New approaches to problems in the fields of mycotoxin and stress tolerance research

Bayer CropScience held a workshop at "Bayer's Perspective on Innovation 2006" to present new research approaches in the field of plant health. The event focussed on the topics of "Securing harvests and healthy food: The fight against mycotoxins" and "Plants under stress: Helping crops grow under difficult conditions". Both subjects belong to the main areas of research at Bayer CropScience which, with an R&D budget of around EUR 630 million in 2006, is one of the most research-intensive companies in the industry.

"For us, innovation is the central key to long-term success in the market for agrochemicals, seeds and plant biotechnology," explained Dr. Alexander Klausener, Head of Research in the Executive Committee of Bayer CropScience AG. The company is therefore planning extensive investments in research and development in the coming years, with the annual budget scheduled to rise to EUR 750 million by 2015. Bayer Crop Science's focus is on the development of innovative crop protection products and novel plant traits.

Slides 1-5

New options in the fight against mycotoxins

One particular challenge facing the crop protection industry at present is the fight against Fusarium in international cereal growing. Fusarium is a species of mold that frequently occurs in cereals, animal feed and food. In the first part of the workshop, Dr. Isolde Häuser-Hahn, who is responsible for Product-related Research in the Fungicides Business Unit of Bayer CropScience AG, explained: "Infestation of cereals with Fusarium is a worldwide problem with complex repercussions for agriculture in the countries affected. It is estimated that the economic damage in North America alone amounts up to US$ 1 billion each year."

Most varieties of Fusarium are plant parasites that can form fungal toxins known as mycotoxins. Mycotoxins in food can cause massive problems for humans and animals, including acute symptoms of poisoning, nerve damage, immune disorders and an increased risk of cancer. For this reason, the European Union, for example, recently specified threshold limits for certain toxins in unprocessed cereals. For efficient control of the pathogen, it is necessary to employ a combination of all the crop management techniques to rule out the risk of infestation of cereals as far as possible, thus preventing the formation of mycotoxins.

In her presentation, Isolde Häuser-Hahn described prothioconazole, Bayer CropScience's cereals fungicide that is currently in the launch phase, as the "new gold standard in

Fusarium control”. Studies have confirmed that this active ingredient from the new chemical class of triazolinthiones is markedly more effective against fusariosis than other products available in the market so far. Products based on prothioconazole such as Proline®, Prosaro® and Input®, also perform better than reference compounds from the azole class of substances in reducing levels of harmful mycotoxins, added Häuser-Hahn.

High-precision rapid test for cereal diagnosis developed

During the workshop, the Bayer CropScience scientist also presented a new, high-precision, rapid diagnostic test for mycotoxins. Existing tests to determine potential contamination with toxins either take too long, require expensive testing equipment or are relatively imprecise, explained Häuser-Hahn, as they are unable to provide quantitative information on the toxins. This will soon be a thing of the past, however: specialists at Bayer CropScience and Bayer Technology Services are currently developing a measurement device that can provide precise results within 20 minutes. The device is based on a tiny biochip using planar waveguide technology which Bayer is also developing for medical diagnostic applications. The chip can test for several toxins at the same time and other diagnostic applications in the food industry are also feasible. Häuser-Hahn expects that this diagnostic kit will be available on the market within the next three years.

Slides 6-16

Research to help plants cope with stress better

The second part of the workshop on plant health was dedicated to the topic of “Plants under stress: Helping crops grow under difficult conditions”.

Just like humans and animals, plants are exposed to numerous stress factors. Plant growth can be severely compromised by both biotic and abiotic stress factors. These stress factors can reduce the optimal achievable yield of plant crops by up to 80 percent. Biotic stress factors include, for example, attacks by insects, fungi, weeds, bacteria or viruses and can cause large yield losses in modern agriculture unless specific cop protection agents are employed to defend against these dangers. Modern crop protection research has already achieved a high standard of therapy to combat biotic factors, but much less research has been conducted into abiotic stress resistance. However, abiotic stress factors such as drought, heat, cold or soil salinity are the cause of sometimes dramatic yield losses in many regions of the world.

In order to safeguard high harvest yields and the good quality of plant-based products, Bayer CropScience is conducting two specific research projects into abiotic stress control: one approach based on classic active ingredient synthesis and one solution model based on the application of plant biotechnology.

