Standby Statement

On the INTEON® technology

Background

Syngenta has implemented stewardship programs over many years to support the safe and effective use of its products, among them Gramoxone®. More than 1 million farmers per year are trained by Syngenta in developing countries. In the context of its stewardship programs Syngenta developed INTEON® technology as an additional element to further promote the safe use of paraquat products.

The primary goal of INTEON® was to eliminate deaths from accidental ingestion and to significantly increase the chance of survival after misuse by deliberate ingestion of paraquat-containing products. To this end three components were combined in the INTEON® technology: an alginate, an increased emetic and a purgative. The alginate was to form a gel under the acidic conditions of the stomach. This would slow the release of paraquat and its passage to the small intestine. The increased emetic content was designed to invoke more effective vomiting of the stomach contents. The purgative was added to provide faster removal of paraquat that may have reached the small intestine.

The INTEON® technology was assessed by benchmarking the oral toxicity of the new Gramoxone® INTEON® against data for older products. From this initial benchmarking Syngenta concluded that a significant difference existed between Gramoxone® INTEON® and conventional Gramoxone® formulations with regard to oral toxicity and that there were potential benefits in relation to eye and skin irritation.

Latest Research

Recent studies have provided new insights into the dose-response for the acute toxicity of Gramoxone® products in animal model studies. The dose response for conventional Gramoxone® formulations is not linear and the formulations are less toxic at certain doses than previously expected. The non-linear dose response, indicates latest research, may be a reflection of the co-administration of increasing doses of both paraquat and emetic, although this is still a hypothesis at this time.

All available data show consistently that Gramoxone® INTEON® formulations are at least as safe as conventional Gramoxone® formulations. Because the reference benchmark for Gramoxone formulations has changed, we are not able to conclude that there is as significant and consistent a safening effect over conventional Gramoxone formulations as originally expected. However, it is prudent to assume that the degree of safening of INTEON® formulations is consistent with the published results of a monitoring survey in Sri Lanka which showed an approximately two-fold reduction in toxicity.

Syngenta is sharing latest research on Gramoxone® INTEON® with regulators in relevant countries (e.g. the USA and South Korea).

Basel, 17th April 2008

Questions and Answers
on the INTEON® **technology**

Q&A's relevant in contacts with the media

1. What are alginates?

Alginates are natural, non-toxic products extracted from seaweed. They are commonly used in the food and pharmaceutical industry, e.g. in ice cream and as heartburn treatments. They are known for their wound healing properties.

2. Why did you initiate the development of Gramoxone® INTEON®?

The novel formulation technology used in Gramoxone® INTEON® was designed to complement stewardship programs by eliminating deaths from accidental ingestion and by significantly increasing the chance of survival after misuse by deliberate ingestion of paraquat-containing products. These properties, according to the working hypothesis, would be the result of proprietary technology using alginates. Through this a higher industry standard for the protection of users might be established while providing the same effective broad-spectrum weed control offered by traditional Gramoxone® formulations.

3. Why did you develop Gramoxone® INTEON® when a similar safening can be achieved by diluting conventional Gramoxone®?

Diluting paraquat-based products has a safening effect, particularly in deliberate ingestion scenarios. Syngenta initiated the development of the INTEON® technology for two reasons. Firstly because the initial benchmark indicated a more significant safening effect with this technology compared to simple dilution. Secondly, a more concentrated product has agronomic benefits: there are smaller volumes of product to be handled, stored and transported and also fewer packages to dispose of.

4. In communications on the INTEON® technology you kept talking about safening effects of Gramoxone® INTEON® as compared to conventional Gramoxone® formulations. What do you mean with safening effect?

When we talk about safening by a factor of e.g. x we mean that we have reduced the amount of paraquat taken into the blood stream by a factor of x; it is like swallowing a xth of the intended amount.

