



Gramoxone PLT

10 Apr 2001

Regulatory update

- Griffin
- Parkinsonism
- Switzerland
- US Dust mist filter
- Ongoing regulatory issues

syngenta

Griffin US Update

- 12th April 2001
 - Withdraw pending petition to deny
 - Submit petition to cancel (stop sale, use, removal order)
- Terpyridine analysis
 - Syngenta analysis =
two isomers at 9 and 14 ppm (submitted 2nd Feb)
 - Independent analysis Montana State University =
9.6 ppm for isomer #1 and 16.4 ppm for isomer #2
 - EPA analysis at Fort Meade Laboratory due end April

syngenta

Griffin Brazil Update

- We know their petition is at best misleading and at worst fraudulent
 - Manufacture
 - Valdorta GA USA
 - Houston TX USA
 - Triwest Manufacturing Inc. Guatemala
- We are developing a strategy about how and when to challenge to deliver best result.

syngenta

Parkinsonism

- We are being vigilant and taking the potential impact on Gramoxone seriously
 - Lewis Smith, Head of HAES in Syngenta and Ted Lock the specialist on paraquat who has been following developments with the Parkinsonism research, were both at the SOT meeting.
- Parkinsonism is the issue of the day and is likely to remain so for the foreseeable future.
 - The theme of the 19th Neurotox conference to be held in Colorado in August is "Parkinson's Disease, Environment and Genes". Again we will ensure appropriate representation from Syngenta.
 - Research into environmental causes will continue to increase as a result of the high scientific profile and the research that suggests there is not a predominantly genetic element to the condition.
 - There will also continue to be a high media interest due to newsworthy sufferers like the Pope, Mohammad Ali, Janet Reno and Michael J. Fox.

syngenta

Parkinsonism

- Presentations are essentially based on good science but lack perspective on pesticide exposure and therefore emotive for the industry
- Main drivers
 - Genuine belief that there is an opportunity to understand and cure PD through new technologies such as genomics
 - Reinforcement that environmental factors (e.g. Pesticides) are involved
 - Opportunity for research funding (available from NIEHS)
- Concerns
 - New data showing dose related neuronal cell loss in substantia nigra in C57Bl mouse following paraquat administration down to 1mg/kg IP once per week for 3 weeks
 - Claim of interactions between pesticides

syngenta

Parkinsonism

- Our strategy is under review
 - Our efforts will be to steer the focus of serious research away from paraquat which is an interesting academic model (because of its crude similarities to the Parkinsonism like agent MPTP) and on to other agents that have neurotoxicity and exposure profiles more consistent with being a potential causative or contributory agent.
 - Syngenta is forming a steering group and evaluating support for an industry wide initiative
 - We have commissioned a review paper of all the epidemiology studies investigating environmental causes for Parkinsonism including those that claimed to make an association with pesticides. Once this is completed we will evaluate options for publication and/or further studies to discredit assertions that paraquat is in any way implicated.

syngenta

Why does Syngenta not have a Gramoxone registration in its home market of Switzerland ?

- Syngenta was formed in Nov 2000 from the merger of Novartis Agribusiness (Switzerland) and Zeneca Agrochemicals (UK).
- Gramoxone came to Syngenta from the UK based legacy company.
- Gramoxone is registered in the UK, USA and China where it is manufactured.
- The commercial opportunity in Switzerland has always been small.
- In 1990 the registration was not renewed.
- Paraquat is an agricultural herbicide and is among the most widely registered pesticides in the world. It is registered and/or sold in over 120 countries including all the major agricultural markets with the most demanding regulatory systems such as Canada, Australia, USA, Japan, UK, France, Germany, Brazil and the Netherlands.

syngenta

Worldwide paraquat registrations

Algeria	Costa Rica	Guyana	Macedonia	Paraguay	Sudan
Angola	Croatia	Haiti	Madagascar	Peru	Surinam
Antigua	Cuba	Holland	Malawi	Philippines	Swaziland
Argentina	Czech Republic	Honduras	Malaysia	Portugal	Taiwan
Australia	Dominica	Hong Kong	Mali	Puerto Rico	Tanzania
Bahrain	Dominican Republic	India	Malta	Romania	Thailand
Bangladesh	Ecuador	Indonesia	Mauritius	Rwanda	Togo
Barbados	Egypt	Iran	Mexico	Sao Tome	Trinidad
Belgium	El Salvador	Iraq	Montserrat	St Kitts	Turkey
Belize	Ethiopia	Ireland	Morocco	St Lucia	Uganda
Bolivia	Fiji	Israel	Mozambique	St Vincent	United Kingdom
Botswana	France	Italy	Myanmar	Senegal	USA
Brazil	Gabon	Ivory Coast	Namibia	Sierra Leone	Uruguay
Burkina Faso	Gambia	Jamaica	New Zealand	Singapore	Venezuela
Burundi	Germany	Japan	Nicaragua	Slovakia	Vietnam
Cameroons	Ghana	Jordan	Nigeria	Somalia	Yemen
Canada	Greece	Korea	Oman	South Africa	Yugoslavian Federation
Chile	Grenada	Kenya	Pakistan	South Korea	Zaire
China	Guatemala	Lebanon	Panama	Spain	Zambia
Colombia	Guinea	Liberia	Papua New Guinea	Sri Lanka	Zimbabwe

syngenta

Regulatory options

- 1 Maintain and explain current status
- 2 Pursue a Swiss registration but don't sell
- 3 Pursue a Swiss registration and sell
 - Option 1 is considered to be sustainable from a regulatory perspective (feedback AP and LATAM)
 - Option 2 is considered to deliver no significant additional benefit and could be seen as under hand
 - Option 3 is considered to present serious risks. The market and hence benefits case in Switzerland is small. Our experience is that registrations in these situations are difficult to maintain. A ban would present a serious threat.

syngenta

US requirement for dust mist filter

– Californian requirement

- Challenged
- Accept no inhalation exposure
- Want filter because of nose bleeds



– Now request to put on Federal label

- Assessing impact in US and ROW

– Developing strategy

- Understanding and challenge at Federal level
- Contraindicated (encourages hand to face contact, addressing poor spray practice with PPE)
- Following up on incidents data
- Do not challenge further with CDPR at this time and instead accept a separate label run

syngenta

Ongoing regulatory activities

- Regulatory workshop for Gramoxone (Bipyridyls)
 - AP and LATAM successfully completed
 - US / NAFTA tentatively w/c 21st May
 - EU / EAME tentatively June
- Regulatory Development Team meeting (RDT)
 - Tentatively w/c 11th June
 - HAES / Global and regional regulatory group to develop Gramoxone techno/regulatory strategy and options
- Following up on erroneous internet sites
 - Extoxnet
 - IRIS database

syngenta

Ongoing regulatory activities

- Validating / developing alerting agent regulatory requirements and strategy options
 - Nationally (India specifically)
- Developing TG formulation strategy
 - Test market opportunity
 - How to manage
- Supporting preparation of 2nd edition of Gramoxone enquiry guide
- Revision of Green book (IPCS H & S Guide No 51)
 - Evaluate how to facilitate, timing, how to manage risks

syngenta

Ongoing regulatory activities

- Audit of registration, classification and labelling position
 - LATAM
 - Registered in all countries
 - all yellow band (except Colombia strategy in place)
 - AP
 - more varied classification situation
 - Developing strategies to address variance
- Follow up activities in various territories
 - Mauritius, W Samoa, Taiwan, Korea, Vietnam, Chile

syngenta