Approaches to Measuring and Modeling Indoor Human Exposure to Chemicals in Consumer Products

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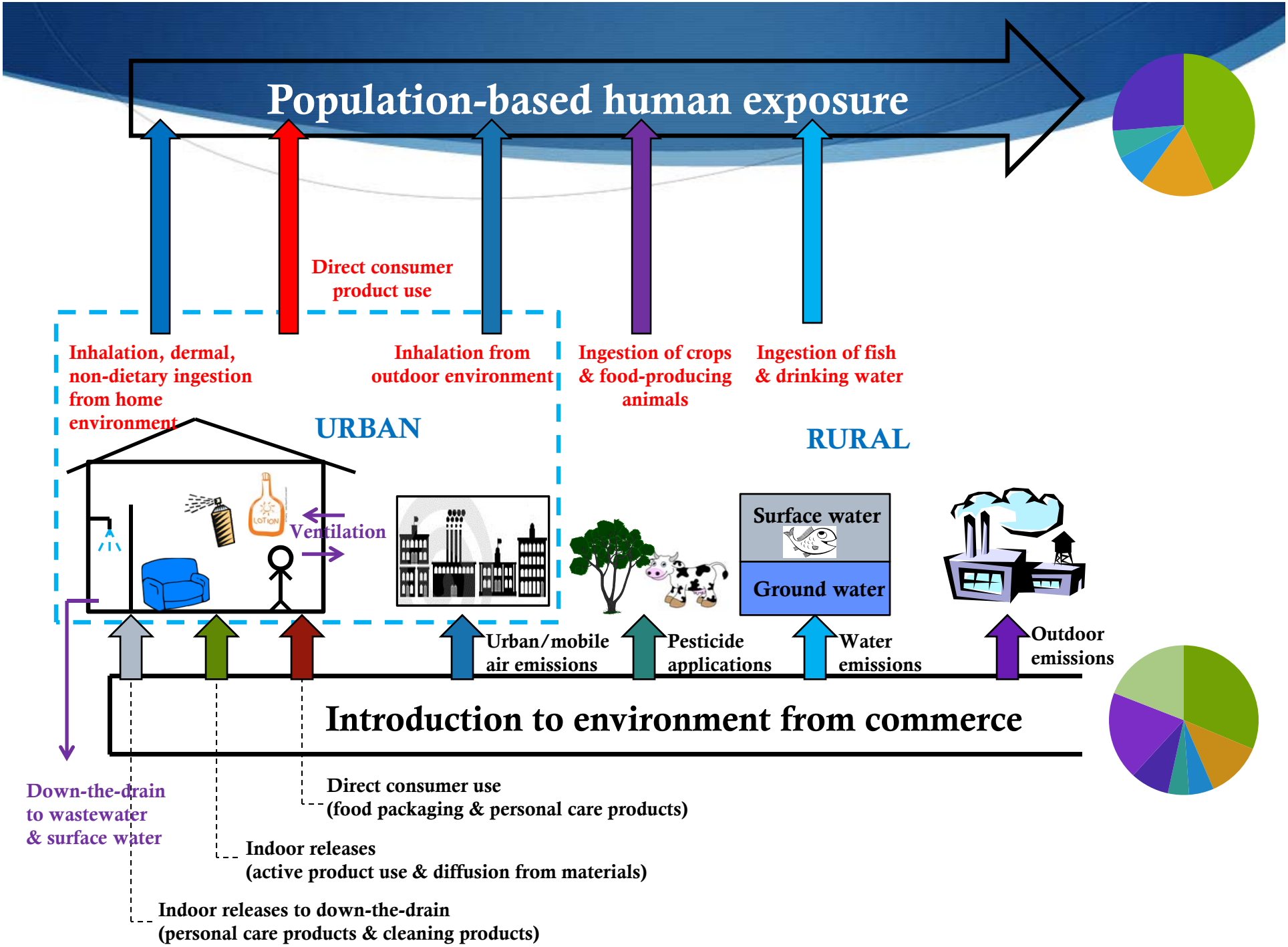

Population-based human exposure
Direct consumer product use
Inhalation, dermal, non-dietary ingestion from home environment
Inhalation from outdoor environment
Ingestion of crops & food-producing animals
Ingestion of fish & drinking water
URBAN
RURAL
Ventilation
Surface water
Ground water
Urban/mobile air emissions
Pesticide applications
Water emissions
Outdoor emissions
Introduction to environment from commerce
Down-the-drain to wastewater & surface water
Direct consumer use (food packaging & personal care products)
Indoor releases (active product use & diffusion from materials)
Indoor releases to down-the-drain (personal care products & cleaning products)

Residential Indoor Sources of Organic Compounds

What is in our home?

