



# An Update on the EFSA Bt Opinion and the Role of Microbials in Sustainable Agriculture

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Creative Hybrid Chemistry

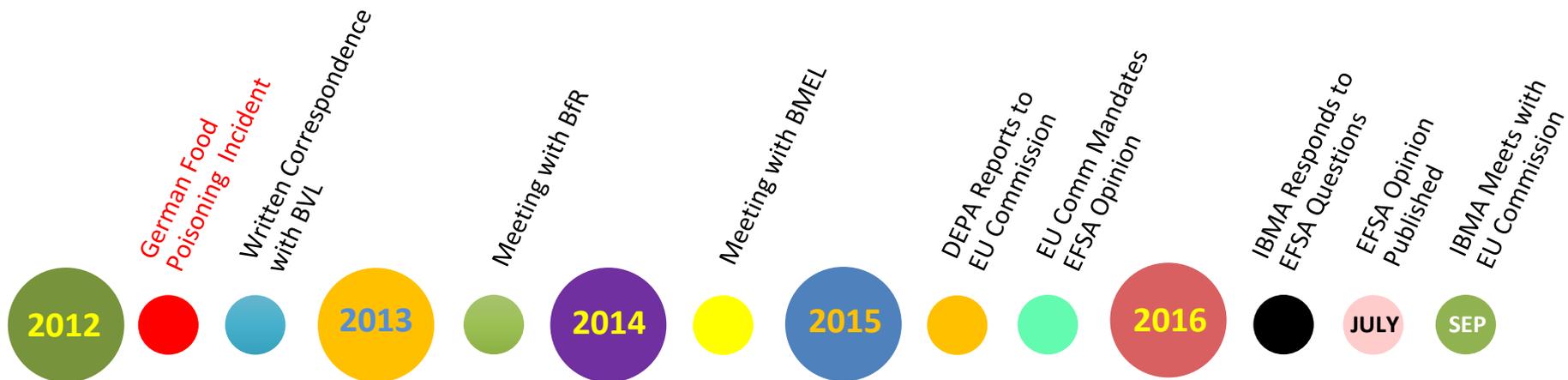
## Presentation Summary

**Everyone in this room shares one fundamental objective:**

We all want to bring **safe** and **useful** products to the market that will bring **value** to growers and the **entire food value chain**.

That objective is being undermined in Europe as the safety of Bt – one of our industry's flagship products – is being challenged based on flawed and incomplete information.

# EFSA Opinion Timeline





## German Food Poisoning Incident - 2012

- Members of a German family became sick in the night after eating a dinner of salad and pasta
  - The lettuce in the salad had been treated with XenTari (Bta ABTS-1857)
- Without a proper clinical and epidemiological investigation, a conclusion was drawn between the presence of Bta ABTS-1857 spores and the sickness
- This incident resulted in the BVL imposing PHIs of up to 9 days for XenTari on certain crops



## Weaknesses in the 2012 Report

### The mere presence of Bt does not imply causation

- A high level of aerobic bacteria ( $10^8$  CFU/g) was found on lettuce acquired from the same producer
- A significant level of Bc ( $6 \times 10^3$  CFU/g ) was found on the pasta
- Poor definition of patient symptoms
- There was no clinical indication of the microbe in the patients



## **Bottom Line: There are Two Points of Contention Stemming from the EFSA Opinion**

1. The implication that Bt is pathogenic: “presumptive Bc”
2. The implication that Bt and Bc cannot be distinguished



## The Science Behind Bt Safety

**The Science does not support either of these contentions**

**Facts supporting the safety (non-pathogenicity) of Bt:**

The evolutionary pathways of Bc and Bt into distinct ecological niches and resulting differentiation:

- The origin of commercial Bt strains relates to their specificity
- The presence of Cry toxins with relation to spore coat and germination
- Qualities of Bc group bacteria that govern diarrheal pathogenicity
- Lack of Bt proliferation in food and the environment
- Conditions for survival, germination, and toxin production in the human gut



## The Science Behind Bt Safety

### Bt and Bc: Differentiation through their Ecological Niches

- **Bt is, first and foremost, an insect pathogen**

Commercial Bt strains have been specifically selected based on potency against Lepidopteran larvae (or Diptera in the case of Bti)

- As a result, most Bt strains are better adapted to complete their life cycle in susceptible insect hosts than in other environments
- Bt spore germination rates in soil and Bt survival rates on plant surfaces are extremely low. Bt requires specific nutrients and pH for germination