5. On what basis did you anticipate Gramoxone® INTEON® to be safer than conventional Gramoxone®?

Syngenta had developed a database of toxicity studies with both Gramoxone® INTEON® and conventional Gramoxone® formulations. These data characterized the relationship between blood levels of paraquat and toxicity. Based on these early studies it was concluded that a significant difference existed between the oral toxicity of INTEON®, and that of conventional Gramoxone® formulations.

6. Are you saying that after years of development you have been unable to demonstrate the postulated safening in animal studies?

The new studies demonstrate differences in the dose-responses of Gramoxone® INTEON® versus conventional Gramoxone® formulations, but these differences are smaller than previously estimated. In the new studies the oral toxicity of Gramoxone® INTEON® has remained consistently low. However, the new studies have revealed new insights on non-INTEON® formulations namely that they are less toxic at certain doses than originally assumed. Consequently the difference between Gramoxone® INTEON® and non-INTEON® formulations over a broad range of doses is less than our initial data indicated.

7. What was the purpose of the survey in Sri Lanka?

The survey published in 'PLoS Medicine' compared the outcome of paraquat self-poisoning with the standard formulation against the new Gramoxone® INTEON® formulation following its introduction in Sri Lanka.

8. Are you satisfied with the safening you achieved with Gramoxone® INTEON®?

In the first year following the introduction of Gramoxone® INTEON® up to 30 lives may have been saved in Sri Lanka. This is a great achievement of which we are proud. The fact that the safening is not as significant and consistent as expected requires a re-assessment of the situation.

9. And what will you do with Gramoxone® INTEON®?

We are assessing our options with regard to offering equivalent safening to that which we have achieved with Gramoxone® INTEON®. This will take a few weeks to complete and will take into account the feedback from contacts with regulatory authorities in relevant countries.

10. Why are initial results of studies with Gramoxone® INTEON® different from more recent results?

Results of initial and more recent studies with Gramoxone® INTEON® are consistent. The more recent studies have extended the breadth of formulations and dose ranges tested. The non-linear dose-response for conventional Gramoxone® found in this research provided a new benchmark for Gramoxone INTEON.

11. In addition to the non-linear dose-response which other factors contributed to this significantly lower safening effect of Gramoxone® INTEON®?

The potential safening from the individual components of the INTEON® technology (i.e. alginates, emetic, purgative) has not been fully characterized.

12. You anticipated benefits of Gramoxone® INTEON® with regard to acute oral toxicity as well as eye and skin irritation. You have discussed the limited safening of oral toxicity, but what about irritation?

Some Gramoxone® INTEON® will qualify for more favorable classification under certain schemes, but the product remains an irritant to eyes and skin.

13. We take from your information that Gramoxone® INTEON® fails to provide the expected safening effects over traditional Gramoxone®. How could a company like Syngenta not foresee such a failure?

It is incorrect that Gramoxone® INTEON® does not provide safening effects over Gramoxone®. The independent monitoring survey in Sri Lanka suggests that within the sample population up to 30 lives may have been saved in the first year following the introduction of the new formulation in this country. This would indicate that the formulation offers a measurable improvement in oral toxicity, particularly after misuse by deliberate ingestion, which is a problem specifically in countries like Sri Lanka and South Korea.

14. Previous Syngenta communications talked about the mode of action of Gramoxone® INTEON® and how the gelling of the alginates would slow absorption of paraquat. Is this hypothesis still correct?

The potential safening from the individual components of the INTEON® technology (i.e. alginates, emetic, purgative) has not been fully characterized. This means not only the alginate but also the higher emetic concentration in INTEON® may be one of the parameters responsible for the differences seen in latest studies.

15. Does this mean that the limited safening of Gramoxone® INTEON® could come entirely from the increased concentration of the emetic?

We have no data at this time which would either support or disprove such a conclusion. Latest research indicates that the non-linear dose response may be a reflection of the co-administration of increasing doses of both paraquat and emetic; the former delivering increased exposure to a toxic substance and the latter inducing increased reduction of this exposure, but this is no more than a hypothesis at this time.