- Very little data on chemicals used in commerce
  - Composition
  - Product formulation
  - Distribution of total production volumes
  - Exposure
  - Toxicity

Objectives

- Measure concentrations of a broad spectrum of target and non-target SVOCs in indoor dust
- Estimate emission rates from dust levels and predict resulting exposures
- Refine and evaluate a multi-compartment indoor fate, transport, and exposure model
- Evaluate air-to-skin transdermal uptake models

Why Dust?

- Correlated with blood or urine samples
  - Pyrethroid Pesticides
  - Flame retardants
  - PFCs
- More practical (compared to air samples)
  - Can be collected in a single visit
  - Compounds with low VP are likely to have levels that exceed LOD in dust
- Chemical reservoirs
  - Potentially reflecting chemical loading in the home over a long period
  - Indicator of source strength as it integrates emissions from all sources

Compounds Measured in Dust

- Typical compounds
  - Phthalates
  - PBDEs
  - Pesticides
  - PFCs
  - Other flame retardants
- Other personal care product ingredients
  - Fragrance ingredients (AHTN, HHCB)
  - Sun-blocking agents (OMC, ODP)
  - Triclosan

- Non-targeted analysis will greatly expand what we know

Exposure Pathways

- Inhalation
- Dermal uptake
  - air-to-skin transdermal uptake
  - a series of discrete transfers from each contact with a contaminated medium
- Non-dietary dust ingestion
  - a series of discrete transfers from hand- and object-to-mouth activities
  - a product of dust ingestion rate (68 mg/day) and chemical concentration in dust

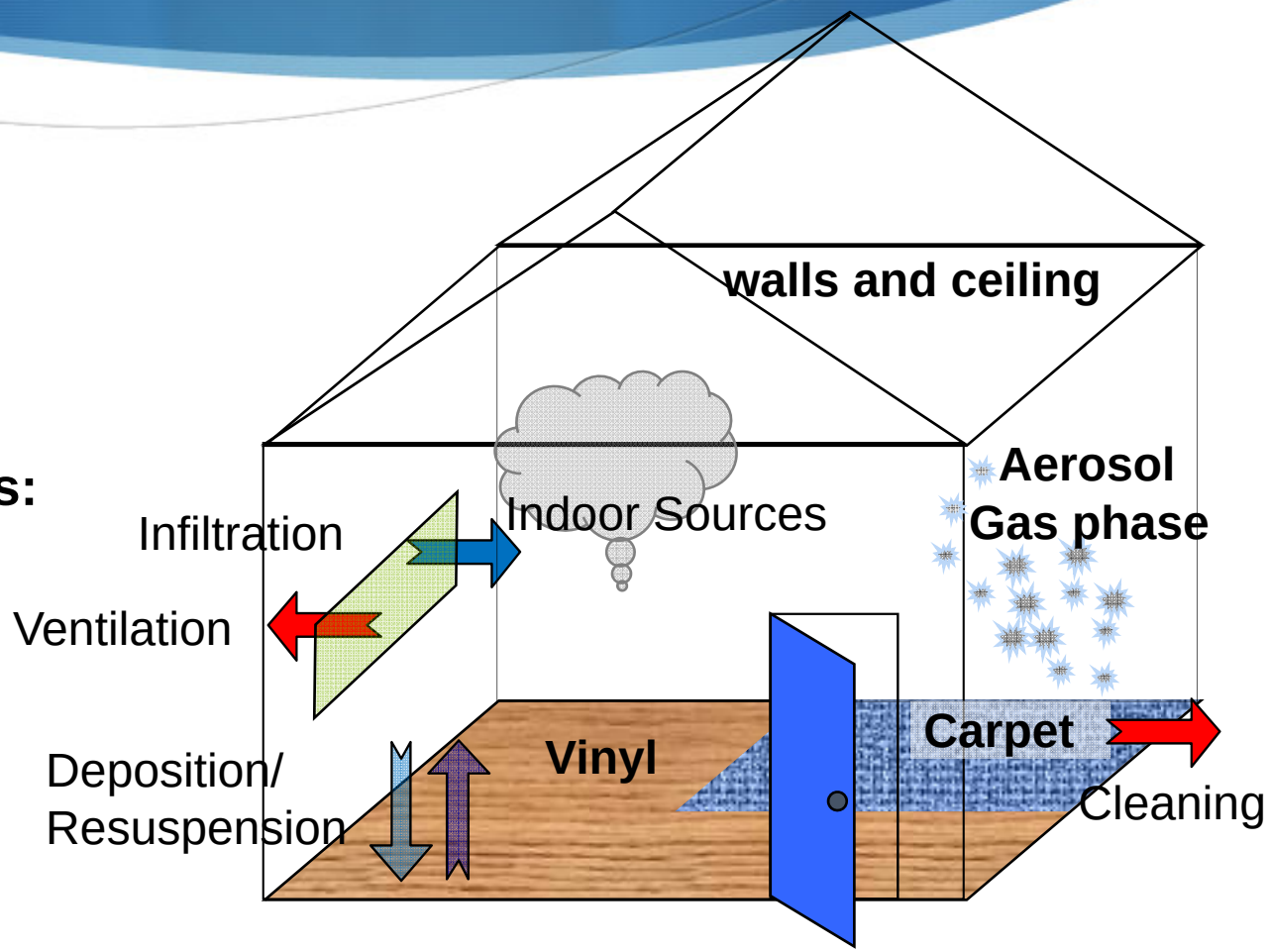
Fugacity-Based Indoor Model

Compartments:

- air (gas + particles)
- carpet
- vinyl flooring
- walls and ceiling

Mass transfer factors:

- diffusive
- advective



Residence Times of SVOCs

Decreasing volatility →

Property name	diazinon	chlorpyrifos	pbde-47	pbde-99	permethrin
Log VP (Pa)	-2.0	-2.7	-3.3	-4.5	-6.0
Log Koa	8.0	8.7	10.0	11.2	13.0
Mass (%)					
air (gas +particles)	**0.01**	**0.03**	0.001	0.0001	0.00001
dust on carpet	0.1	0.2	1.3	**2.0**	**6.6**
carpet	98.7	98.8	97.8	97.4	93.0
Removal (%)					
ventilation	**99.1**	**96.0**	57.5	24.3	19.9
carpet cleaning	0.9	3.9	40.9	**72.8**	**76.9**
Steady-state Residence time (years)					
	6.7	**19.0**	**16.2**	**13.7**	**3.9**

Estimate Source Strength from Fugacity-Based Indoor Model

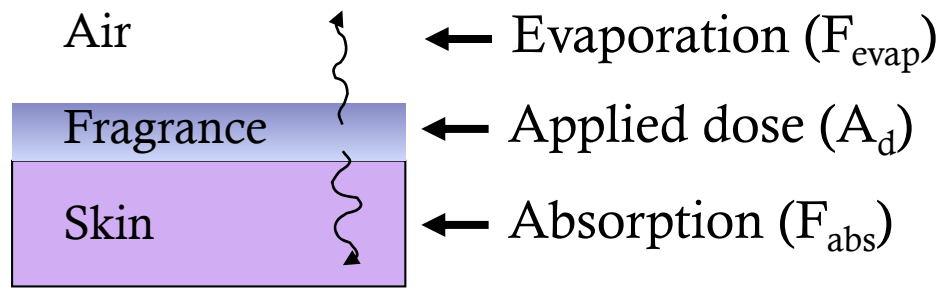
- Set up mass balance equation for each compartment
  - Source = Mass * (portion removed each day)
- Assumptions
  - The mass in each compartment is at steady state (e.g., dMa/dt = 0)
  - Each phase in a given compartment is in chemical equilibrium (e.g., fugacity in the carpet fiber = fugacity in the carpet dust)
- Solve for *S* (emission rate) in the air compartment

Alternate Approaches to Estimate Source Strength

- Evaporation from Personal Care Product Use

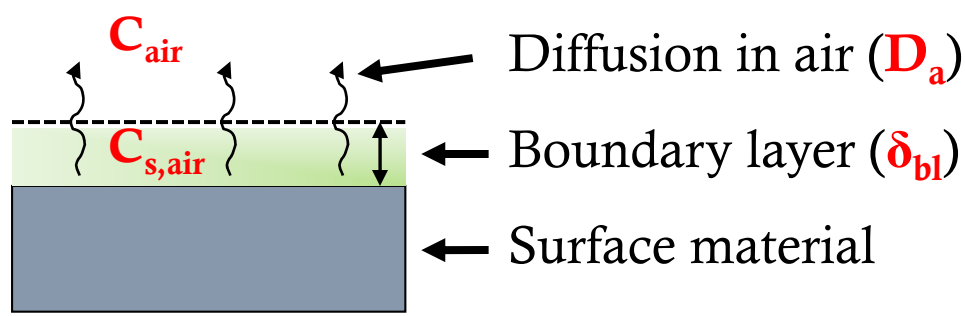
$$S_{pcp} = A_d \cdot F_{evap} \cdot f_{retention}$$