## The Science Behind Bt Safety

Registrants and EFSA agree that pathogenicity of bacteria is multifaceted and is, therefore, strain-specific. Pathogenicity depends on:

- **Proliferation** in the environment
- **Survival** in the gastric passage
- **Germination** in the host
- **Adhesion** to the intestinal wall
- **Multiplication/growth** in the host
- **Production** of toxins

## The Science Behind Bt Safety

### It is not the genetic information, it is the level of **EXPRESSION**

- **Damgaard (1995)** presented differences in the level of toxin production between commercial Bt strains and pathogenic Bc strains:
- The potential for virulence of *B. cereus* does not depend on the presence of genetic information for any of the enterotoxins, but rather in their level of expression (**Bellinzona, 2010**)
- In addition, the expression of these toxins is controlled in response to environmental conditions (pH, temperature, oxygen tension), nutrient availability and metabolic state of the cell (**Stenfors Arnesen et al., 2008**).
- Our data shows that **even under ideal growth conditions (during manufacturing) these toxins are not expressed**
- We have the ability to differentiate between our commercial strains and Bc quickly and reliably - **today**



## The Science Behind Bt Safety

### Empirical Evidence that Bt is Safe:

Fischer and Rosner (1959)

- 18 human volunteers ingested 1 g of formulated Bt (Thuricide®) daily for five days
- Five volunteers inhaled 100 mg of formulated Bt daily for five days
- Subjects were tested before and after exposure (including X-rays for those who inhaled product)
- **Researchers did not find any changes** in evaluations of the genitourinary, gastrointestinal, cardiorespiratory, or nervous systems



## The Science Behind Bt Safety

### From the IBMA Response to EFSA Opinion (September 2016)

*“It is contradictory to presume that the presence of Bt group bacteria automatically indicates a causal agent relationship in a food poisoning event given that Bt is ubiquitous in the environment and can be found in stool samples of healthy, as well as afflicted, individuals. This ubiquitous nature of Bt, its ecological niche as an insect pathogen, and the lack of a single, definitive Bt-caused food poisoning incident after approximately 50 years of commercial use of Bt as a plant protection product provides **an overwhelming weight of evidence** that commercial Bt strains are unlikely to cause illness from food poisoning.”*



## (Not so) Abstract

The EFSA July 21, 2016 Opinion Includes an **Abstract** that (in the estimation of the IBMA Microbials Working Group) is **inconsistent** with the body of the Opinion document.

### From the Abstract:

*“Bacillus cereus and B. thuringiensis strains are usually not discriminated in clinical diagnostics or food microbiology. Thus, the actual contribution of the two species to gastrointestinal and non-gastrointestinal diseases is currently unknown...”*

*“The levels of B. cereus that can be considered as a risk for consumers are also valid for B. thuringiensis.”*

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*“Bacillus cereus and B. thuringiensis strains are usually not discriminated in clinical diagnostics or food microbiology. Thus, the actual contribution of the two species to gastrointestinal and non-gastrointestinal diseases is currently unknown.”*

### From the Opinion:

*“The levels of B. cereus group posing a health risk to consumers are highly strain-dependent due to the highly diverse pathogenic potential.”*

## (Not so) Abstract

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### **From the Abstract:**

*“The levels of B. cereus that can be considered as a risk for consumers are also valid for B. thuringiensis.”*

### **From the Abstract:**

*“There is no evidence that B. thuringiensis has the genetic determinants for the emetic toxin cereulide.”*

# EFSA's Seven Recommendations & IBMA Responses

## EFSA Recommendation

Obtain information through whole genome sequencing in order to provide unambiguous identification of strains used as biopesticides and assist further safety assessment.

## Registrant Response

It is critical to remove all ambiguity by correctly identifying commercial Bt strains used as biopesticides and distinguishing them from pathogenic Bc strains. Information regarding these commercial strains is currently available. Complete sequences are being provided to the European regulators as part of AIR4 dossiers.

## EFSA's Seven Recommendations & IBMA Responses

### EFSA Recommendation

In cases of food-borne outbreaks associated with the Bc group, characterise strains in detail allowing discrimination of Bt from Bc, as well as the identification of strains related to commercial Bt used as biopesticides.

