

Application EFSA-GMO-NL-2008-51 (GHB614 Cotton)			Annex G	
Comments and opinions submitted by Member States during the three-months consultation period				
Country	Organisation	Reference	Comment	EFSA GMO Panel response
Comments from National Competent Authorities under Regulation (EC) No 1829/2003				
Austria	Ministry of Health, Family and Youth	General comments	Detection method According to the CRL-Homepage (http://gmo-crl.jrc.it/statusofdoss.htm), the Validation process is currently under step 2. Therefore it has to be stated that before the validation process is not completed, no approval to the placing of the market of this product should be given.	Outside the remit of the GMO Panel.
Austria	Ministry of Health, Family and Youth	D, 07.02 Field trials	Field trials were performed at 17 locations in 2004 and 2005. The conclusion drawn from these trials, that "The few differences observed were regional differences and not consistent across all locations and the overall performance of GHB614 was equal to or better than that of the non-transgenic counterpart" are not understandable. The yields of the GM-cotton were significantly lower in 7 comparisons and not significantly lower in most of the cases. Therefore the interpretation of the data is highly questionable.	The GMO Panel noted that differences were observed in some instances with regard to several characteristics related to yield, lint percentage, and reproduction. However, these differences did not occur consistently in the various studies and, therefore, were not considered to be related to the genetic modification.

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Austria	Ministry of Health, Family and Youth	D, 07.03 Selection of compounds for analysis	There were statistically significant differences in fatty acid contents[Dr. R. Oberdörfer: Nutritional Impact Assessment Report on Glyphosate Tolerant Cotton transformation Event GHB614; 2007] , indicating lower values for the GM variant. Comparing the fatty acid contents of different plant parts the following differences can be observed in the GM variant: <ul style="list-style-type: none"> • less fat %dm in whole linted cotton seed (Tabl. 5.9.1) • sign. less fat%dm in linters (Tabl. 5.10.1) • sign. more fat%dm in hulls, even outside the reference ranges (Tabl. 5.11.1) These results indicate a change in the fatty acid metabolism of the GM plant.	The GMO Panel has primarily assessed the compositional data derived from the raw agricultural commodity. The observed differences between the fatty acid compositions of cotton GHB614 and the non-GM comparator were extremely small and therefore not considered biologically and nutritionally relevant. The Panel concluded that cotton GHB614 was compositionally and also agronomically equivalent to conventional cotton, except for the introduced transgenic trait. The GMO Panel had no reason to assume that the characteristics of cotton GHB614 and derived processed products would be different from those of the respective products derived from conventional cotton. The compositional data available for processed products do not indicate nutritionally relevant differences. Fat is not considered nutritionally relevant in linters and hulls and represents a residue of the technological process.

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Austria	Ministry of Health, Family and Youth	D, 07.08 Toxicology	<p>Oral toxicity studies The oral toxicity study was performed with 5 female mice per group with the E.coli produced mEPSPS. The number of test animals was very low and both sexes should be included. Furthermore the test substance should be obtained from the GM plant. Therefore these studies can not be regarded as state of the art. Whole feed conversion studies A 42 day broiler feeding study with toasted cottonseed meal derived from GHB614 Cotton, its non-transgenic counterpart and commercial non-GM varieties was conducted. The control variety is designated as "Non-transgenic "near isogenic" variety". Thus it could be the parental line or any breeding tree derived line. This is important since potential pleiotropic effects are only excluded when the parental plant, into which the gene cassette has been inserted, is used for the comparison. Therefore clarification is needed. Additionally it has to be stated that no toxicologically relevant studies were performed by the notifier which can not be regarded as state of the art.</p>	<p>Although the GMO Panel does not advocate this type of study, an acute oral toxicity study using the protein 2mEPSPS was provided. This study was conducted in accordance with the OECD Guideline 425. Female animals are normally used in this study since experience has shown that usually there is little difference in sensitivity between sexes, but in those cases where differences are observed, females are generally slightly more sensitive.</p> <p>Comparison of the 2mEPSPS protein produced in <i>E. coli</i> with the protein expressed in GM cotton GHB614 has shown the structural and functional equivalence of these proteins. Thus the GMO Panel has accepted the microbial protein as a suitable substitute for the plant protein to be used in the safety studies (see section 4.2.3.1 in the scientific opinion).</p> <p>On request of the GMO Panel the applicant indicated that Coker312 was used as the non-GM counterpart in the 42-day broiler feeding study.</p> <p>With regards to the toxicological assessment it is referred to Section 4 of the scientific opinion.</p>

