

# Product Chemistry and Active Ingredient Characterization

**Brian Portoni**

**Chemistry and Microbiology Program**

**Pesticide Evaluation Branch**

**Department of Pesticide Regulation (DPR)**

# What is the active ingredient?

## ▶ Biochemicals

- ▶ Unique chemical structure, protein sequence, or genetic (RNA/DNA) sequence
- ▶ Unique conformational aspects of the active ingredient that is apart of the function
  - ▶ Protein sequence and genetic sequence folded into an active 3-D shape

## ▶ Microbial Pesticide

- ▶ Each isolate is considered a new active ingredient according to US EPA
- ▶ Genetic sequence of the microbial is needed to establish specific unique identity
  - ▶ Genetics of a microbial pesticide do not significantly change over time
  - ▶ Nomenclature of a microbial pesticide will change over time as taxonomy changes
- ▶ How differentiate the microbial pesticide from heterotrophic microorganisms in the environment?
- ▶ How differentiate the microbial pesticide from other isolates of the same taxonomy?

# How is the active ingredient produced?

## ▶ **Biochemicals**

- ▶ Manufacturing methods used to produce active ingredient
  - ▶ Chemical manufacturing methods or biological manufacturing methods
- ▶ Chemical contamination present with active ingredient
  - ▶ Excess chemicals used in manufacturing, biological by-products, etc...
- ▶ Biological contamination present with active ingredient
  - ▶ Bacteria, fungi, virus, parasite, or other biologic contaminations

## ▶ **Microbial Pesticide**

- ▶ Type of growth method used to grow the active ingredient
  - ▶ Solid fermentation, liquid fermentation, tissue culture, biological host or other method
- ▶ Chemical contamination present with active ingredient
  - ▶ Biological by-products of fermentation, tissue culture by-products, spent growth media, etc...
- ▶ Biological contamination present with the active ingredient
  - ▶ Bacteria, fungi, virus, parasite, or other biologic contaminations

# How stable is the active ingredient?

- ▶ **Biochemicals and Microbial Pesticides**

- ▶ Storage stability of the active ingredient at optimal storage conditions
  - ▶ Stable over days, weeks, months, or year(s)
- ▶ Storage stability of the active ingredient at non-optimal field storage conditions
  - ▶ Stable at elevated temperatures over days, weeks, months, or year(s) to match California climatic field conditions

# Key Product Chemistry Elements

## ▶ Product Identity

- ▶ Composition active ingredient – Unique Sequence or Unique shape
  - ▶ Nomenclature
- ▶ Differentiation of active ingredient – Environment & Similar active ingredients
  - ▶ “Enforcement Method”

## ▶ “5-Batch” Analysis

- ▶ Manufacture Methods
- ▶ Contamination – Chemical and Biological (Bacterial, Fungal, etc...)

## ▶ Stability Over Time – Time & Temperature

- ▶ Label’s Storage Use-Directions
- ▶ California Field Storage Conditions

# Documents Submitted for Review

- ▶ **Public Literature** - Not considered Confidential Business Information (CBI)
  - ▶ Journal Articles
    - ▶ Complete articles in electronic format (example: PDF) with highlights of relevant information
      - ▶ CalPEST
      - ▶ No citation only, need submission of complete literature
  - ▶ Published Books
    - ▶ Complete chapter(s) in electronic format (example: PDF) with highlights of relevant information
      - ▶ No citation only, need submission of complete literature
- ▶ **Non-Public Information**
  - ▶ Complete laboratory reports with raw data in electronic format (example: PDF) with highlights of relevant information
    - ▶ Method(s) used need to be detailed in report(s)

# Common Issues that Slows Evaluation Process

- ▶ Names used in Documents and Labels
  - ▶ Active Ingredient
  - ▶ Subject Product
- ▶ Documents and Label Text
  - ▶ Too small to read and/or Too blurry to read
  - ▶ Unable to differentiate text due to background
- ▶ Color documents submitted as Black/White
  - ▶ If color, submit as color
- ▶ Spelling errors
- ▶ Incomplete or Missing Documents
  - ▶ Missing or omitted pages in documents
  - ▶ Missing documents
    - ▶ Referenced MRID that were not submitted for review
    - ▶ Referenced EPA documents that were not submitted for review

# Case Studies

- ▶ Differentiating Active Ingredients
- ▶ Taxonomy Changes of Active Ingredients Over Time





# Differentiating Active Ingredients

- ▶ Register a New Strain of *Beauveria bassiana* in California
- ▶ What do you need for “Product Identity” of the new active microbial?

