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**From:** Clapp Mike GBAP  
**Sent:** 28 January 2003 09:47  
**To:** Su Tiffany TWTP; Gampp Harald CHBS  
**Cc:** Osten Hans-Dieter CNHK; Wheals Ian CHBS; Streit Luc THBK; Sheldon Ros GBAP; Hsu Wesley TWTP; Hsu Eric TWTP  
**Subject:** RE: FAO Spec. of PQT

Tiffany,  
Please find attached a summary of the emetic data which was used to support EU re-registration which I think will cover the data you require. Let me know if you wish to discuss.  
Regards, Mike



Extract from EU  
submission MII...

-----Original Message-----

**From:** Su Tiffany TWTP  
**Sent:** 28 January 2003 01:44  
**To:** Clapp Mike GBAP; Gampp Harald CHBS  
**Cc:** Osten Hans-Dieter CNHK; Wheals Ian CHBS; Streit Luc THBK; Sheldon Ros GBAP; Hsu Wesley TWTP; Hsu Eric TWTP  
**Subject:** RE: FAO Spec. of PQT

Dear Mike,

Thanks for the information.

The authority is asking local manufacturer to offer related information on Antimony potassium tartrate, meanwhile, we are requested to submit the same data of PP 796, especially its effect on gastrointestinal, its acting via brain, its absorbance compared to PQT, lasting effect of vomiting( it'd be better not longer than 2 hours) and its toxicity data(such as acute toxicity).

Thanks and best regards,

Tiffany

-----Original Message-----

**From:** Clapp Mike GBAP  
**Sent:** Monday, January 27, 2003 7:37 PM  
**To:** Su Tiffany TWTP; Gampp Harald CHBS  
**Cc:** Osten Hans-Dieter CNHK; Wheals Ian CHBS; Streit Luc THBK; Sheldon Ros GBAP  
**Subject:** RE: FAO Spec. of PQT

Tiffany,

You raised the question of the use of Antimony Sodium tartrate as an alternative emetic in gramoxone formulations. The notes below indicate that this would not be viable.

Antimony salts (e.g. antimony potassium tartrate) have been used for centuries as medicinals, to induce emesis and treat other conditions, however over the last century there has been concern over antimony

toxicity and therefore they are no longer the choice of modern day medics and have been superseded by other better products.

Absorption from the gastrointestinal tract is relatively low and it is unlikely to be acting centrally via the brain as is the case with PP796. More likely to be acting locally. In addition the dose needed to cause emesis appears to be high stated as 33mg/kg antimony potassium tartrate; at least an order of magnitude higher than with PP796. It should also be noted that there appears to be little data specifically on Antimony sodium tartrate, although it was shown to have some genotoxicity in vitro (induced chromosomal aberrations in cultured human leukocytes and lymphocytes).

Hence it would not appear to be a viable alternative to PP796. Further specific tests would be needed to demonstrate its effectiveness and safety if this were to be considered further.

Regards, Mike

Dr M.J.L.Clapp  
Health Assessment lead for NSH.

-----Original Message-----

**From:** Gampp Harald CHBS  
**Sent:** 22 January 2003 08:24  
**To:** Clapp Mike GBAP; Sheldon Ros GBAP  
**Subject:** FW: FAO Spec. of PQT

Mike and/or Ros,  
Can you please answer to Tiffany's question.

Best regards,  
Harald

-----Original Message-----

**From:** Gampp Harald CHBS  
**Sent:** Mittwoch, 22. Januar 2003 09:09  
**To:** Su Tiffany TWTP  
**Cc:** Osten Hans-Dieter CNHK; Wheals Ian CHBS; Streit Luc THBK  
**Subject:** RE: FAO Spec. of PQT

Dear Tiffany,

Antimony Sodium tartrate is a well known chemical (a salt of tartraic acid). It is also known that it is an emetic. However, I cannot tell you whether or not this emetic works in the case of paraquat. It could easily be that by the time it works, paraquat has already entered the system. Therefore, I leave that to the tox specialists.

