BioStimulants/Biologicals: What CROs Need To Know

Dr. Brian Cornelious
About Me

Brian Cornelious, PhD

Director of Applied Sciences, Agricen (2011-Present)
Regional Sales Manager, Stine Seed Company (2009-2011)
Station Manager, Mertec, LLC (2004-2009)

Education:

The University of Arkansas, Fayetteville
PhD, Plant Breeding & Genetics (2000-2004)

The University of Arkansas, Fayetteville
MS, Plant Breeding & Genetics (1997-2000)

The University of Arkansas, Pine Bluff

Background:

As Director of Applied Sciences, Dr. Brian Cornelious brings to Agricen nearly two decades of research expertise. His experience spans corn and soybean breeding and development, seed sales and marketing and field plot design, preparation and maintenance.

Prior to joining Agricen, Brian managed regional sales at Stine Seed Company. Previously, he worked as a soybean breeder and station manager at Mertec, LLC. He has also held research positions in the AR Soybean Breeding Program and within the Formulations/Bioevaluations and Product Development Groups at Monsanto Company.

Brian currently serves as a board chairman for the Arkansas Land and Farm Development Corporation and a board member of the Crittenden County 4H. He is a past board chairman of the Commercial Soybean Breeders Association.
My Goal Here Today

• To bring awareness to the changing landscape of the BioStimulant/Biologicals sector
## Comparison of Technologies for Fertilizer Efficiency

<table>
<thead>
<tr>
<th>Technology</th>
<th>Primary Mechanism</th>
<th>Primary Mode of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow and Controlled Release</td>
<td>Physical</td>
<td>Meter out nitrogen</td>
</tr>
<tr>
<td>Stabilizers</td>
<td>Chemical</td>
<td>Inhibits a specific bacterium or enzyme</td>
</tr>
<tr>
<td>Biostimulants</td>
<td>Various</td>
<td>Hormonal, Stimulatory (Sugars) Stressed Relief (Kelp), Organic Acids, etc.</td>
</tr>
<tr>
<td>Microbial</td>
<td>Biological</td>
<td>Indirectly stimulates bacterial, nutrient and plant function</td>
</tr>
<tr>
<td>Biochemical</td>
<td>Biological</td>
<td>Directly stimulates bacterial, nutrient and plant function</td>
</tr>
</tbody>
</table>
The Term “Biostimulant”

- Name first appeared in industry publications in 1997, when Zhang and Schmidt at Va Tech talked about their use in turf and hort
- 1st peer-reviewed journal reference in 2007 (Kauffman at Penn State) described uses much as the industry associations describe them today
- Began to gain broader acceptances in 2010 – 2011 with founding of EBIC (June 2011), BC (July 2011)
- 1st world congress on biostimulants in Nov 2013 in Strasbourg, France
Plant Biostimulants: What Are They?

**Analyst’s view:**

- “Biologically derived crop chemistry…”, from:
  - Naturally occurring microorganisms,
  - Plant extracts, and
  - Organic material
- Crop protectors (aka biopesticides)
- Crop enhancers (aka biostimulants)

Biostimulants: Working Definitions*

**EBIC:**

Plant biostimulants contain substance(s) and/or micro-organisms whose function when applied to plants or the rhizosphere is to stimulate natural processes to enhance/benefit nutrient uptake, nutrient efficiency, tolerance to abiotic stress, and crop quality.

**US Biostimulant Coalition:**

Plant biostimulant means a material which contains substance(s) and/or microorganisms whose function when applied to plants or the rhizosphere is to stimulate natural processes to benefit nutrient uptake, nutrient efficiency, tolerance to abiotic stress, and/or crop quality, independently of its nutrient content”.

* Currently, no agreed definition exists for legal / regulatory purposes
“Biostimulant (n.) – A material derived from biological origin that, when applied to a plant, seed, soil or growing media, enhances the plants ability to use nutrients, reduces nutrient losses to the environment, or provides other direct or indirect benefits to plant development or stress response, but is not regulated as a fertilizer or pesticide.”