Imidacloprid: much more than just the world's best-selling insecticide

Dr. Wolfgang Thielert, responsible for Product-related Research in the Insecticides Business Unit at Bayer CropScience in Monheim, Germany, first outlined the findings of recent research into imidacloprid, a conventional crop protection agent first launched by Bayer CropScience in 1994. Marketed under brands such as Confidor®, Gaucho® and Admire®, the compound achieves annual sales of about EUR 600 million, making it the world's best-selling insecticide. Studies carried out in the context of an international research cooperation project with scientists from Germany, Belgium, the Netherlands and the United States have shown that imidacloprid confers a special protective effect against stress.

"Even in the absence of plant infestation with insects, imidacloprid markedly improves the growth picture and also demonstrated positive effects on crop yields," explained Thielert in regard to the research findings. Studies of barley and cotton exposed to drought stress, for example, showed that plants treated with imidacloprid exhibited greater leaf growth even during the drought phase and were therefore able to generate more energy for production of the yield over an extended period of time.

"What was also surprising was that the plants treated with imidacloprid also produced markedly more endogenous proteins to defend themselves against fungal diseases. Imidacloprid therefore not only exerts its verifiable insecticidal action but also a supportive, fungicidal and stress-reducing protective effect," said Thielert in summary of the properties of imidacloprid.

Bayer CropScience recently started marketing imidacloprid-based active ingredient formulations in combination with the new O-TEQ formulation technology specially developed for this application under the label "Confidor® Stress Shield Inside". This novel formulation technology combines the benefits of a suspension with the biological advantages of an emulsion, and reliably transports the active ingredient into the plant. The active ingredient strengthens the plant's resistance to stress factors and helps to improve its health, thus safeguarding yields in terms of both quality and quantity. Added Thielert, "The name 'Stress Shield' graphically symbolizes the contribution that a product like Confidor® OD can make to maintaining crop health."

Slides 17-27

New strategies in stress research: the PARP metabolic pathway

Dr. Michael Metzlaff, Head of the Crop Productivity research group at Bayer CropScience's Innovation Center in Gent, Belgium, then explained the latest findings on the development of stress in plants and outlined a specific plant biotechnology approach towards improving stress tolerance which is currently being investigated by Bayer CropScience.

Plants react to stress by consuming large quantities of energy which can then no longer be used for vital physiological processes such as growth and carbon fixation in photosynthesis, explained Metzlaff to the audience at the workshop. The effects of moderate stress over extended periods of time or short-term episodes of extreme stress can completely drain the plant's energy reserves. The result can be irreversible damage to the plant or even death, said the Gent-based researcher.

Bayer CropScience's plant biotechnology research is therefore looking for new ways to counteract the loss of energy in plants under stress. This research aims to improve crop performance and thus boost both yields and product quality. A key protein in the stress response of all higher organisms, including plants, is what is known as PARP [*poly(ADP-ribose)polymerase*]. PARP controls the activity of several proteins involved in the stress response and consumes a great deal of biological energy in doing so.

In trials involving oilseed rape plants, Dr. Metzlaff's research group has succeeded in reducing the PARP activity to a level which provides the plant with adequate protection against stress yet simultaneously offers significant energy savings. Numerous laboratory tests have confirmed that the plants with fewer PARP proteins were better able to survive drought, high-intensity light, heat and cold than reference plants with a high PARP protein content. The research team used a novel technology known as gene silencing or RNAi to reduce PARP activity.

Said Dr. Metzlaff, "Field trials in 2005 and 2006 have shown that oilseed rape plants with a reduced PARP protein level are better able to withstand drought conditions. "In addition, field trial results for the summer 2006 harvest show a significant relative yield difference. We will further investigate this effect in the course of the project." Bayer CropScience is currently conducting research work with the new RNAi-PARP technology in corn, cotton, oilseed rape and rice, with the objective of developing a new generation of stress-tolerant, high-

performance crop varieties. Metzlaff believes that it may be possible to launch this technology on the market within the next ten years. Bayer CropScience is also currently investigating the possibility of combining the ‘Stress Shield’ effect of imidacloprid with new, stress-tolerant plant varieties from the company’s breeding research, as dual protection against stress for crops.

Slides 28-36