$f_{retention}$ = 1.00 for body lotion
0.05 for body wash



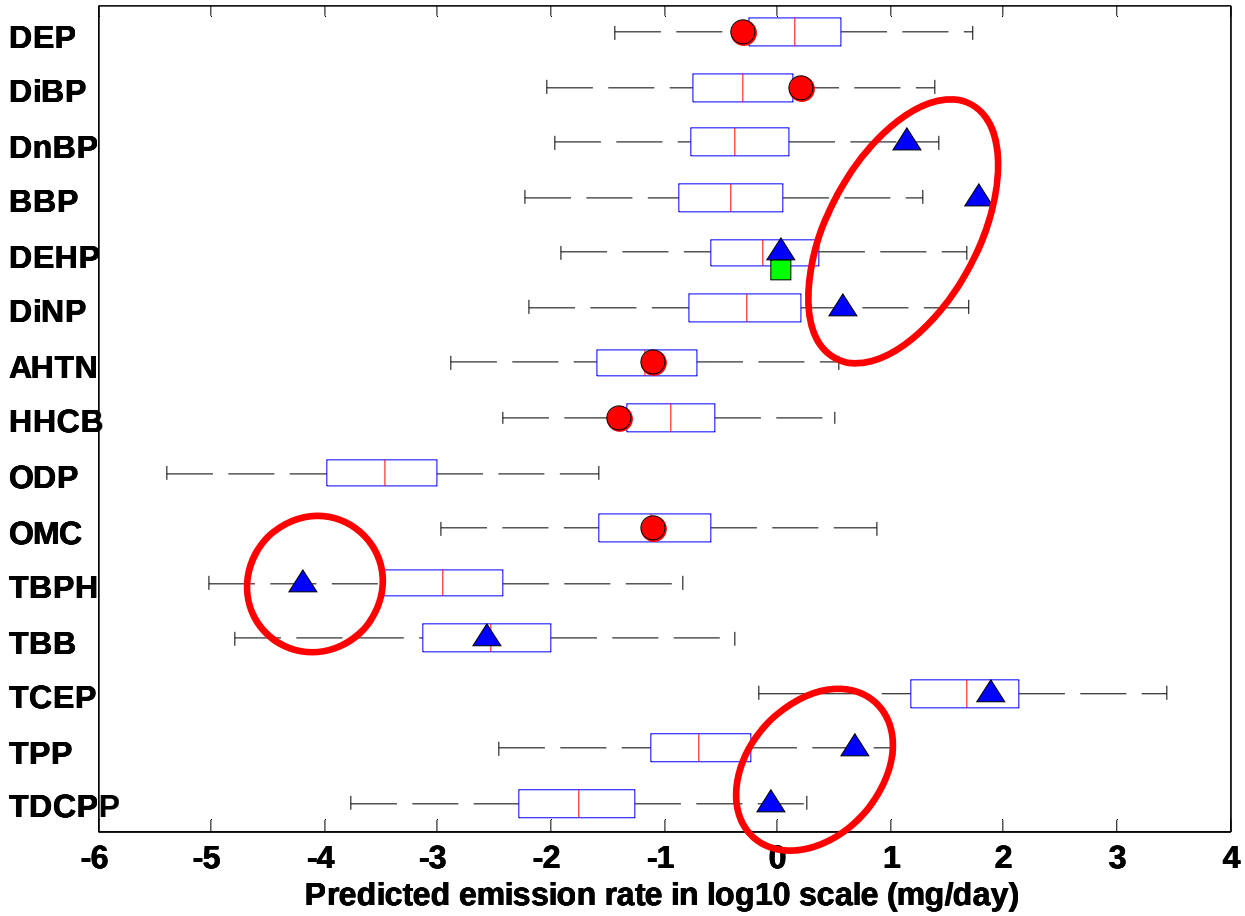
- Diffusive Transfers from Surface Materials

$$S_{surf,i} = J_i \cdot A_i = D_a \frac{(C_{s,air} - C_{air})}{\delta_{bl}} \cdot A_i$$