### Registrant Response

First and foremost, adherence to full epidemiological protocols is necessary in cases of food-borne outbreaks to correctly identify causal agents. Just as it is critical to characterize virulent *B. cereus* group strains, it is likewise critical to characterize non-pathogenic *B. cereus* group strains in order that European food producers continue to have access to proven and sustainable crop protection tools.

# EFSA's Seven Recommendations & IBMA Responses

## **EFSA Recommendation**

Maintain Bc group food-borne outbreak strains in accessible culture collections preferentially managed by reference laboratories.

## **Registrant Response**

Once pathogenicity is confirmed using appropriate and accepted epidemiological protocols, those strains should consistently be maintained by reference laboratories.

# EFSA's Seven Recommendations & IBMA Responses

## EFSA Recommendation

Identify markers for commercial Bt strains to allow regular monitoring and easy differentiation in suspect outbreak situations.

## Registrant Response

The full genome is available for identification of commercial Bt strains, and can be used in suspect outbreak situations. Additional genomic methods are already available to regulators to carry out this differentiation.



## EFSA's Seven Recommendations & IBMA Responses

### EFSA Recommendation

Promote field studies after application of Bt biopesticides in order to inform the possible establishment of pre-harvest intervals.

### Registrant Response

We believe that a lack of pathogenicity has been sufficiently established for commercial Bt strains through a weight of evidence and a volume of scientific data, therefore no studies or pre-harvest intervals are warranted.



## EFSA's Seven Recommendations & IBMA Responses

### EFSA Recommendation

Develop research on dose–response and behavioural characteristics of Bc group strains and specifically of Bt, to facilitate risk characterisation.

### Registrant Response

IBMA cannot comment on other *B. cereus* group strains, however we believe a lack of pathogenicity has been established for commercial Bt strains and thus the need for risk characterization has already been met.

## EFSA's Seven Recommendations & IBMA Responses

### EFSA Recommendation

Develop studies to monitor and characterise the factors that lead to/favour the transfer of the Bc group and specifically Bt from the environment to foodstuffs and identify the routes and critical steps of contamination in the food industry.

### Registrant Response

IBMA cannot comment on other *B. cereus* group strains, however we believe that a lack of pathogenicity has been established for commercial Bt strains through a weight of evidence and a volume of scientific data, hence their presence on foodstuffs is a non-issue.



## Implications to the Biocontrols Industry and the Importance of Bt to Sustainable Agriculture

In an environment where mandatory reductions in the use of synthetic pesticides is the norm, Bt's lack of mammalian toxicity and low environmental impact make it among the most important tools for the future of sustainable production agriculture

Bt was introduced more than 50 years ago and is the **Paragon of Biocontrols**

Bt is the #1 selling biopesticide in the world

Bt is exempt from tolerance in more than 100 countries around the world

US EPA and other leading regulatory agencies recognize numerous studies that indicate Bt toxins are non-pathogenic to mammals

Studies also indicate a lack of toxicity to fish, pollinators, and other non-target organisms

Bt is critical to resistance management programs that help preserve the product life of today's softer chemistries



## Implications to the Biocontrols Industry and the Importance of Bt to Sustainable Agriculture

Bt exhibits all of the most desirable traits upon which designs for sustainable agriculture are founded:

- It is naturally occurring
- It is highly effective
- It is highly specific
- It is not toxic to mammals, fish, or bees
- It has built-in resistance management qualities
- It has little to no impact on workers
- It has little to no impact on the environment

**We must stand behind Bt as an INDUSTRY**



## **Implications to the Biocontrols Industry and the Importance of Bt to Sustainable Agriculture**

**What would it mean if we lost Bt in Europe or if new label restrictions were imposed?**

**Business and Society would both suffer if Bt is needlessly/over/regulated/restricted in Europe:**

- European consumers and growers would be at a severe disadvantage in the global marketplace
- Such restrictions would send a clear message to the biocontrols industry: While important, the EU is a risky place to introduce new technologies
- It would surely affect future product development decisions for Europe
- It would surely affect minor uses in Europe



## Takeaway and Call to Action

Remember that it is MEMBER STATES, not EFSA, who votes and decides on whether Crop Protection products should be bound to a tolerance, and on what that tolerance should be, based on a rigorous process.

- IBMA and Bt registrants are in the process of meeting with Member State representatives as possible
- Stakeholder groups have agreed in principle to host an event in Q1 2017 for food companies and growers groups to share the technical information surrounding this issue to further galvanize support of this technology

**Thank you for your kind attention**

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