The BIT Experience: “How did this happen?”

PUBLIC/PRIVATE RESPONSE TO THE RESCUE

BACK-TO-BASICS:
This presentation is for marketing and information purposes only. By this presentation, ADAMA Agricultural Solutions (the “Company”) does not intend to give, and the presentation does not constitute, professional or business advice. The accuracy, completeness and/or adequacy of the content of this presentation, as well as any estimation and/or assessment included in this presentation, if at all, is not warranted or guaranteed and the Company disclaims any intention and/or obligation to comply with such content. The Company may make improvements and/or changes in the features or content presented herein at any time. The Company shall not be liable for any loss, claim, liability or damage of any kind resulting from your reliance on, or reference to, any detail, fact or opinion presented herein. This presentation contains proprietary information of the Company and may not be reproduced, copied, disclosed or utilized in any way, in whole or in part, without the prior written consent of the Company.
Industrial Parks where precursor to BIT is synthesized are shut down by Chinese provincial government in summer 2018.

2-Chlorobenzonitrile (2-Chloro-phenyl cyanide) \( \rightarrow \) 1,2-benzisothiazol-3-one (BIT)

Effective antimicrobial and sporicidal preservatives are critical formulants in aqueous-suspensions and suspoemulsions if the End-Product (“EP”) is to remain shelf-stable in all but for the shortest-term storage and to inhibit possible contamination upon opening multi-dose packaging as well.
The impact of BIT supply disruption is felt across industries

The Pesticide and Adjuvant Industry was not alone:

- Household & Commercial Products Association issued an advisory to its members when the extent of the shortage became known (Steve Bennett, SVP of Scientific Affairs HCPA)

  ➢ BIT users, must reformulate “…to make sure their products perform as expected…”

  ➢ The Agency could receive thousands of reformulation requests in a short period of time
Did Industry put all its eggs in one basket?

A supply disruption requiring multiple remedies:

- 2019 production season was looming
  - *Inertia*, owing to very few instances of crop protection chemicals suffering short shelf-life, there was scant study of alternatives

- Unknown performance and durability so a new microbiocide would require dose-finding

- Would a substitute preservative have the same pH tolerance and durability or have an effect on physical properties of any of the EPs?

- How much burden could be placed on EPA in fielding literally thousands of duplicative MFAs?
Public/Private leadership addresses the imminent and shared challenge

Actions taken:

• CLA/RISE/CPDA members and leadership mobilized and surveyed their communities for input to propose a consensus set of potential solutions to EPA

• A database of formulated microbiocides was screened for already-approved options

• CITAB’s Kerry Leifer was engaged from the outset in formulating policy options for OPP and OGC consideration

• Open channels of communication between OPP/RD leadership and Industry through Ray McAllister’s office enabled responsive relief measures to be rapidly developed

• EPA rolled out a series of policy notices anchored to its administrative requirements while responsive to the measured relief Industry had requested
The series of policy notices from EPA include BIT combinations and non-BIT preservatives:

- BIT preservatives from registered source can be substituted via self-certification by notifying EPA
- BIT + 2nd biocide are approved for use in aq. products provided the partner preservative holds a 910, 920 or 950 classification for food-crop use and does not exceed its respective rate limitation
- BIT can be replaced entirely with several non-BIT preservatives approved for food-crop use by submitting to RD a MFA with a 8570-1 that identifies the EPA Reg No. of the EP so modified
- Adjustments to the filler’s content in an EP or the addition of buffers and/or pH adjustments for stability are permitted (provided the adjustment is ≤1% in aggregate)
- Dec 21 Agency response offers a prescriptive list of options by tradename and Reg. No. (in Table B) to husband remaining inventory of BIT since timing and reliability of BIT replenishment remains uncertain in the near- to mid-term
- The preservative options made available to the Industry besides BIT standalone, number 35, and comprise standalone preservatives or combinations of 6 already-registered microbiocides for food- and non-crop use
Objective: A variety of neat EPs were inoculated with specified microorganisms individually to simulate high levels of contamination

