



Citrus Research and
Development Foundation, Inc.

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Management of Huanglongbing: An Outline of the Antimicrobial Strategy

The industry, through CRDF, has been investigating solutions to HLB for 5 years now, and most recently has been provided the opportunity to invest state resources in accelerating those tools that are close to field-ready. Additional field-ready tools are needed for use in managing the HLB vector, Asian citrus psyllid, reducing or eliminating the inoculum from infected trees, and having available citrus trees and production practices that maintain health and productivity in the presence of continued HLB pressure.

We have invested heavily in nutritional treatments, both as citrus growers and in the research arena. Continuing research has two main goals, the first of which is to demonstrate the benefit of supplemental nutrient treatments and allied materials. This will help growers determine among available products, rates, timing, and potentially the return on investment of this set of tools. The second goal is mechanistic; to understand the cause/effect relationships of nutritional treatments, with an eye to reduction to those components which are most useful in the varying environments of Florida citrus groves. Regarding the need for near-term therapies that specifically reduce the levels of bacteria in infected citrus trees, there have been many strategies pursued that collectively address reversing disease impacts.

- We are trying to understand the effects of heat therapy in reducing HLB symptoms and reducing tree decline. On-going research is synchronized with grower innovation, and together, evidence is accumulating for how solarization within tree covers can reduce *CLAs* titer and stimulate positive tree growth response. Research projects are designed to quantify the variables at play and to contemplate commercialization strategies (scale-up to rows and groves).
- Biological treatments are being evaluated in field research, with many potential objectives being considered. Among these are beneficial microbe products, many of which are available for use in citrus, and for which little performance evidence exists. Like the nutritional treatments, there are questions of what can be expected from their use, as well as how they can be optimized and integrated into overall citrus management in the era of HLB. Other biological approaches include use of the CTV vector as a delivery tool and investigation of phages (bacterial viruses).
- All of these tools and other approaches which involve ACP reduction or development of plant tolerance/resistance, need to be evaluated under field conditions to determine their individual and collective effects on citrus production in the current season and beyond.
- Finally these therapies and other tools must be capable of overcoming challenges in new plantings, providing growers with the confidence to move ahead with resetting and replanting.



Antimicrobial Strategy:

Since the NRC study and its publication in 2009, CRDF has backed research in antibacterial compounds including antibiotics that are used in human and animal health. Initially research focused on development of expanded screening assays, since HLB and *CLas* offer unique challenges to researchers. This work has yielded a reproducible citrus graft assay, and more recently, a surrogate bacterial laboratory assay using the closely related *Candidatus Liberibacter crescens*. The latter allows for high throughput evaluation of antimicrobial candidates. Finally, a soil assay also has been developed to investigate activity of soil-borne microbes or their by-products.

The InnoCentive™ promotion showed the breadth of chemical compounds that have good activity. The Innocentive Challenge was a reward-based attempt to seek solvers who had candidate antimicrobial materials that they felt might be useful against *CLas*. Based on screening the candidates submitted, and subsequent discussions with commercial partners, we have narrowed these submissions to 11 compounds to evaluate further. In turn this has guided our development of 5 strategies for advancement to field trials and possible registration. Each of these strategies, referenced in the table below, face different regulatory, technical and commercial risks.

At a recent CRDF Commercial Product Delivery Committee Meeting, the following information was summarized and strategies given favorable consideration to move forward.

- 1) Antibiotics: Streptomycin and Oxytetracycline are considered most likely to be approved among conventional antibiotics, since there is precedence for their use in agriculture. CRDF reports that corporate research is committed to move these two antibiotics forward.
- 2) Agricultural Antibiotics used on food crops in other countries: These candidates offer another opportunity for therapy against *CLas*, while posing unique challenges, including unraveling intellectual property issues.
- 3) New Molecular Entities: Compounds with specificity and potency customized to treat HLB and not used for human or animal health. These might be referred to as non-antibiotics.
- 4) Biopesticides: One class of compounds in this category is used in agriculture but not formulated for vascular disease of trees. CRDF is in discussion with the dominant industry patent holder.
- 5) GRAS-like: Simple plant essential oils. Sponsored-research is underway to formulate and deliver compounds that qualify for the GRAS-like status (Generally Regarded As Safe). The appeal of this category is the potential for more rapid deployment through a reduced commercialization and regulatory pathway if the laboratory evidence for efficacy of these materials is translated into the field.

In summarizing the status of this antimicrobial strategy, it is important to balance multiple dimensions of risk inherent in developing a product that is safe, effective and can be registered for agricultural use through federal and state agencies. In addition to regulatory concerns, we have to optimize dosages that are non-phytotoxic but still effective.

While this and other strategies for combatting ACP, *CLas* and the disease, HLB that they these organisms cause, it is **Critically important that growers Only use materials that are labeled for use in citrus, and use them in accordance with the label.** While it should go without saying, the seriousness of possible repercussions of misuse demand that this message be communicated clearly.