16. Have all Gramoxone® INTEON® studies been carried out in Syngenta laboratories?

The initial studies with Gramoxone® INTEON® were conducted in Syngenta laboratories. More recent studies were conducted by contract research laboratories.

17. A Syngenta sponsored study in Sri Lanka reports a reduction of fatalities following intentional ingestion of Gramoxone® INTEON® over similar cases with conventional Gramoxone®. What is the significance of these data?

The independent survey in Sri Lanka points to the benefits of Gramoxone® INTEON® over conventional Gramoxone®. Within the sample population it appears that up to 30 lives may have been saved after deliberate ingestion following the introduction of the new formulation. This would indicate a measurable improvement towards reducing fatalities after deliberate ingestion of paraquat based formulations, a problem specific to Sri Lanka and a few other countries.

18. Are the results from animal studies consistent with the results from the Sri Lanka survey phase 1?

The degree of safening in animal model studies is seen to be consistent with the results of the monitoring survey in Sri Lanka, which showed an approximate two-fold reduction in toxicity for Gramoxone® INTEON®.

19. How do you expect regulatory agencies to react to the latest research on Gramoxone® INTEON®?

We do not speculate on the outcome of the independent reviews by regulatory authorities. Syngenta has always communicated openly on the state of research with regard to Gramoxone® INTEON®, and we continue to work in this spirit with the latest submissions.

20. Gramoxone® INTEON® failed to meet the standards of regulators in Sri Lanka, particularly with regard to a significant increase in the chance of survival after deliberate ingestion of paraquat containing products. Evidence is the phase-out of paraquat containing products in Sri Lanka. Is there not an obligation for Syngenta to also withdraw the product in South Korea?

Gramoxone® is a highly important product in South Korean agriculture, particularly appreciated by producers of vegetables and several other crops. The INTEON technology was developed as one element of a much broader Syngenta stewardship program addressing pesticide users as well as other stakeholders. The decision taken by regulators in South Korea was to allow introduction of Gramoxone® INTEON® in the market at its original strength (200 g/l) and request dilution to <70 g/l for all other paraquat-based products. This decision is consistent with data from the survey in Sri Lanka, which suggested a roughly 10% reduction of fatalities with Gramoxone® INTEON® after misuse by deliberate ingestion compared to Gramoxone® formulations.

21. In earlier communications you talked about cost of roughly $ 50 mio for the development of Gramoxone® INTEON®. How do you justify such expenses for a concept that does not work?

The decision to develop Gramoxone® INTEON® and engage in entirely new formulation technology demonstrates that Syngenta is taking product stewardship very seriously and does not shy away even from challenging projects. The company has always been aware of the technical challenges involved in the development of this new technology. For this reason INTEON® has always been just one element among several to assure the safe use of paraquat based products.

22. Your latest research fails to show the level of safening effect of Gramoxone® INTEON® formulations over conventional Gramoxone® formulations that was previously expected. Have you misled regulatory authorities on Gramoxone® INTEON® with premature promises?

No, we did not. Syngenta has always been completely transparent with regard to the working hypothesis and the data supporting it. We have shared with regulators progress and results of this project and we continue with this open approach with the current update of regulators on the INTEON® technology.

23. Was the development of Gramoxone® INTEON® driven by your own doubts about the safety of conventional Gramoxone®?

No. Gramoxone® has been used safely and effectively for more than 40 years, particularly after Syngenta included an emetic, a blue dye and an alerting agent into the formulation. Gramoxone® INTEON® was designed as a further enhancement to this product. It was intended to set a higher industry standard for the protection of those who accidentally or deliberately ingest the product while offering the same effective broad-spectrum weed control as the traditional Gramoxone® formulation.

24. Your communication says that the dose-response for conventional Gramoxone® formulations is not linear. What does this mean?

Acute oral toxicity of a product typically increases in a more or less linear way with increasing dosage. Gramoxone® was discovered to be different: signs of toxicity are variable over a wide range of doses making it difficult to draw comparisons between formulations. Latest research indicates that this non-linear dose response may be a reflection of the co-administration of increasing doses of both paraquat and emetic; the former delivering increased exposure to a toxic substance and the latter delivering an increased reduction of this exposure although this is still a hypothesis at this time.

