq 10\%$
  - MDL: 161  $\leq 10$  ppb, 2  $> 20$  ppb
  - Linearity (100 ppb % Rec): 166 @  $\pm 30\%$ ,
  - Range (1 ppm % Rec): 169 @  $\pm 50\%$

## Methodology

- Q x LC-MS/MS Collaboration Results
  - Matrix Effects:

<b>Matrix</b>	<b>Avg</b>	<b>Min</b>	<b>Max</b>
Summary	99	45	142
Orange	91	45	134
Carrot	100	69	137
Spinach	106	59	142

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## Methodology

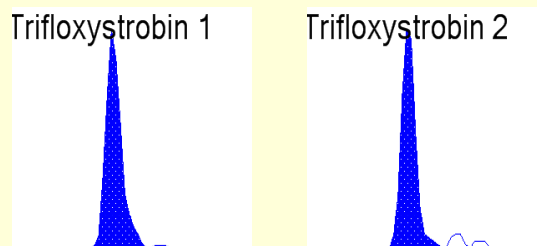
- Q x LC-MS/MS Residues in BF pears

<b>Pesticide</b>	<b>PPB</b>	<b>Pesticide</b>	<b>PPB</b>
Acetamiprid	2.5	Imidacloprid	1.9
Bifenazate	0.4	Methoxyfenozide	1.6
Carbendazim	1.8	Pyrimethanil	0.6
Chlorantraniliprole	1.2	Spinetoram	2.2
Clothianidin	0.3	Thiabendazole	0.2
Diflubenzuron	2.8	Thiacloprid	2.2

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## Methodology

- Q x LC-MS/MS Residues



Trifloxystrobin @ 0.2 ppb in BF applesauce

## Methodology

- LAMM – Los Angeles Micro Method
  - 10 g + 10 mL acetone, shake
  - add 1 mL pet ether, shake
  - Combined saltout/cleanup
    - 4 g MgSO<sub>4</sub>
    - 4 g fructose
    - 8 g NaCl
    - 1 g C18
    - 2 g PSA

## Methodology

- LAMM
  - Three versions: fatty, low and high moisture
  - Validation
    - 118 compounds by GC: Avg 94 % recoveries
    - 150 compounds by LC-MS/MS @ 6 ppb: 70-130 %
    - Comparable to Luke and QuEChERS
  - See poster 33

## Looking to the Future

### LC-MS Orbitrap

- uHPLC-High Resolution Exactive MS
- Screen 500+ pesticides @  $\leq 10$  ppb
- Expand to other chemical contaminants: mycotoxins, plant toxins, veterinary drugs, dyes, emerging organic pollutants, and unknown contaminants.

## Looking to the Future

- GC-MS/MS:
  - Scope: 250 – 300 pesticides in 20 minutes
  - MRM (2-3 transitions)
  - LOQ: 10 ppb
  - 10-25 x more sensitive than GC-MS(SIM)
  - Successfully applied to botanicals
- Other GC-MS technologies
  - GCxGC-TOF-MS
  - GC-MS full scan methods for unknowns

## Looking to the Future

- LC-MS/MS
  - Negative ionization
  - Pesticide libraries of product ion spectra on LC-QTRAP-MS
  - LC-APPI-MS for analysis of PAHs in seafood products

## Looking to the Future

- Sample preparation
  - Extension of QuEChERS to fatty matrices
  - DPX (disposable pipette extraction)
  - Automation

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