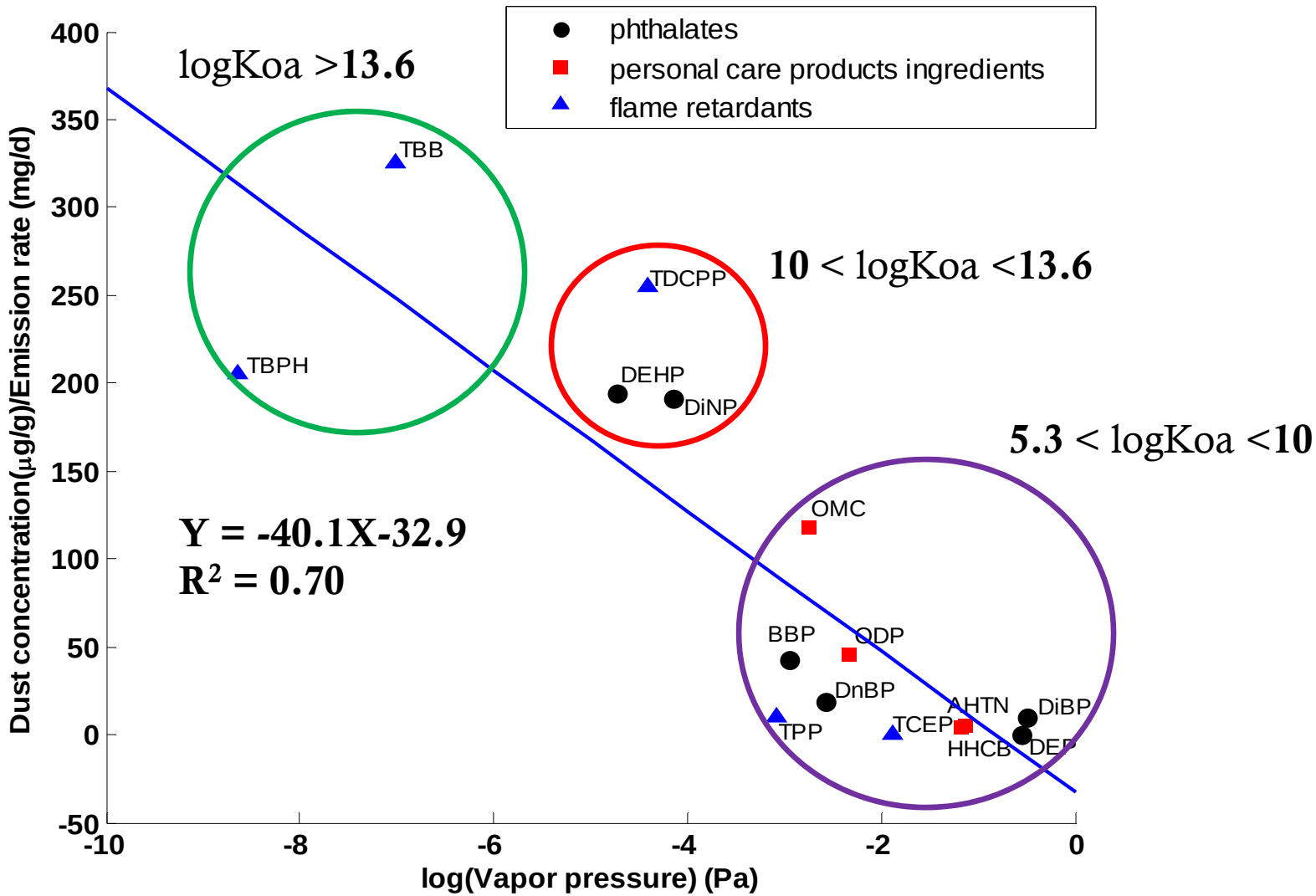
$C_{s,air}$ = VP·MW/(R·T)

Predicted Emission Rate (mg/day)



- Monte Carlo simulation
- Reported value from experiments (Xu et al. 2009)
- Predicted from personal care product use behaviors
- Predicted from diffusive transfers of surface materials

Log (VP) vs. the ratio of the measured dust concentration to the estimated emission rate



Two Populations will be included in this effort

- CHARGE study (PI: Hertz-Picciotto)
  - ***CH***ildhood ***A***utism ***R***isk from ***G***enetics and ***E***nvironment
  - A population-based autism case-control study that has enrolled over 1600 index children and their families
  - Provides a large number of cases and controls along with other samples and endpoints when their child is 2 to 4 years old
- New population
  - Will be recruited for the current project to examine chemical concentration changes over time for validation

Autism

- Developmental disability characterized by:
  - Impairments in social interaction, communication, and/or cognition
  - Repetitive behaviors
- Current CDC estimate is 1 in 68 children (ADDM Network)
- 5 times more common among boys (1 in 42) than among girls (1 in 189)
- Can be reliably diagnosed by 2 years of age, with some signs recognizable in the first year of life
- In some cases, there may be typical developmental trajectory until 18-24 months then loss of skills (regression) or no gain of new skills (plateau).

CHARGE Overview

- Immunologic
- Metabolic
- Genetic
- Epigenetic

Endogenous Factors

- Chemicals
- Nutrients
- Infectious agents
- Pharmaceuticals

Exogenous Factors

- Parental education/occupation
- Access to care
- Familial, cultural

Social Context

CHARGE Study Design

- **Population-based case-control**
  - California-born children 24-60 months + parents and siblings
  - Cases (autism and developmental delay w/o autism) - California Department of Developmental Services (DDS)
  - Controls (typical development) - randomly selected from California births, age, sex and geographically matched to cases
- **Specimen and data collection provides rich comparisons**
  - Blood, urine, saliva, hair, shed teeth, newborn blood spots, stool, dust
  - Questionnaires - personal care products, housing information, cleaning products, nutrition
  - Blood is being analyzed for PBDEs, most likely PFCs
  - *Dust can be compared to existing data to determine what predicts levels*
  - *D*evelopmental assessment by clinicians, medical records, immune markers, GI symptoms, allergies, DNA, RNA, methylation, microflora, thyroid function, metabolic panel
  - *Outcomes can be compared to dust levels to see if any compounds are elevated for mid- or endpoints*

