CORTEVA™ agriscience

# Innovations in Sustainable Agrochemistry

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# *What Does Farming Look Like in 2020?*

# Agrochemistry Challenges & Opportunities

## Discovery

*Novel Mode of Action*

*(non)-Target Site Biochemical Data*

## Process & Product Development

*Green Chemistry Manufacturing Principles*

*Renewable & Safe Raw Materials*

## Application Technology

*Precision Ag*

*Drone Technology*

## Product Stewardship

*Farmer Training*

*Integrated Solutions*

***Sustainability is not only about the active ingredient!***

# Crop Protection Discovery

**Strategic Platform of Active Generation Approaches**

- Natural Products
- Bioactive Hypotheses
- Competition Inspired

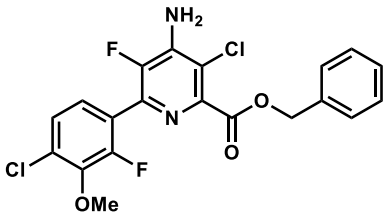
**Design-Build-Test approach to analog design & optimization**

1. Active Generation
2. Lead Generation
3. Lead Optimization
4. Staged Molecules

**Products**

## Control weeds

Herbicides help control weeds that compete with crops for light, moisture, and nutrients

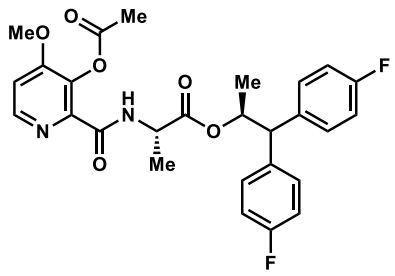



Rinskor™ herbicide (2018)

GREEN CHEMISTRY

## Manage diseases

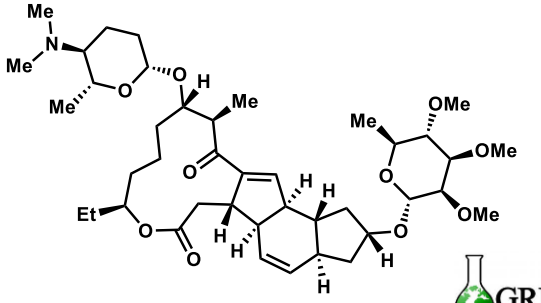
Fungicides help prevent or cure fungal diseases; fungi are the #1 cause of crop loss worldwide[1]




Adavelt™ fungicide

## Control crop-damaging pests

By managing harmful insects and nematodes, farmers protect yields and the health of their crops




Spinosad insecticide (1999)