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Austria	Ministry of Health, Family and Youth	D, 07.09 Allergenicity	In Part 1 Techn. Dossier p. 88 it is stated that "The in silico approach enabled the search of the potential N-glycosylation sites often found on allergens. The results showed that such sites of potential post-translational glycosylations were not found on the 2mEPSPS protein (Rouquié, 2006e)." But the cited study of Rouquié (2006e) points out that "Two potential N-glycosylation sites were identified on the amino acid sequence of the 2mEPSPS protein. Only an experimental approach could confirm an effective N-glycosylation on the protein." These two statements seem contradictory and clarification is needed.	The GMO Panel agrees that these two statements are contradictory. Rouquié (2006) identified two potential glycosylation sites in the amino acid sequence of the 2mEPSPS protein. However, a glycosylation study using SDS-PAGE followed by glycoprotein staining was provided (Currier and Hendricks, 2007), which indicated no glycosylation of the E. coli and the plant 2mEPSPS proteins. [Regarding the faint signals corresponding to the proteins 2mEPSPS from GHB614 cotton, 2mEPSPS produced by E. coli (which is not expected to be glycosylated), phosphorylase B and carbonic anhydrase (the negative controls) in relation to the very strong signals corresponding to the positive controls alpha1-acidic glycoprotein and avidin, the GMO Panel agrees with the conclusion drawn by the authors.
Belgium	Belgian Biosafety Advisory Council	General comments	Useful references supporting some of the comments made by the Belgian Biosafety Advisory Council (Belgium) Aelvoet J., Freyssinnet M. (2007). GLY TOL cotton : assessment of pollen flow under European conditions, Catalonia, 2006. (Bayer CropScience) Freyssinnet M., Trolinder-Wright (2006). Agronomic performance of glyphosate tolerant cotton based upon transformation event GHB614. 2004-2005 USA production seasons. (Bayer CropScience). Hofs JL et al (2006). Conséquences écologiques et agro-économiques de l'introduction de cotonniers transgéniques dans un agrosystème tropical: le cas du coton Bt chez les petits paysans des Makhathini Flats (Afrique du Sud). In : Premier séminaire de	Relevant references have been included in the scientific opinion of the GMO Panel.

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			<p>restitution du programme ANR-OGM, 14&15 décembre 2006. Paris : ANR. 81-84. Hofs J.-L., Klein E., Pierre J., Chèvre A.M., Hau B. (2007). GM cotton gene flow in small-scale farming systems : Probable impact on organic cotton production in Africa. Third International Conference on Coexistence between GM and non-GM based Agricultural Supply Chains. Seville (Spain), 20-21 November 2007. JRC and IPTS. Stein A.J. and Rodriguez-Cerezo E. (Eds), 87-90. Lançon J., Klassou C. (1988). Mise au point sur graines de coton (<i>Gossypium hirsutum</i> L.) d'une méthode de germination en laboratoire. <i>Cot.Fib.Trop.</i> 43 (4) :311-317. Lavigne C., Klein E.K., Vallée P., Pierre J., Godelle B., Renard M. (1998). A pollen-dispersal experiment with transgenic oilseed rape. Estimation of the average pollen dispersal of an individual plant within a field. <i>Theor. Appl. Genet.</i> 96:886-896. Van Deynze A.E., Sundstrom F.J., Bradford K.J. (2005). Pollen-mediated gene flow in California Cotton depends on pollinator activity. <i>Crop Sci.</i> 45: 1565-1570.</p>	
Belgium	Belgian Biosafety Advisory Council	A. General information	If cottonseed are used mainly for making oil, should the scope of the application not also be "Food produced from GM plants or containing ingredients produced from GM plants", in addition to "GM plant for food use".	This issue has been considered in the scientific opinion.

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Belgium	Belgian Biosafety Advisory Council	B. Information relating to (a) the recipient or (b) parental plants	In Table 1 under paragraph 5 (geographical distribution and cultivation of the plant), the area harvested in China is somewhat lower but almost similar to the area harvested in USA; however the quantity produced in metric tons is unusually high (11400.00 in 1000 metric tons): is this figure correct ?	Outside the remit of the GMO Panel.
Belgium	Belgian Biosafety Advisory Council	B. Information relating to (a) the recipient or (b) parental plants	B3. Survivability: In mild and dry winter conditions the existence of feral perennial populations of <i>G. hirsutum</i> along roadsides is highly probable (Hofs et al. 2006; Hofs et al., 2007). Their persistence depends on the national or regional infrastructure maintenance policy; which is highly variable in Southern Europe.	The GMO Panel is aware that, due to the physical characteristics of cotton seeds and methods of transportation, accidental spillage is unavoidable. Therefore, the GMO Panel recommends that, within general surveillance, specific measures are introduced to actively monitor the occurrence of feral cotton plants in areas where seed spillage is likely to occur. In addition, the applicant noted that cotton GHB614 will be imported as mostly non-viable seed. Therefore, the likelihood that some imported seed could escape and germinate is very low. Please note that in relation to the monitoring plan, the GMO Panel gives its opinion on the scientific quality of post-market environmental monitoring (PMEM) activities proposed by applicants. The definitive and final endorsement of PMEM activities is under the responsibility of risk managers.
Belgium	Belgian Biosafety Advisory Council	B. Information relating to (a) the recipient or (b) parental	Under "3. Survivability – Ability to form structures for survival or dormancy" it is mentioned that "Cultivated cotton does not produce seeds which can persist in the environment for long periods of time, furthermore cotton seed lacks the ability to develop dormancy." Our question is : are there	In line with the observations made by Eastick and Hearnden (2006), the GMO Panel has concluded that the seed-mediated establishment of cotton and its survival outside of cultivation in Europe is mainly limited by a combination of absence of a dormancy phase, low competitiveness, and susceptibility to diseases and cold climate conditions. Adequate soil moisture is an additional factor affecting the survival of feral cotton