Collected Dust Samples

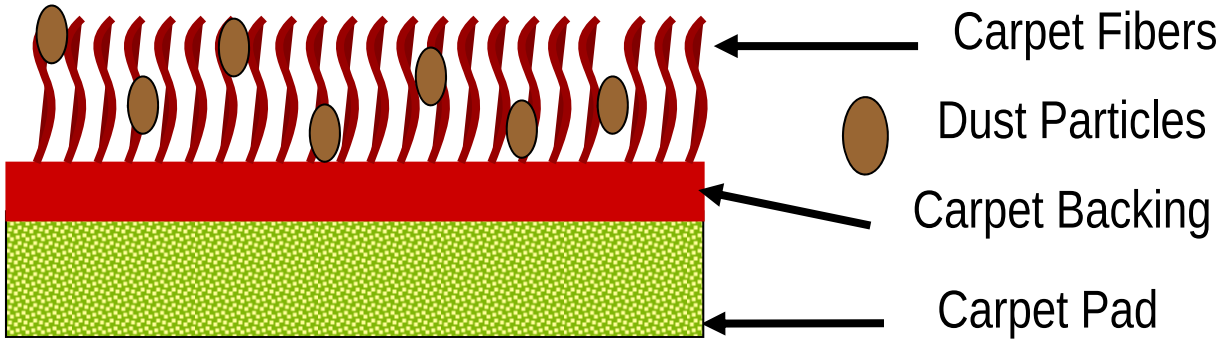
- These will be used for non-targeted analysis to determine what compounds are in home
- Approaches of current project (field sampling + modeling)
  - Provide information on distribution and co-occurrence of chemicals in the indoor environment
  - Improve understanding of what chemicals and which pathways result in current exposures to the U.S. populations
- Benefits CHARGE because it provides another measure of exposure

New Population

- Eligibility
  - People who have purchased a new couch within the last year
- Objectives
  - Determine how much of the chemicals in old couch get into dust and how much they change over time (half-life indoors)
  - Provide a model validation data set

Refine Model Parameters

- Dust loading
  - Surface dust (easily removable dust from standard vacuuming)
  - Deeply embedded dust
- Dust removal rates (from vacuum cleaners)
  - Collect all dust removed over two 1-month periods from all 20 homes
  - Determine how much dust is typically removed from homes during cleaning
- Further evaluation of air-dust partitioning models



Air-to-Skin Transdermal Uptake

- Measure concentrations of chemicals in skin obtained as surgical waste
  - Skin will be collected from patients who undergo plastic surgery from the UCDMC Plastic Surgery Department
- Evaluate air-to-skin transdermal uptake models
  - Compare measured concentrations to model predictions