“Plant biostimulant mean a material which contains substance(s) and/or microorganisms whose function when applied to plants or the rhizosphere is to stimulate natural processes to benefit nutrient uptake, nutrient use efficiency, tolerance to abiotic stress, and/or crop quality, independently of its nutrient content.”
Companies Working Together

Agricen, A Loveland Products Company*
Arysta LifeScience North America
Chemical Dynamics, Inc.
DeltAg Formulations
Fast2Grow
Horizon Ag-Products

Lebanon Seaboard Corporation*
Loveland Products
Ocean Organics
Spring Valley USA*
Valagro S.p.a.
Kadant GranTek, Inc.

* Founding Members
Global Biostimulants Market – Opportunities in Key Application Sectors by 2025

By Hiren Samani  -  January 17, 2018

On account of the increasing need for non-toxic agricultural stimulants, the global biostimulants market offers commendable growth opportunities for market players. The most noticeable trend in the market is the formation of strategic alliances amongst market players. Established regional players are keen on partnering with global market players to gain a worldwide presence. Further, the stupendous market potential is attracting the entry of new players into the market. This is expected to fragment the market due to the presence of large-, small-, and medium-sized players. The renowned market players are Koppert Biological Systems, Italpollina spa, Agrinos, Biolchim S.p.A., Syngenta, Premier Tech Ltd., Valagro, Novozyme, Agricen, Agriculture Solutions Inc., and Kelpgrow. These market players are anticipated to invent a range of innovative business strategies that could give them an upper hand over competitors.
Why Should We Care?

- Important contributions to sustainable agriculture
  - Feeding the world on today’s production acreage
- Surge of investment to build R&D, applied research capacity
  - All along the market value chain, from majors to start-ups

**Early Stage**
- Marrone
- AgBiome
- BioConsortia
- Indigo

**Mid-Size**
- More than 60 member companies in US / EU industry groups

**Majors**
- Monsanto
- BASF
- Syngenta
- Bayer M&A activity

**Soil & Crop Technology:**
$161M VC Investments in 1H2016
Up 290% over 2015

**Flurry of Transactions**
Over $2.5B in deals in 2012-13 alone
Biostimulants Market Expected to Grow to Over $2.5B by 2021

Market Forecast – 2016 through 2021
Estimates of Six Market Analysts

Biostimulants represent roughly 40% of total Ag Biologicals sales
CAGR through period of 10 to 12%

Source: Agricen Sciences’ analysis of six separate market analyst forecasts
# Descriptors of Main Biostimulant Categories

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</tr>
</thead>
<tbody>
<tr>
<td><strong>Existence of Plant Analogs</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Action inside the plant</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Action outside the plant</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Physical or physio-chemical effects</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Metabolic effects</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Hormonal effects</strong></td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Physiological effects on nutrition efficiency</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Physiological effects on abiotic stress response</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Physiological effect on biotic stress response</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tbody>
</table>
Plant Biostimulants: What are the Claimed Benefits?

**Improve nutrient use efficiency**
- Mobilization of nutrients (in soil)
- Recruitment / acquisition of nutrients (e.g., stimulate root function, nutrient sensing, N-fixation)
- Improved uptake
- Transport, storage and assimilation

**Improve abiotic stress tolerance**
- Performance under physical or chemical stresses
- Common targets are heat, cold, water (flooding or drought), salinity

**Improve crop quality traits**
- Nutritional / nutraceutical value, color / cosmetics, shelf life, sizing, grade, pounds solids, etc.
Where Do They Fit the Regulatory Landscape?

FIFRA, Section 2(v)

<table>
<thead>
<tr>
<th>Regulated</th>
<th>Excluded from Regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Plant regulators&quot;:</td>
<td>Substances intended as:</td>
</tr>
<tr>
<td>• Substances or mixtures</td>
<td>• Plant nutrients</td>
</tr>
<tr>
<td>• Intended by physiological action</td>
<td>• Trace elements</td>
</tr>
<tr>
<td>• Meant to accelerate or retard rate of growth or maturation</td>
<td>• Nutritional chemicals</td>
</tr>
<tr>
<td>• Or otherwise altering the behavior of plants</td>
<td>• Inoculants</td>
</tr>
<tr>
<td></td>
<td>• Soil amendments</td>
</tr>
</tbody>
</table>

EPA is currently drafting initial regulatory guidance (with more to follow)
The Regulatory Challenges / Ongoing Issues

• FIFRA – 1950’s legislation (Major updates in 1972 & 2012)
  – What was the thinking at the time?
  – Limitations of the (then) available science?