25. Will you do further studies to clarify the contribution of individual components in the safening of the INTEON® technology over conventional Gramoxone®?

In view of the less striking safening effect of the combined components of the INTEON® technology it is unlikely that Syngenta will attempt to characterize the impact of each individual component (alginate, increased emetic content and purgative). Instead we will focus efforts on assessing our options in relation to delivery of the safening achieved with Gramoxone® INTEON®.

26. Is there only one Gramoxone® INTEON® or are there variants of this product?

The brand Gramoxone® INTEON® applies to a number of products of different strength, depending on market needs. The concentration of the active ingredient paraquat varies from 135 g/l to 240 g/l.

27. Where is Gramoxone® INTEON® registered and sold?

Gramoxone® INTEON® is registered and sold in the U.S.A., South Korea, Sri Lanka, and the Pacific Islands. In addition we have registrations for Gramoxone® INTEON® in New Zealand, Mexico, Belize, Dominican Republic, El Salvador, Guatemala, Nicaragua, Panama and Cameroon. In this group of countries we have not started marketing the product.

28. In Gramoxone® INTEON® you increased the dose of the emetic compared to conventional Gramoxone®. Does this mean you knew that a higher dose would offer a safening effect by itself?

The design of Gramoxone® INTEON® was based on the hypothesis of a combined effect of the gelling alginate under acidic conditions slowing the release of paraquat and the more effective vomiting as a result of the increased dose of the emetic.

29. Sri Lankan and South Korean authorities have requested the dilution of paraquat-based products to reduce the number of fatalities after deliberate ingestions. How does the safening of dilution compare with the safening of Gramoxone® INTEON®?

Syngenta has no data enabling a direct comparison to be made of conventional Gramoxone®, diluted conventional Gramoxone® and Gramoxone® INTEON® and is therefore unable to answer this question based on the available facts.

30. Is Gramoxone® INTEON® Syngenta's way of preventing generic competition?

No. Syngenta hoped to set a new industry safety standard with Gramoxone® INTEON® for all paraquat-based products, and believed that it would offer growers a better product. To develop innovative products such as INTEON is simply good business.

31. In South Korea Gramoxone® INTEON® is less stringently classified compared to conventional Gramoxone®. Why could South Korean regulators come to such a decision when a proper scientific evaluation of Gramoxone® INTEON® was not available at the time the decision was taken?

Gramoxone® is a highly important product in South Korean agriculture, particularly appreciated by producers of vegetables and several other crops. Together with regulators in South Korea Syngenta has been committed to come up with a safer formulation of this important tool for agricultural production in their country and one that would also help address the problem of misuse of the product. Although Gramoxone® INTEON® does not fully meet the original level of expectations with regard to safening effects, the independent Sri Lankan survey demonstrated measurable improvements with regard to the chance of survival after misuse by deliberate ingestion of paraquat containing products. This result fully justifies the decision of South Korean regulators to register Gramoxone® INTEON®.

Basel, 17th April 2008

Questions and Answers on the INTEON® **technology**

Q&A's relevant in contacts with regulators

32. Will you continue with the Sri Lanka survey phase 2?

At this time phase 2 of the Gramoxone® INTEON® survey in Sri Lanka continues but we are concerned that latest regulatory decisions in Sri Lanka may prevent completion. Data which has been collected over many months will be of limited value should proper completion of the survey prove impossible.

33. Will you do further studies to clarify the contribution of individual components in the safening of the INTEON® technology over conventional Gramoxone®?

In view of an approximately two-fold reduction in toxicity of the combined components of the INTEON® technology (alginate, increased content of emetic, purgative) Syngenta has no plans at this time to characterize the impact of each of them individually.