Here's the MSDS of the emetic in Gramoxone:

<< File: emetic.pdf >>

-----Original Message-----

**From:** Su Tiffany TWTP  
**Sent:** Mittwoch, 22. Januar 2003 02:35  
**To:** Gampp Harald CHBS  
**Cc:** Osten Hans-Dieter CNHK; Wheals Ian CHBS; Streit Luc THBK  
**Subject:** RE: FAO Spec. of PQT

Dear Harald,

Appreciate for your response and comments on this matter.

Thanks and best regards,

Tiffany

-----Original Message-----

**From:** Streit Luc THBK  
**Sent:** Monday, January 20, 2003 6:48 PM  
**To:** Su Tiffany TWTP; Gampp Harald CHBS  
**Cc:** Osten Hans-Dieter CNHK; Wheals Ian CHBS  
**Subject:** RE: FAO Spec. of PQT

Tiffany and Harald,

I do not have any data on this, nor was I able to check antimony potassium tartrate in the Merck index (access problems).

We therefore rely entirely on Harald's help.

Many thanks and best regards

Luc

-----Original Message-----

**From:** Su Tiffany TWTP  
**Sent:** 20 January 2003 17:03  
**To:** Wheals Ian CHBS; Streit Luc THBK  
**Cc:** Gampp Harald CHBS; Osten Hans-Dieter CNHK  
**Subject:** RE: FAO Spec. of PQT  
**Importance:** High

Dear Ian, dear Luc,

Regarding the emetic in PQT specification, we were requested by our authority to offer them the toxicological data (acute toxicity), MSDS and physical-chemical property data of PP 796, and the characters of PP 796 why makes it fit to be the emetic of PQT.

Meanwhile, the local formulators have proposed " antimony potassium tartarate " as another choice for emetic of PQT. They've claimed the chemical is very safe and useful as emetic. Do you have any idea what it is?

Thanks for a quick response at your earliest convenience.

Best regards,  
Tiffany

-----Original Message-----

**From:** Wheals Ian CHBS  
**Sent:** Saturday, November 09, 2002 1:05 AM  
**To:** Streit Luc THBK; Su Tiffany TWTP  
**Cc:** Gampp Harald CHBS  
**Subject:** RE: FAO Spec. of PQT

Tiffany / Luc,

I support the proposal by the Taiwanese authorities regarding the specification for paraquat products. I have a few comments and suggestions.

Their proposal is consistent with the existing FAO specification for paraquat

The existing FAO specification for paraquat does not mention PP796 by name. So I am pleased to hear that the Taiwanese authorities intend to name PP796 as the example even if they do not exclusively insist on PP796.

Regarding alternative emetics Syngenta's position is that PP796 is the only emetic to have been demonstrated to meet the FAO specification's effective emetic criteria.

Recently Syngenta made a submission to FAO requesting that a new FAO specification for paraquat be established according to new FAO procedure that was adopted in January 1999 and is now jointly operated by FAO and WHO.

I attach the new specifications that Syngenta have proposed for your information.

Technical :

<< File: 2nd Draft Paraquat TK spec 2002.doc >>

Liquid formulations :

<< File: Paraquat FAO SL specification\_draft4revision 1.doc >>

Solid formulations :

<< File: PQ SG\_draft specification\_draft5.doc >>

As well as an e-mail outlining the background

<< Message: Generic paraquat - FAO specifications >>

Syngenta's submission is now being reviewed by an expert nominated by FAO, Alan Hanks in the USA. Roger Parker is a consultant to Syngenta who has been asked to manage the interactions with Alan Hanks and FAO for this project. We hope the proposed new specifications will be adopted at the June 2003 FAO meeting.

The key points in addition to those in the old FAO specification are.