• Plant regulators
  – Definition of “altering the behavior of the plant”?

• Ongoing issues:
  – The “nutritional chemicals” exclusion
  – The natural continuum of claims
  – Complex organics and “dual use” materials
  – Safety standards and industry stewardship role

BPIA and US Biostimulant Coalition collaborating in work with EPA
“Dual Use” Questions: An Example

Consider the humble Bacillus:

With a range of possible functions...
- Organic matter degradation
- Nutrient processing/cycling
- Plant growth promotion
- Biochemical signaling
- ISR/SAR
- Antibiosis/disease control
- Insect/nematode control

...determined by a variety of factors:
- Concentration/“titer” (in CFU/ml)
- Use context/rates
- Fermentation approach:
  - e.g., optimal for metabolite production?
- Genetic capability of the strain(s)
  - Possess or lack a functional gene?
- Formulation/applications approach
- Whole broth versus metabolites
- Deactivation/lysing of cells?

When is a biocontrol product...not a biocontrol product?
The Emerging Landscape of Products – Broad and (Potentially) Confusing

- **Acids**
  - Humic substances
  - Fulvic acids
- **Humins**
- **Microbials**
  - Mycorrhizae, Trichoderma, other beneficial fungi
  - PGPR’s
  - Rhizobium
  - Complex communities / consortia
- **Extracts**
  - Laminarin, alginates, other polysaccharides
  - Polyphenols
  - Botanicals
- **Other**
  - Protein hydrolysates
  - Nitrogenous compounds
  - Phosphites
  - Enzymatic extracts
  - Other organic matter extracts
  - Chitin / chitosan
  - Betaines
  - Carboxyls
  - Phytohormones
- **Proteins**
- **Inorganic salts**
- **Beneficial elements (Si, Na, Co, etc.)**
- **B Vitamins**
- **Proteins**
- **Other organic acids**
- **Amino acids**
- **Fatty acids / lipids**
- **Peptides**
- **Cytokinins**
- **Phytohormones**

Source: Agricen Sciences' analysis of market analysts, survey papers on Biostimulants
Acids and Extracts are the Dominant Product Categories (by Market Share)

Percent of Sales (est., 2018) ~1.8B @ 10.8% annual growth

- **Acids**
  - Microorganisms
  - Chitosan, other biopolymers
  - Protein hydrolysates
  - Other inorganic / organic compounds
  - Kelp / Seaweed
  - Plants (Botanicals)

- **Extracts**
  ~$170m

- **Other**
  ~$750m

- **Humic**
- **Fulvic**
- **Other organic**
- **Amino**

Sources: MarketsandMarkets Analysis; P. du Jardin analysis of Plant Biostimulants 2015
## Other Examples of Emerging Biostimulants

**Substances**

- Amino acids / peptides (e.g., glycine betaine)
- Organic matter fermentation products
- Protein hyrolysates
- Chitosan / other biopolymers
- Inorganic salts (e.g., silicates, carbamates)

**Researched Effects**

- Stimulate enzyme production for nitrate uptake
- Production of flavonoids, lignins under salt stress
- Plant defense elicitors
- Stress response signaling
- Regulation of osmotic stress
- Improved transpiration, stoma functioning
Research-driven approaches to “wellness” for plants
• System optimization and management
• Integrated with conventional practices

The lines blur…between crop protection and managing plant nutrition, vigor, health and productivity
• Will regulatory reform enable it?

A wellspring of discovery:
• Novel bioactive materials, organisms and compounds
• Sourced from plants, organisms, other organic pools

Leveraging precision ag technologies, for focused use and optimal efficiency
If You Are REALLY Hooked…

• Basics on Biostimulants:

• Industry Associations:
  – U.S. Biostimulant Coalition (http://www.biostimulantcoalition.org/)
  – Biopesticide Industry Alliance (BPIA), Biostimulants Integration Committee (http://www.bpia.org/)
  – European Biostimulant Industry Council (EBIC) (http://www.biostimulants.eu/)