34. Do you have alternatives to Gramoxone® INTEON® which offer similar safening effects?

Over recent years we have focused our development efforts fully on Gramoxone® INTEON®. Because we have not achieved our primary goal of a high safening over conventional Gramoxone® we are assessing our options with respect to the offering of an equivalent level of safening to that which we have achieved with Gramoxone® INTEON®. It will take a few more weeks to complete this assessment.

35. Is this new data the reason why Sri Lanka took regulatory actions in November 2007?

Regulatory actions in Sri Lanka have been taken in relation to a number of products, paraquat is just one of them. Decisions were made before the latest data on Gramoxone® INTEON® became available, which means the decision on paraquat is unrelated to these new data.

36. In the light of these new data is Syngenta going to continue to market Gramoxone® INTEON® ?

The independent study in Sri Lanka demonstrates a benefit of Gramoxone® INTEON® over conventional Gramoxone® primarily after misuse by deliberate ingestion. It appears that within the sample population up to 30 lives may have been saved in the year following the introduction of the new formulation. This would indicate a measurable improvement towards reducing fatalities after deliberate

ingestion of paraquat based products. Syngenta is assessing its options with respect to the delivery of this benefit through its product offer.

37. In the light of these new data is Syngenta going to continue with Gramoxone® INTEON® registrations anywhere. If yes, where and why?

Registrations for Gramoxone® INTEON® have been received in a number of countries, among them South Korea and the USA. We expect to continue with these products while we discuss with regulatory authorities and assess our options in relation to offering the safening achieved with Gramoxone® INTEON®.

38. Is the concentration of emetic in current conventional products effective?

Historical data in dogs demonstrate a safening effect of an emetic added to a paraquat-based formulation compared to a non-emeticized paraquat-based product.

39. What is Syngenta's understanding of the importance of built in wetter in the formulation with respect to its inherent toxicity?

Wetted and unwetted products have never been tested in dogs side-by-side, therefore an answer to this point is not possible.

40. Is a two-fold reduction in toxicity going to make an impact on accidental ingestion scenarios?

Syngenta does not have the data to come to a final conclusion on the impact of Gramoxone® INTEON® over conventional Gramoxone® in accidental ingestion scenarios. However, the Sri Lanka survey shows a reduction in fatalities after primarily deliberate ingestions. This result provides a strong indication for similar positive effects after accidental ingestion.

41. Is a two-fold reduction in toxicity going to make an impact on deliberate ingestion scenarios?

The independent study in Sri Lanka demonstrates a benefit of Gramoxone® INTEON® over conventional Gramoxone® after primarily deliberate ingestion. It appears that within the sample population up to 30 lives may have been saved in the year following the introduction of the new formulation. This would indicate a measurable improvement towards reducing fatalities after deliberate ingestions of paraquat based products.

42. Does Syngenta have further dog studies ongoing at this time? If so, what is the objective of these studies?

Syngenta has no further dog studies on Gramoxone® or Gramoxone® INTEON® ongoing at this time. The company has decided to update regulators on latest data before making decisions on any further studies.

43. Does Syngenta know the results of the observational monitoring survey in Sri Lanka (phase 2)?

The Sri Lanka survey phase 2 on Gramoxone® INTEON® is incomplete. Therefore we are not yet in a position to draw conclusions. Latest regulatory decisions in the country may prevent completion of the study and without proper completion it will be of limited value.

44. Has Syngenta completed any observational monitoring survey following introduction of Gramoxone® INTEON® and is there evidence that the proposed safening is effective?

Phase 1 of the independent survey in Sri Lanka is the only piece of research that has been completed and published very recently in the peer-reviewed online journal PLoS Medicine. Two more surveys are still running at this time, one of them is phase 2 of the Sri Lanka survey and we are concerned that latest regulatory decisions in Sri Lanka may prevent completion. The second survey still in progress is in South Korea. It is of a different quality because Gramoxone® INTEON® and other, more diluted products are on sale in the Korean market. Unlike the survey in Sri Lanka, the Gramoxone® INTEON® sold in Korea does not contain a biomarker to enable it to be differentiated from other products. Therefore, it will be difficult to differentiate the safening effect of the INTEON technology from product dilution, which was mandated by regulators for all paraquat-based products except Gramoxone® INTEON® at the launch of the latter.