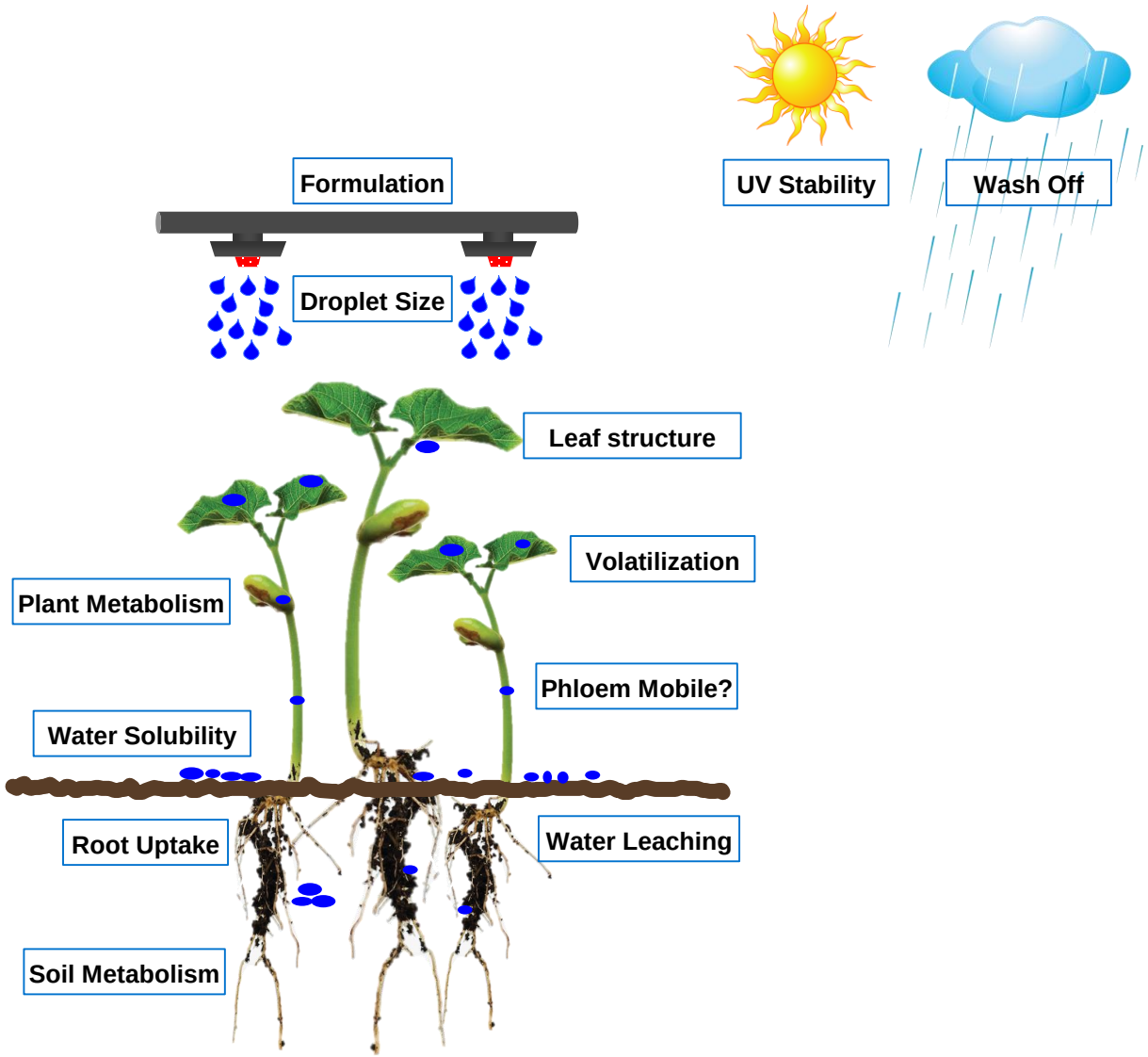
GREEN CHEMISTRY

# *Difficulty of Delivering an Agrochemical Solution*

- **Absorption**
- **Distribution/Translation**
- **Metabolism**
- **Degradation**

**Many variables before and after spraying**

**Essential properties differ depending on research area**



# Sustainable Active Ingredient Design

## Product Design

Crop protection products are designed for high efficacy and minimal environmental impact

- *Aquatic toxicity*
- *Mammalian toxicity*
- *Beneficial insect safety*
- *Ground water leaching*
- *Soil degradation*

### *Tools & Capabilities*

*Early High Throughput Screening*

*Mode of Action Determination Assays*

*Biochemical Assays for Resistance Type*

*in-Silico Models*

*Machine Learning*

## Presidential Green Chemistry Challenge Awards

GREEN CHEMISTRY CHALLENGE
A U.S. EPA Program

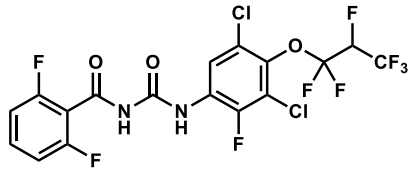
**6-time Recipient**

| 1998 | 1999 | 2000 | 2008 | 2016 | 2018 |
|---|---|---|---|---|---|
| Confirm™ (as Rohm and Haas) | Spinosad | Sentricon™ Termite Colony Elimination System | Spinetoram | Instinct® technology | Rinskor™ active |