Outcome: Scored growth or inhibition of select bacteria, mold and fungus at defined intervals over the course of 28-days (based on CFU/gram)

Independent Variables: Alternative registered preservatives, biocide content in EP, durability of effect, compatibility with other components of EP, effect on pH of EP

Dependent Variable: Log reductions as follows:
- 1 log reduction = 90% reduction
- 2 log reduction = 99% reduction
- 3 log reduction = 99.9% reduction and so forth thru log reduction series

If the preservative achieves at least a 2 log reduction by 14-days post-inoculation with no increase from 14-day count until test’s end then it meets acceptance criteria
## USP <51>
**Herbicide Aqueous Suspension Sans Polysaccharide**
**No Preservative Added**

<table>
<thead>
<tr>
<th>Test Substance</th>
<th>Contact Time</th>
<th>Data Description</th>
<th><em>E. coli</em> 8739</th>
<th><em>P. aeruginosa</em> 9027</th>
<th><em>S. aureus</em> 6538</th>
<th><em>A. brasiliensis</em> 16404</th>
<th><em>C. albicans</em> 10231</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biosub-RCC-45n No preservative</strong></td>
<td>Time Zero</td>
<td>CFU/g</td>
<td>9.35E+05</td>
<td>4.60 E+05</td>
<td>7.30 E+05</td>
<td>5.55 E+05</td>
<td>2.75 E+05</td>
</tr>
<tr>
<td>Day 7</td>
<td>CFU/g</td>
<td>2.52E+04</td>
<td>1.09 E+04</td>
<td>&lt;5.00 E+01</td>
<td>6.95 E+05</td>
<td>&lt;5.00 E+01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Log₁₀ Reduction</td>
<td>1.57</td>
<td>1.63</td>
<td>&gt;4.16</td>
<td>None</td>
<td>&gt;3.74</td>
<td></td>
</tr>
<tr>
<td>Day 14</td>
<td>CFU/g</td>
<td>2.50E+02</td>
<td>3.93 E+05</td>
<td>&lt;5.00 E+01</td>
<td>6.65 E+05</td>
<td>&lt;5.00 E+01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Log₁₀ Reduction</td>
<td>3.57</td>
<td>0.07</td>
<td>&gt;4.16</td>
<td>None</td>
<td>&gt;3.74</td>
<td></td>
</tr>
<tr>
<td>Day 28</td>
<td>CFU/g</td>
<td>&lt;5.00E+01</td>
<td>3.00 E+02</td>
<td>&lt;5.00 E+01</td>
<td>6.30 E+05</td>
<td>&lt;5.00 E+01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Log₁₀ Reduction</td>
<td>&gt;4.27</td>
<td>3.19</td>
<td>&gt;4.16</td>
<td>None</td>
<td>&gt;3.74</td>
<td></td>
</tr>
</tbody>
</table>
USP <51>
Herbicide Aqueous Suspension Sans Polysaccharide
No Preservative

![Graph showing bacterial growth over time](image-url)
USP <51>
Herbicide Aqueous Suspension Sans Polysaccharide with BIT-Free Alternate Preservative

<table>
<thead>
<tr>
<th>Test Microorganism</th>
<th>CFU/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>1.00E+00</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>1.00E+01</td>
</tr>
<tr>
<td>S. aureus</td>
<td>1.00E+02</td>
</tr>
<tr>
<td>A. brasiliensis</td>
<td>1.00E+03</td>
</tr>
<tr>
<td>C. albicans</td>
<td>1.00E+04</td>
</tr>
</tbody>
</table>

**Time Zero**
- E. coli: 1.00E+00
- P. aeruginosa: 1.00E+01
- S. aureus: 1.00E+02
- A. brasiliensis: 1.00E+03
- C. albicans: 1.00E+04