45. The safening effects of Gramoxone® INTEON® are smaller than previously expected. Will you now consider phasing out paraquat based products from the market?

With conventional Gramoxone® Syngenta has a product in the market, which has been used safely over many decades and plays an important role particularly in sustainable weed management programs. It controls glyphosate-resistant weeds and is fundamental in minimum tillage practices which help to preserve soil moisture and structure, and reduces erosion. Gramoxone® INTEON® and Gramoxone® are both safe products when used as recommended and their safety record in normal use would not point to their phase-out .

Basel, 17th April 2008

Questions and Answers
on the INTEON® **technology**

Q&A's to be used only when there are direct questions to the points addressed.

46. Why is the dog rather than the rat the correct animal model to compare toxicity of products like Gramoxone® and Gramoxone® INTEON®?

An emetic is an integral part of the products Gramoxone® INTEON® and Gramoxone®. The effectiveness of emesis can only be tested in a vomiting animal species. Dogs are such a species while mice and rats are not.

47. How did you discover that the historical data might not be relevant as a benchmark for Gramoxone® INTEON®?

During an extensive data review Syngenta realized that a previous estimate of the safening effect of Gramoxone® INTEON® was derived from comparison to non-emeticized Gramoxone® formulations. These non-emeticized formulations were therefore not appropriate references to make these estimations, which led to the decision to conduct additional studies on dogs to strengthen the supporting data for Gramoxone® INTEON®.

48. How do you justify the fact that the Sri Lanka survey was initiated when there were no confirmed animal data on the safening of Gramoxone® INTEON® over conventional Gramoxone® ?

Prior to the survey in Sri Lanka Syngenta did a detailed assessment of available data to ensure that Gramoxone® INTEON® would be as safe as or safer than conventional Gramoxone®. Only once safety was confirmed did the company apply to authorities in Sri Lanka to support the survey. At the initiation of the survey the open question was how much safer Gramoxone® INTEON® would be compared to conventional Gramoxone®.

49. Your monitoring survey in Sri Lanka shows that you had been fully aware of the high number of deliberate ingestions of Gramoxone® in that country. How could you justify the introduction of a new formulation when the withdrawal of Gramoxone® would have saved many more lives?

The INTEON ® technology was developed and introduced in Sri Lanka as one element of a much broader Syngenta stewardship program addressing pesticide users as well as other stakeholders. Among several other measures including training in safe use, a safe storage initiative was launched by Syngenta, together with international NGO's. This initiative aims at preventing deliberate ingestion of pesticides including Gramoxone® by reducing access to such products. Only by combining preventative and protective measures is there a real possibility of

reaching the goal to significantly reduce misuse by deliberate ingestion of pesticides including Gramoxone® and Gramoxone ® INTEON® and increase the rate of survival where such misuse occurs despite the preventative measures.

50. When you first introduced the emetic in Gramoxone® formulations did you test the effectiveness of more than one concentration and if so what were the results?

The introduction of the emetic PP 796 in Gramoxone® formulations dates back to 1976/77. The decision on the concentration was made based on studies with a range of dosages of PP 796 in pigs, dogs and monkeys. Additionally because PP796 was a development product in clinical testing by ICI Pharmaceutical Division, there was the possibility to also take into account data in man.

51. Why did you carry out additional studies after the submission of the Gramoxone® INTEON® registration dossier to US EPA?

US-EPA felt unable to come to a final conclusion on the safening of Gramoxone® INTEON® as compared to conventional Gramoxone®. The agency questioned in particular the benchmark formulation for Gramoxone® INTEON® and the contribution of individual components like the alginate, the emetic and purgative. During an extensive data review in response to questions from the agency Syngenta realized that the estimate of the safening effect of Gramoxone® INTEON® was derived from non-emeticized Gramoxone formulations. This discovery triggered additional studies to clarify open questions.

Basel, 17th April 2008.