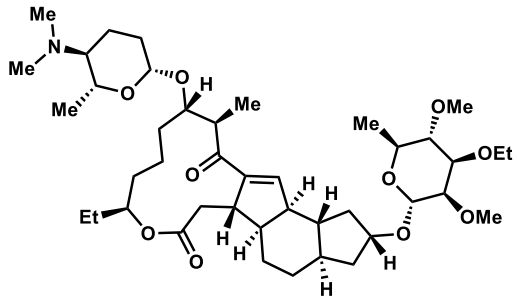
*The Design of Greener Pathways*

*The Design of Greener Reaction Conditions Award*

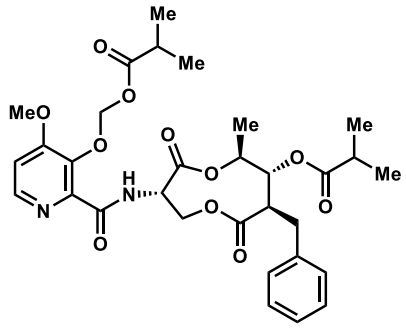
*The Design of Greener Chemicals Award*




**Noviflumuron insecticide (2000)**

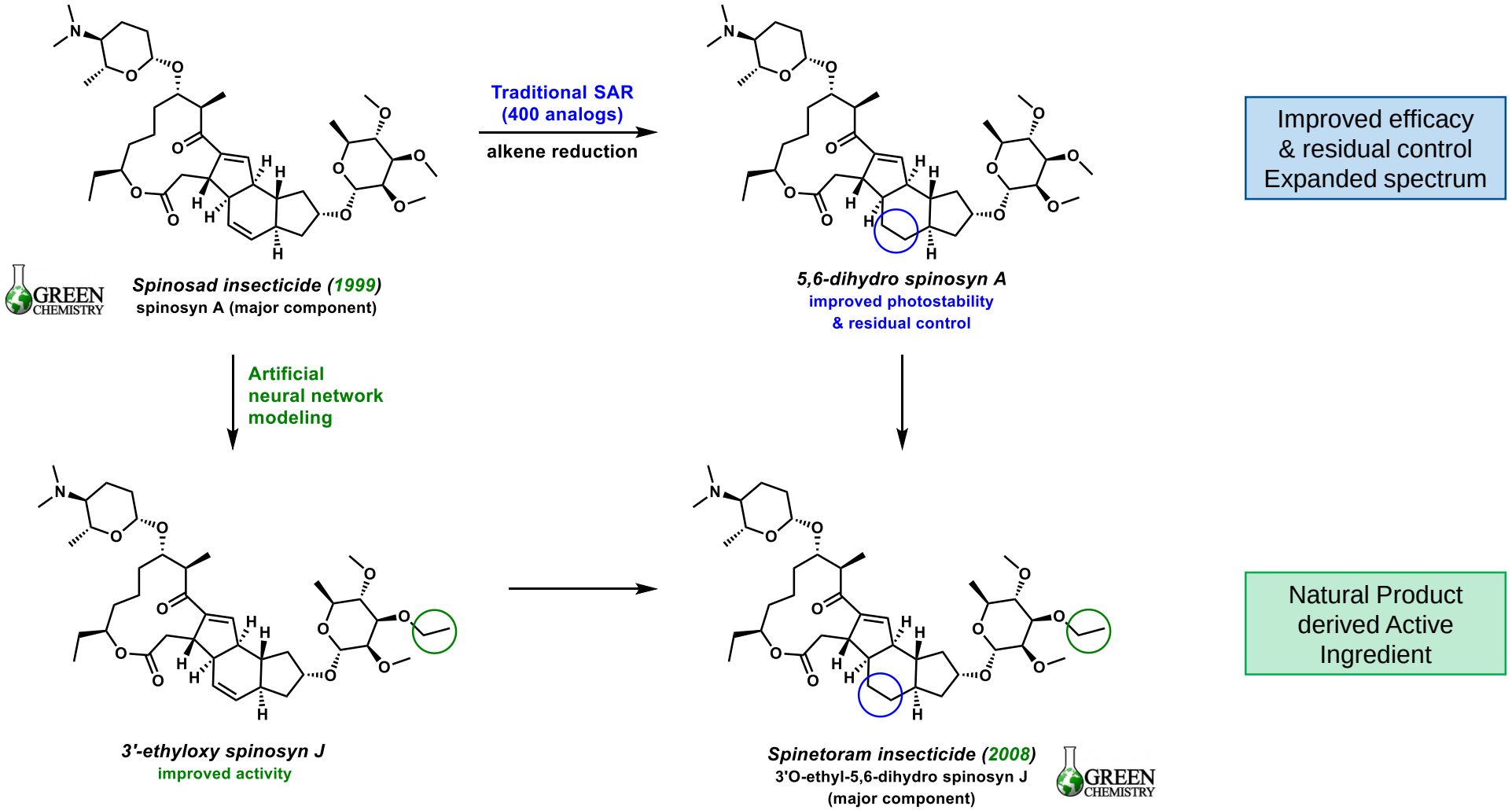



**Spinetoram insecticide (2008)**




**Inatreq™ fungicide (Natural Product-based)**

# Combining Traditional Design With Computer-Aided Design




Improved efficacy
& residual control
Expanded spectrum

Natural Product
derived Active
Ingredient

J. Dripps, et. al. 2008, Plant Management Network

# *On-Going Discovery Challenges*

*Novel Mode of Action*

*(non)-Target Site Biochemical Data*

Dearth of protein crystal structures related to plants, insects, & fungi

Limited funding for academic research in agrochemistry compared to pharmaceuticals

Basic research in organic chemistry and chemical biology not applied to crop protection

# *Sustainability with Manufacturing Process in Mind*

## Process Design

Production volumes are much higher than pharma although structural complexity is similar

- *Global glyphosate use in 2014 was 750,000 MT*[1]
- *Other top products are ~10,000 MT/yr*