# Differentiating Active Ingredients

- ▶ Currently Registered *Beauveria bassiana*
  - ▶ HF23 (DPR Chemical Code: 5976)
  - ▶ GHA (DPR Chemical Code: 3993)
  - ▶ ANT-03 (DPR Chemical Code: 6137)
  - ▶ PPRI 5339 (DPR Chemical Code: 6217)
  - ▶ 203 (DPR Chemical Code: 6575)
  - ▶ BW149 (DPR Chemical Code: 6603)

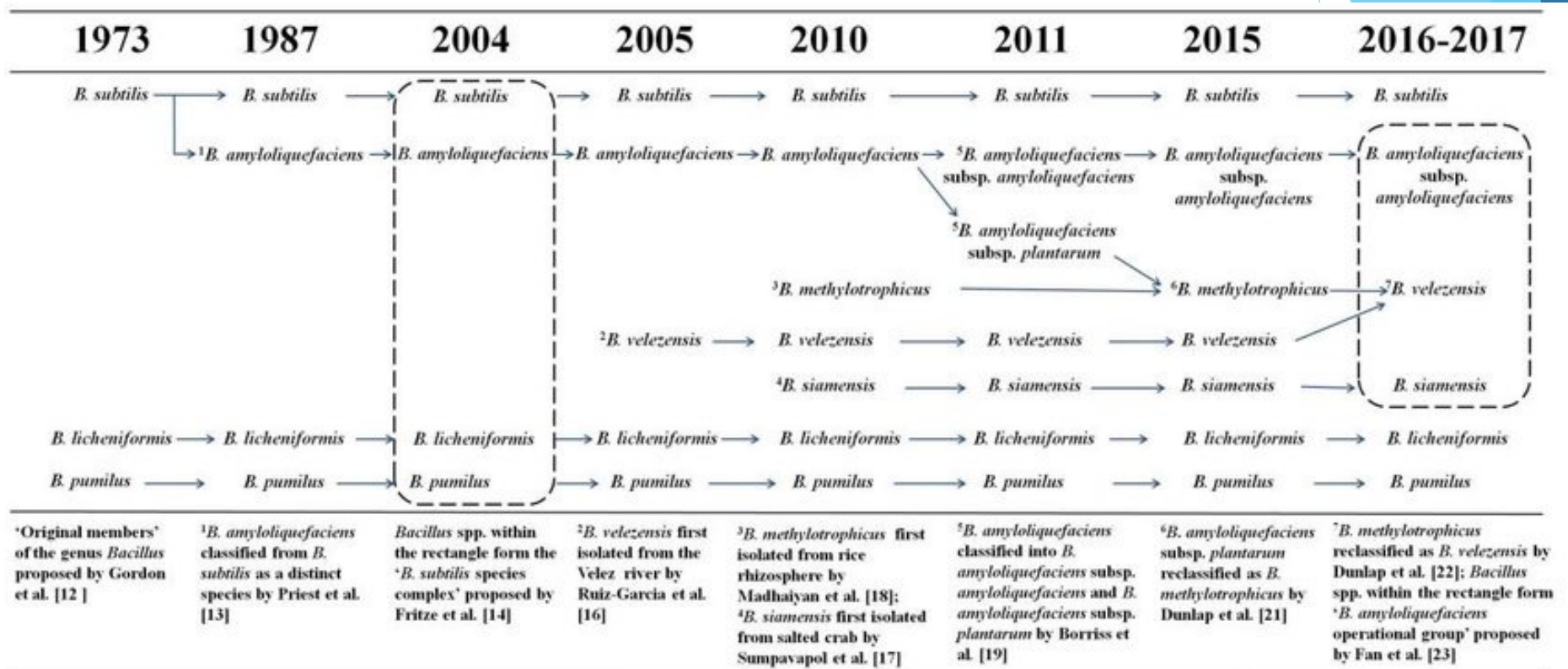
# Common Ways of Differentiating Active Ingredients