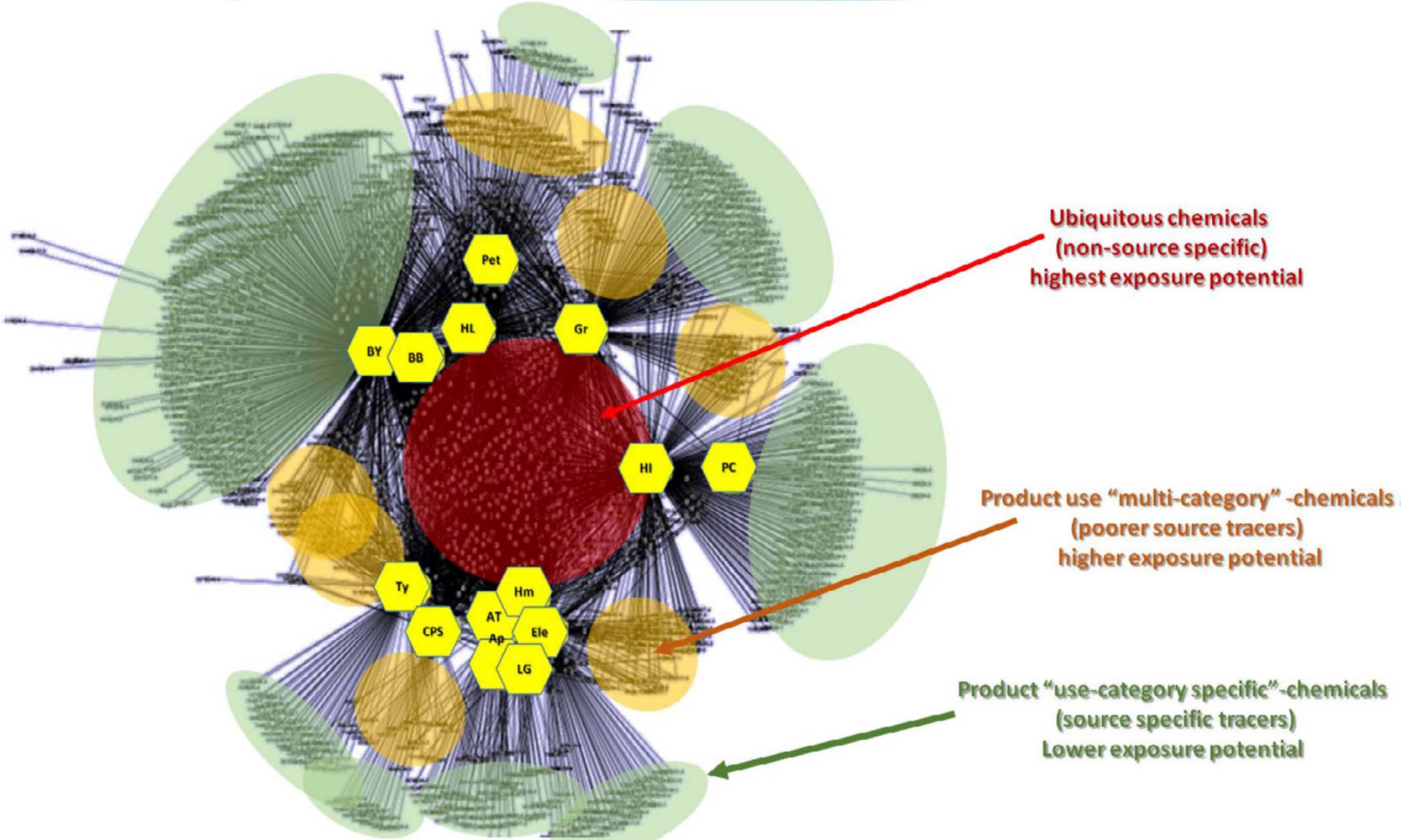
Goals of HRMS Chemical Analysis

- Support validation of indoor exposure model
  - Include chemicals with diverse physical-chemical properties and indoor residence times
- Provide information on exposure pathways
  - Select tracer compounds found in a limited number of product categories
- Identify transformation products or unexpected compounds (e.g., "trade secrets")
- Connect chemical results to presence of biomarkers

General Approach

- Perform organic extractions of dust samples from participating homes
- Analyze extracts on two HRMS platforms
  - LC-QTOF-MS: Agilent 6530
  - GC-QTOF-MS: Agilent 7200
- Quantify concentrations of 50 target chemicals
- Identify non-target chemicals present at high abundance or that correlate with observed biomarkers