***Process Optimization Tools***

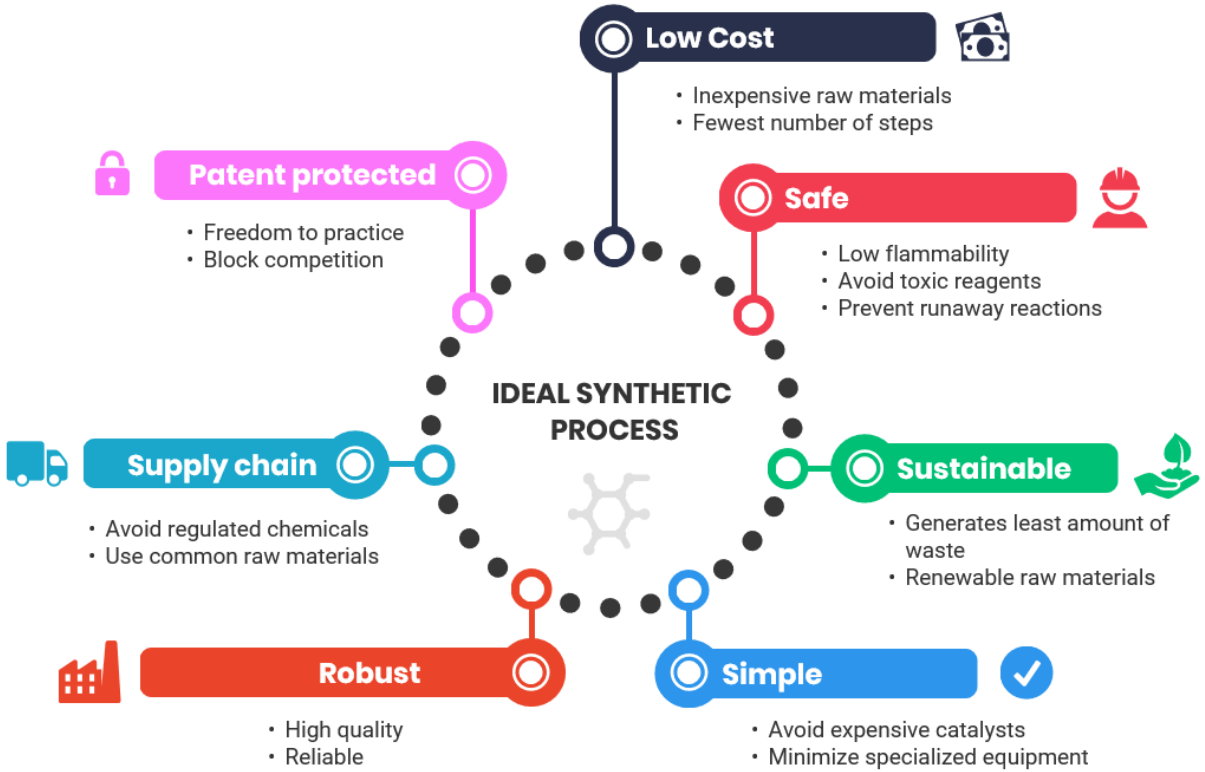
*High-Throughput Experimentation & Design of Experiments*