**Day 7**
- E. coli: 1.00E+00
- P. aeruginosa: 1.00E+01
- S. aureus: 1.00E+02
- A. brasiliensis: 1.00E+03
- C. albicans: 1.00E+04

**Day 14**
- E. coli: 1.00E+00
- P. aeruginosa: 1.00E+01
- S. aureus: 1.00E+02
- A. brasiliensis: 1.00E+03
- C. albicans: 1.00E+04

**Day 28**
- E. coli: 1.00E+00
- P. aeruginosa: 1.00E+01
- S. aureus: 1.00E+02
- A. brasiliensis: 1.00E+03
- C. albicans: 1.00E+04
Sample was pre-exposed to 54 °C for 1 week prior to challenge testing to evaluate if breakdown of other formulants provides a more favorable growth medium for foulers.
USP <51>
Insecticide Aqueous Suspension with *BIT Preservative*

<table>
<thead>
<tr>
<th>Test Microorganism</th>
<th>CFU/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>1.00E+06</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>1.00E+05</td>
</tr>
<tr>
<td>S. aureus</td>
<td>1.00E+05</td>
</tr>
<tr>
<td>A. brasiliensis</td>
<td>1.00E+04</td>
</tr>
<tr>
<td>C. albicans</td>
<td>1.00E+04</td>
</tr>
</tbody>
</table>

- **Time Zero**
- **Day 7**
- **Day 14**
- **Day 28**
USP <51>
Insecticide Aqueous Suspension with *BIT-Free Preservative #1*

<table>
<thead>
<tr>
<th>Test Microorganism</th>
<th>CFU/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>1.00E+06</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>1.00E+06</td>
</tr>
<tr>
<td>S. aureus</td>
<td>1.00E+06</td>
</tr>
<tr>
<td>A. brasiensis</td>
<td>1.00E+06</td>
</tr>
<tr>
<td>C. albicans</td>
<td>1.00E+06</td>
</tr>
</tbody>
</table>

- **Time Zero**
- **Day 7**
- **Day 14**
- **Day 28**

ADAMA
The rapid response was of global importance to Adama’s extended supply chain.
Challenges/Opportunities Ahead

Triage Priorities

Thorny Issue Index

Supply Chain Complexity

EPA Resource Trend

Time >>>

CAPABILITY DEFICIT
Learnings from the BIT Experience

Streamlining and self-certification:

• Aqueous suspensions bring many benefits however shelf-life is *not* one; formulants that make minor contribution to formulas mediate their stability and handling properties

• Distributed supply chains of RMs, inert components and MUPs are more global than ever

• With extended supply lines, chains that were once efficient can break without notice

• Advances in sustainable chemistry and manufacturing will spawn new functional materials from new sources burdening an already taxed scientific review resource

• The BIT experience demonstrates how self-certification and batched processes that reduce paperwork for submitters and EPA can eliminate redundant CSF amendments

• Among reasonable areas to pilot self-certification:
  - Commodity chemicals and inert substances with qualifying criteria and a well-defined list
  - Fertilizer blends, where applicants self-certify that the nutrient carrier in the CSF is drawn from the list of ingredients described and vetted as fertilizer by AAPFCO.
A QUICK RECAP

1. A KEY POINT

A shortage of crop protection chemicals in 2019 was averted by the combined judgment and rapid response of EPA and the Industry it regulates.

2. ANOTHER KEY POINT

The ability of CLA/RISE/CPDA to unite behind one set of proposals served the Industry and EPA. The stewarding of our Nation’s safe and abundant food supply is the responsibility of an efficient Public/Private partnership that builds in flexibility to maintain ecosystem stability.

3. ONE LAST THOUGHT

Given the interconnected nature of our supply chains, and the trend for governments to promulgate sustainable production policies that disrupt existing supply chains, efficient vetting of secondary sources of formulants will become ever more critical in the future.