Selecting Target Chemicals: Consumer Products

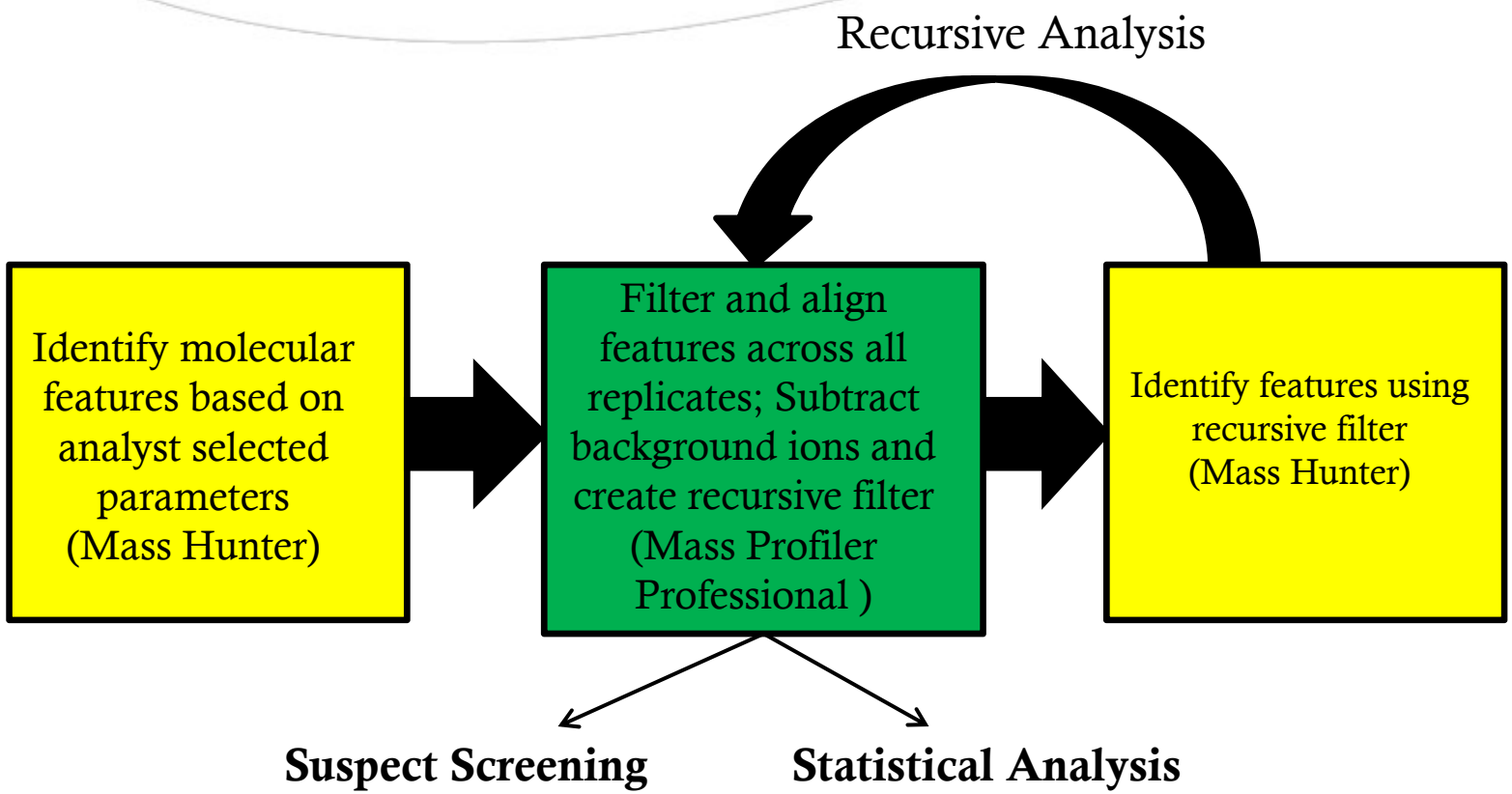


Goldsmith et al., *Food and Chem. Toxicol.*, 65, 269 (2014)

Target Compound Selection Criteria

- Ubiquitous indoor exposure known or suspected
  - Central "node" on previous diagram (e.g., methyl 4-hydroxybenzoate, propyl 4-hydroxybenzoate)
  - On EPA high production volume chemical list
  - Likely precursor of widely detected biomarker
- Chemicals likely to be good source tracers
  - Ethofenprox (pets: flea and tick control)
  - 5-tert-butyl-1,3-benzoxazole (toys: drawing and coloring)

Non-target Compounds: Feature Identification and Filtering



Non-target Chemical ID Strategies

- Presence in database of consumer products or high production volume chemicals
- Documented metabolites and environmental TPs from literature searches
- Anticipated from pathway prediction systems
- Mass defect filters derived from list of target chemicals
- Follow with authentic standards and MS/MS confirmation whenever possible, especially for features correlated with biological effects

Non-target Screening: Database Match

Screen with an exact mass library derived from consumer product database and related sources

Screen possible matches with score filter (exact mass, isotope spacing and abundance)

Filter database matches with retention time filter

MS/MS experiments as needed

Example- Mass Defect Filtering

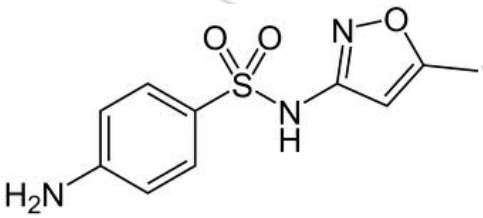
- Mass Defect = Exact Mass – Integer Mass
- Used to identify drug metabolites in biological matrices
- Will apply it to identify byproducts from AOPs and other processes

Table 1. Mass and mass defect shifts for metabolites that have structures similar to the parent drugs[13,52,53]

Mass shift (Da)	Molecular formula change	Mass defect shift (mDa)	Biotransformation reaction[a]
+48	$+O_3$	−0.0153	$RSH \rightarrow RSO_3H$ $3 \times (RH \rightarrow ROH)$
+34	+2OH	+0.0054	$RCH{=}CHR' \rightarrow RCH(OH)-CH(OH)R'$
+32	$+O_2$	−0.0102	$2 \times (RH \rightarrow ROH)$ $RSR' \rightarrow RSO_2R'$
+30	$+OCH_2$ $+O_2, -H_2$	+0.0106 −0.0259	$RH \rightarrow ROH \rightarrow ROCH_3$ $RCH_3 \rightarrow RCOOH$ Quinone formation
+18	$+H_2O$	+0.0106	$RCN \rightarrow RCONH_2$ $RCH{=}CHR' \rightarrow RCH_2CH(OH)R'$ Epoxide hydrolysis

Zhang,et al., Mass defect filter technique and its applications to drug metabolite identification by high-resolution mass spectrometry, *J. Mass. Spectrom.* **2009**, 44, 999–1016

Mass Defect Filtering



Exact Mass	Nominal Mass	Mass Defect
236.09496	236	0.09496

Sulfamethoxazole
$C_{10}H_{11}N_3O_3S$

Mass Shift (Da): +48 Da, -45 Da
Mass Defect Shift (Da): -0.0367, +0.0313

Range of values from Table 1 of Zhang et al. 2009

Sulfamethoxazole MDF

$196 \leq$ Nominal Mass ≤ 284

$0.05346 \leq$ Mass Defect ≤ 0.12796

Effluent ONLY Features	Post MDF Filter	Possible Oxidative Rxn
275	13	1

Thank you for your attention!