***Route Evaluation Metrics***

*Cost-effective ($X/kg)*

*Available on >100 MT*

*Renewable/sustainable*





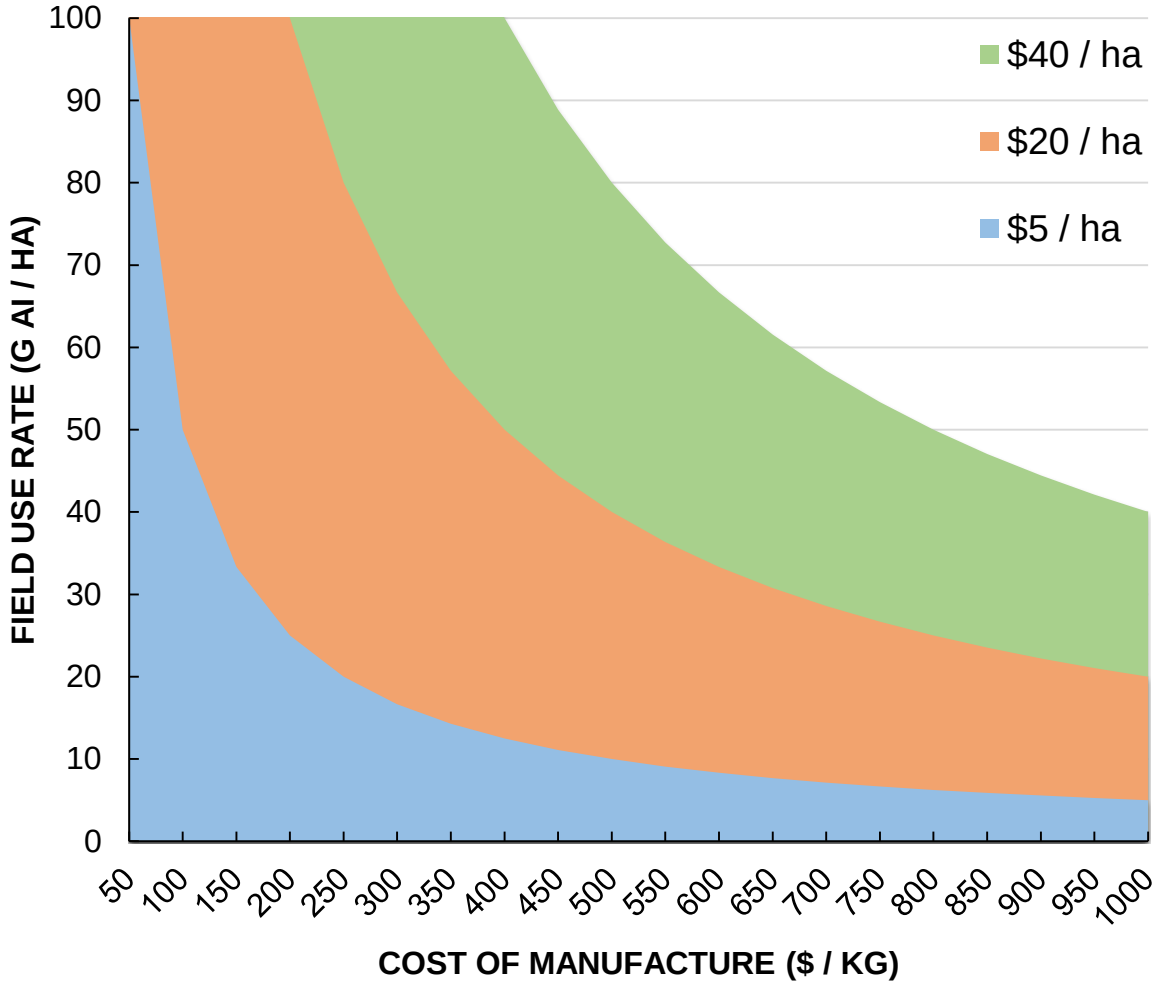

[1]Benbrook, C. M. *Environ Sci Eur* **2016**, *28*, 1; [2]Whiteker. G. T. *Org. Process Res. Dev.*, **2019**, *23*, 2109-2121

# *Sustainability with Cost of Manufacturing in Mind*

(Field Use Rate) x (COM) = $/ha

$$\frac{x\ g}{ha} \times \frac{\$\ y}{kg} \times \frac{1\ kg}{1000\ g} = \frac{\$}{ha}$$