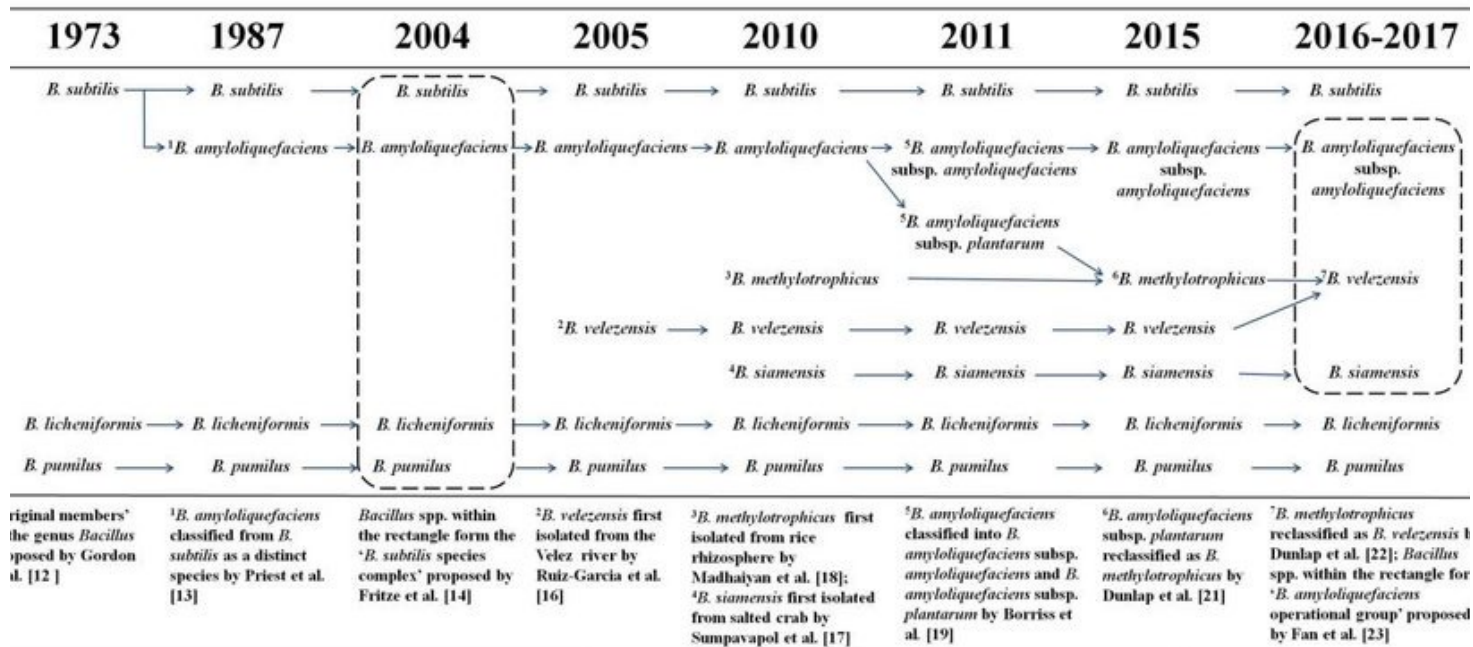
- ▶ **Genetic Sequence**
  - ▶ RNA (mRNA, 16S rRNA, etc...)
  - ▶ Intracellular plasmids
  - ▶ Genomic DNA
  - ▶ Genetic marker sequences
- ▶ **Protein Sequence**
  - ▶ Intracellular marker protein
  - ▶ Membrane bound protein
  - ▶ Secreted protein

# Taxonomy Changes of Microbial Active Ingredients Over Time

- ▶ Registered *Bacillus* in California with outdated nomenclature on labels
- ▶ You are updating the nomenclature of *Bacillus* on the label with California

# Taxonomy Changes of *Bacillus* Over Time





You get a response from California to give supporting evidence for the revision of nomenclature for *Bacillus* on the label

What evidence do you use to support the nomenclature changes?

# Nomenclature Changes of Active Ingredients

- ▶ Best argument at the time of review, using the most current laboratory and literature analysis at the time of review
- ▶ Genetics of a microbial active ingredient are considered constant and not changing over time
- ▶ Nomenclature is constantly changing over time

# CHOCOLATE CHEMISTRY

Whether your preference is dark, milk, or white chocolate, here's handy guide to what's inside



**DARK CHOCOLATE**

**COCOA SOLID: >35%**



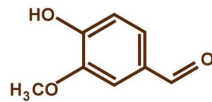
**THEOBROMINE**

Dark chocolate has the highest amount of Cocoa solids, which remain after cocoa butter is extracted from cocoa beans. The solids contain theobromine, toxic to dogs, and phenethylamine, linked to a feel-good effect.



**MILK CHOCOLATE**

**COCOA SOLID: 35-30%**



**VANILLIN**

Confectioners add vanillin to many milk chocolates to enhance their flavor. American brands of chocolate often contain butyric acid, which adds a sour note to the chocolate's taste.



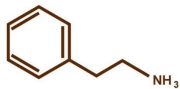
**WHITE CHOCOLATE**

**COCOA SOLID: 0%**

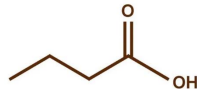


**STEARIC ACID**

White chocolate does not contain any cocoa solids, only cocoa butter, sugar, and milk. Cocoa butter is composed of a number of fats, mainly stearic acid and palmitic acid.



**DARK CHOCOLATE**



**MILK CHOCOLATE**



**WHITE CHOCOLATE**

<https://www.chococraft.in>

Thank you!  
Questions?