- Naming the emetic  
PP 796: 2-amino-4,5-dihydro-6-methyl-4-propyl-s-triazole-(1,5a)pyrimidin-5-one  
An effective emetic must be included. No compound, other than PP796 has been found to be effective in meeting the following criteria:
- Setting a minimum level for the emetic  
Not less than 0.8 g/l (for technical material)  
Not less than 0.4 g/l (for liquid products)  
Not less than 0.3 g/kg (for solid products)
- Inclusion of terpyridyls as a relevant impurity  
Total terpyridyls Maximum: 1.0ppm (0.0001%w/w)

If you have any questions please get back to Harald who will try to provide any further support you need.

Kind regards,

Ian

-----Original Message-----

**From:** Streit Luc THBK  
**Sent:** Donnerstag, 7. November 2002 08:03  
**To:** Wheals Ian CHBS  
**Subject:** FW: FAO Spec. of PQT

Ian,  
Any comments? I'll try to call you.  
Luc

-----Original Message-----

**From:** Su Tiffany TWTP  
**Sent:** Thursday, November 07, 2002 1:57 PM  
**To:** Streit Luc THBK  
**Cc:** Hsu Wesley TWTP; Valmayor Jose THBK  
**Subject:** RE: FAO Spec. of PQT

Dear Luc,

Our authority has proposed spec. of PQT tech. to the industries, and ask for comments before they make the final decision.

Details of the proposal regarding emetic is below:

\* The registrants have to declare the content of emetic (but not necessarily to be 0.1% like Syngenta's spec., the nominal range is +/- 15%.

\*\* The requirements for emetic are:

1. Faster absorbance than PQT, and may induce >50% of patients vomit within 30 minutes.
2. The vomiting effect lasts for only 2~3 hours, to facilitate further treatment.
3. Effect on the vomiting control center in brain.
4. No irritation to stomach and intestine to avoid increasing poisoning of PQT.
5. No toxic risk, short shelf life.
6. Compatible with PQT, stable, and has no controversy effect on PQT field efficacy.

The authority has give PP 796 as the registered example, but it's not mandatory that the emetic has to be PP796.

Do you know any other chemicals except PP796 could meet the requirements? If no, any supporting report will help us to offer to our authority and advise them to put PP796 in the spec. of PQT.

Your fast response is highly appreciated, cause the deadline to react to our authority is end of this December.

Thanks and best regards,

Tiffany

-----Original Message-----

**From:** Streit Luc THBK  
**Sent:** Wednesday, November 06, 2002 12:50 PM  
**To:** Su Tiffany TWTP  
**Cc:** Hsu Wesley TWTP; Valmayor Jose THBK  
**Subject:** RE: FAO Spec. of PQT

Dear Tiffany,

We still do not have the proposed FAO specs in hand. I'll follow up with Ian.  
Luc

-----Original Message-----

**From:** Su Tiffany TWTP

**Sent:** Monday, November 04, 2002 5:32 PM  
**To:** Valmayor Jose THBK; Streit Luc THBK  
**Cc:** Hsu Wesley TWTP  
**Subject:** RE: FAO Spec. of PQT

Dear Jose, dear Luc,

We are going to pay a visit to our authority to discuss about PQT spec., would it be ok that we give to them the spec. that is going to be proposed to FAO next year to our authority.

Could you please send to us the proposed spec. first.

Your comments and quick response are highly appreciated,

Thanks and best regards,

Tiffany

-----Original Message-----

**From:** Su Tiffany TWTP  
**Sent:** Wednesday, October 23, 2002 7:07 PM  
**To:** Streit Luc THBK  
**Cc:** Valmayor Jose THBK; Hsu Wesley TWTP  
**Subject:** FAO Spec. of PQT

Dear Luc,

Our authority has proposed a specification on PQT based on the current FAO guideline, i.e.:

1. Range of emetic: +/- 15%.
2. No specially asking that emetic has to be PP796, but the MSDS of emetic is a must.
3. The % of emetic and which kind of emetic has to be put on the commercialized label.

However, since the proposal is yet to be discussed, could you please send me the specification that we are going to propose to FAO next year, which may could be a very useful reference to our authority.

Thanks and best regards,

*Tiffany Su*

Syngenta Taiwan Co.,Ltd.  
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Taipei 103, Taiwan

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