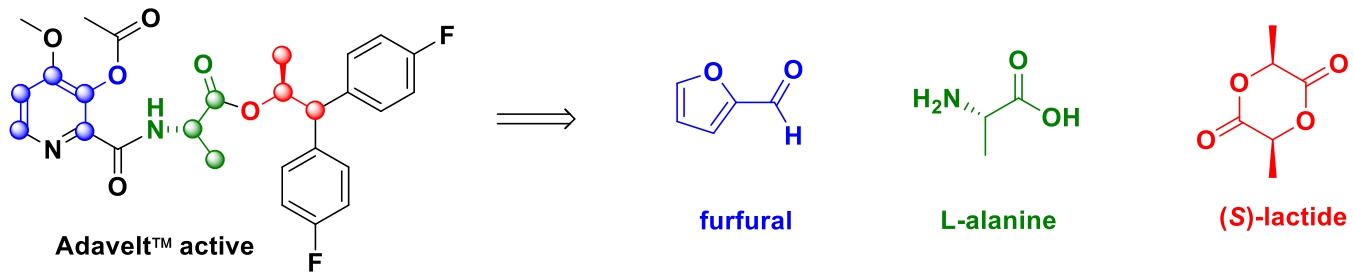
***Farmers have a budget per hectare***




*1 Hectare equals ~ 1 professional baseball field*

# Sustainably-Focused Process Development

## Route Identification




Renewable carbon content = 41%

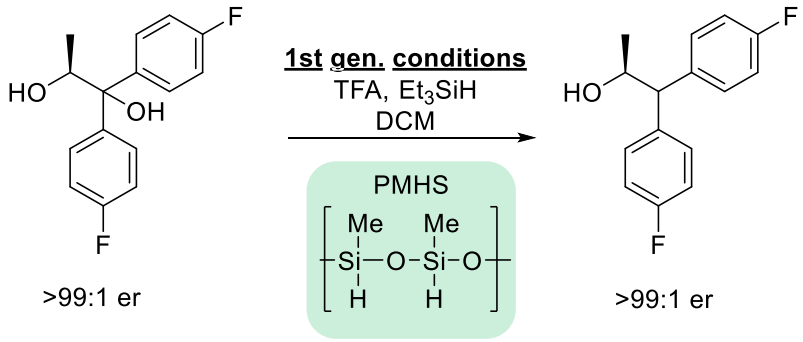
## Furfural raw material

- Renewable Feedstock
- $~1/kg

## Process Optimization: Unchained Labs HTE Instrumentation

- Yield
- Selectivity
- Cost, availability, safety & sustainability of reagents
- Cost, availability, safety & sustainability of solvents

**~400 reactions conducted (acids, reductants, solvents)**




**Replaced $Et_3SiH$ with PMHS**

PMHS ($2/mol hydride) is a by-product of the silicone industry[1]



1. G. L. Larson, Chim. Oggi/Chem. Today, 2009, 27, 25.

# Sustainable Formulation Science Successes

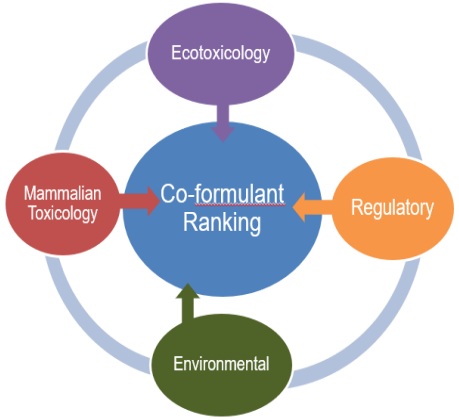
Enlist

## Low Drift Technology

Products are developed with formulation technology that enables products to apply and stay on-target

## Sustainable Ingredients

Co-formulants for all products are chosen with health and safety of people and the environment as primary factors




Resicore® HERBICIDE

Agrow Awards

Simplicity™ GoDRI™ HERBICIDE

Instinct® Optinyte™ technology NITROGEN STABILIZER

2016 R&D 100 WINNER

## Farmer Convenience

Award winning products leverage expertise in product design, multi-component formulations, and controlled release to deliver customer-friendly features

## Local Focus

Products are designed with local conditions and end-users in mind and tested in grower-specific applications.

# *On-Going Process & Product Development Challenges*

*Green Chemistry Manufacturing Principles*

*Renewable & Safe Raw Materials*

“Green” & low-cost catalytic reactions

Ability to synthesize chiral agrochemical products with cost in mind

Limited formulation science education and research in academic settings

# Sustainability of Agrochemistry

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## People

***Next Generation of Farmers***

***Conscience Consumers***

***Fruitful Collaborations***

***Diversity of Scientists, Farmers & Consumers***

# *People Drive Change*

***Farmers Adopting New Sustainable Technologies & Practices***

***Consumers Requesting Sustainably Grown Food***


***Diversity is a Pillar of Sustainability***

# *Collaborations Lead to Success*

***Mode of Action*** | ***Natural Products*** | ***Green Chemistry*** | ***Regulatory*** | ***Machine Learning***

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UNIVERSITY OF MICHIGAN

agPlenus

Berkeley UNIVERSITY OF CALIFORNIA

*Publicly Announced Collaborations

# Conclusion




Sustainability should be a whole system approach

Machine learning and automation will drive the future of sustainable agrochemistry

Numerous sustainable products on the market with many based on natural products

Manufacturing, formulations & “Green Chemistry” are key attributes for a sustainable product

Solving agriculture’s biggest challenges will require **creative scientists** with different skill-sets, **new tools** and **partnerships** from around the world

## Acknowledgements

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