Approved at CPDC meeting 9/18/14

CRDF Post IR-4 Workshop Meeting
September 11, 2014
1:15 – 3:00 pm
The Columbia Room, JW Marriott Hotel
Atlanta, Georgia

Meeting Participants:

CRDF
Tom Jerkins
David Howard
Joe Davis
Larry Black
Peter McClure
Wayne Simmons
Ricke Kress
Tim Anglea
James Dukowitz
Dan Botts

Guest
Ron Williams

FDACS
Anderson "Andy" Rackley (also CRDF)
Davis Daiker
Robert Moore
Greg Hodges

USDA – APHIS
Mary Palm

USDA – IR-4
Dan Kunkel

IFAS
Gary Vallad

EPA
Lois Rossi
Susan Jennings
Barbara Madden

CDC
Jean Patel

FDA
Heather Harbottle

Meeting notes

The meeting was called to order as an information meeting of the Citrus Research and Development Foundation's Product Development Committee by David Howard, Graves Brothers. Several of the CRDF membership present expressed their concerns over the desperate situation facing the Florida Citrus Industry and indicated the need for a therapeutic treatment for infected trees. It was stressed that even a partial solution that provided the ability to retain production on infected trees is critical to ensure the future of the industry.

Dan Botts, in his support role to the Foundation stresses the importance of the collaborative effort and coordinated nature of CRDF's efforts. It was noted that in the short term that "we have to have a therapeutic treatment to the trees". The multifaceted research program of CRDF on Huanglongbing (HLB) is extremely complicated and has been made more difficult by the inability to culture the causal agent outside of the citrus vascular sytem. Infected trees mimic many human pathogens by having a

latency period in the infected tree with visual symptoms not readily apparent in initial stages of the disease. The direct impact on the industry has been demonstrated over the past three seasons by the very large incidence of "drop" of near mature fruit. It is extremely frustrating as fruit drop happens at the very end of the season. He also thanked the meeting participants from EPA, CDC and FDA for their willingness to meet with the industry to follow up on the conference call held in late August. It was noted that the goal of meeting is to establish a dialog around the research to make sure as the results begin to become available the industry can focus its efforts on the most promising lines of treatment options.

Dan's question to the group to begin the discussions was is there anything CRDF and the industry needed to be doing differently, to make sure we are generating the data needed and not to end up, at the end of the day, missing something.

Lois Rossi (EPA) noted that there were two things needed regarding the Streptomycin and Oxytetracycline. Regarding the health risk assessments, she felt there would be room in the risk cup for these uses and that once the residue profile is developed it would be fairly simple to start the process of developing a package allowing a Specific Exemption (Section 18) until the full registration package can be completed. The second item is the 152 analysis process, which can be initiated based on previous work during the reregistration process. Heather C. Harbottle (FDA) also noted the needs for the 152 document and suggested that literature reviews should be initiated and that they will probably give a pretty good indication of any special exposure mitigation that may be necessary to achieve a positive registration decision. Dr. Harbottle did not think that this would require an extraordinary effort and would probably not need additional data generation to develop.

It was agreed by all that getting the residue studies for streptomycin and oxytetracycline initiated as soon as possible is very important. Those studies have been commissioned to Agrosource but the group is still not sure of the delivery method for application. Based on the field research from this past summer, the use pattern may now be understood.

A section 18 for streptomycin on orange is difficult because the data for the grapefruit section 18 is for the disease citrus canker and is limited to foliar applications. There were general discussions regarding what may be needed for mitigation measures (per 152 guidance). Lois noted that it would be similar to what is already required on currently registered uses on these two products and that the review for the Registrations for use on apple could be looked to for examples. Among the potential mitigation measures discussed was applicator exposure minimization, monitoring of resistance development in both soil and plant related microbiological fauna, and potential cross resistance to important human antibiotics.

For streptomycin and oxytetracycline residue studies, the CRDF representatives present stressed that this work was already contracted and underway. CRDF representatives indicated their understanding that the registrant will be working with the Agency to assure that these studies are accomplished as rapidly as possible. It was also noted that studies would start this fall; it was also assumed that the

contractor would have meetings with EPA to discuss the project and agency needs to ensure the project was done properly.

CRDF representatives asked the regulators at the meeting (CDC, FDA and EPA), about the possibility of registration of penicillin in light of the human uses of this antibiotic. Heather C. Harbottle (FDA) noted that resistance potential for that product would be a big problem, and that is aside from the allergen issue. If it is applied by injection then there would be less exposure. Dr. Jean B. Patel (CDC) noted that penicillin isn't used in pharma but there are many other products on the market related to penicillin and that resistance to penicillin would carry over to all of the other related materials being used for treatment today, therefore, the risk for resistance would be greatest with penicillin compared to the other products currently under investigation – streptomycin and oxytetracycline.

Greg Hodges provided an overview of the FDACS study. Much of their research to date has been difficult to analyze and to determine which products may provide the best control because of the variability of tree size and varieties tested. FDACS and EPA are cooperating on protocol development to determine appropriate rates and application methodology. It was indicated that for the treatments that had been made they are testing for penicillin residues in the foliage, fruit, and soil. They are also studying the impacts to the soil flora as well. A grower noted that penicillin was off the table until recently and had been revived because the situation has gotten so dire. Therefore from his perspective the "look and see" study to determine the efficacy and utility of the product is a high priority for the industry. It was agreed that if residues are present in the fruit the product would probably not be a candidate for registration. It was also noted that even if the comparable efficacy is greater than the other active lines of research, and no residues were found, the product would still face a very difficult future due to cross-resistance concerns for important human pathogens. EPA noted that if there are no residues and you proceed with registration, the 152 documentation and all of the other registration review and regulatory decision processes will take a long time. As a new pesticidal active ingredient any registration activity for penicillin would have to go a through a public notice and comment period which will attract the attention of a well-organized activist community that is anti-agricultural use of all antibiotics. EPA compared this process to the ongoing 2,4-D, Dicamba decision that has drawn over 500,000 individual comments. Susan Jennings (EPA) also noted that if penicillin comes out publically for a use on citrus, the negative PR could spill over to affect other products as well.

In addition to the antibiotics discussed above, the group also raised the efforts directed toward the GRAS like substances. There was some discussion on novel formulation activities and the regulatory scrutiny associated with enhanced formulations and the use of nanotechnology to enhance delivery of products to the vascular system of citrus trees. The Agency described the need for regulatory oversight would depend on the specific situation.

The need for regular dialogue was stressed will all of the impacted Federal Agencies present expressing a willingness to work with the industry to most efficiently and effectively deal with this problem.

The meeting adjourned at 3:00 pm.