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		plants	data available to prove this?	seedlings. Since general characteristics of cotton GHB614 are unchanged relative to its conventional counterpart, the inserted herbicide tolerance trait is not likely to provide a selective advantage outside of cultivation in Europe. Moreover, data presented in the application gathered over a series of field trials across the US in 2004 and 2005 indicate that cotton GHB614 has no altered reproductive, dissemination or survivability characteristics compared to its conventional counterpart. In addition to the data presented by the applicant, the GMO Panel is not aware of any scientific report of increased fecundity, persistence (volunteerism) or ferality of GM cotton in regions where it is cultivated. Hence, there is no information to indicate change in survival capacity (including over-wintering). Furthermore, there is no evidence that the herbicide tolerance trait introduced by the genetic modification results in increased persistence and invasiveness of any crop species, except in the presence of glyphosate-based herbicides. Thus escaped plants and genes dispersed to other cotton plants would result in plant populations no different from existing populations and would not create additional agronomic or environmental impacts. In addition, the applicant states that cotton GHB614 will be imported as mostly non-viable seed. Therefore, the likelihood that some imported seed could escape and germinate is very low.

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Belgium	Belgian Biosafety Advisory Council	D, 05 Genetic stability of the insert and phenotypic stability of the GM plant	The presented results confirm the phenotypic and genetic stability of the GM plant. The segregation analysis statistically shows no difference with theoretical segregation ratio of BC2F1. Nevertheless, I am a little worried about this 2/3 R and 1/3 S ratio: couldn't the sample size be bigger? It should be discussed in the application.	Table 12 gives the results of the χ -square goodness-of-fit test of the segregation results. This statistical test validates the conclusions and takes into account sample size.
Belgium	Belgian Biosafety Advisory Council	D, 06 Any change to the ability of the GM plant to transfer genetic material to...	The dispersal trial set-up (Aelvoet & Freyssinnet, 2007) is not accurate enough to detect the "real" impact of pollen dispersal. The "pollen captors" (pollen receiving plants) were harvested only according four directions (SW, NW, SE, NE). To maximize detection, it should have been performed under a 12 x 12 grid experiment set-up, with one plant (pollen captor) at each nod of the grid (see example in Lavigne et al., 1998). Results reported in Van Deynze et al. (2005) are certainly more reliable.	The scope of application EFSA-GMO-NL-2008-51 includes import and processing for food/feed uses of cotton GHB614. Considering the proposed uses of cotton GHB614, excluding cultivation purposes, the environmental risk assessment is concerned with indirect exposure through manure and faeces from gastrointestinal tracts mainly of animals fed on cotton GHB614 and with the unintentional release into the environment of cotton GHB614 seeds during transportation and processing. Since cotton GHB614 will be imported as mostly non-viable seed, there is only a very low probability that that feral cotton GHB614 would establish and produce pollen.
Belgium	Belgian Biosafety Advisory Council	D, 07.01 Comparative assessment	According to Oberdörfer, 2007 phytic acid is also analyzed. This is not mentioned in the technical dossier. Why has this been omitted?	The GMO Panel agrees with Belgium that phytic acid data were not given in the technical dossier. However, the data are available from the Annexes (Oberdörfer, 2007; Rattemeyer-Matschurat, 2007; Haas, 2006; Haas, 2007) and were included in the assessment made by the GMO Panel.

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Belgium	Belgian Biosafety Advisory Council	D, 07.03 Selection of compounds for analysis	All four primary products coming from cottonseed processing, namely oil, meal, hulls and linters were included in the selection of material. The sensitive aromatic amino acids were all analyzed as well as the oil composition or lipid profile. The amount of C18:2 (linoleic acid in the GHB 614 cottonseeds are slightly higher than the levels in Coker 312 cottonseeds but no explanation is given. Also the amount of cyclopropenoid fatty acid are lower in the transgenic samples, and although values are inside the references ranges reported from literature, and the lower levels from this anti-nutritional factor is rather beneficial, a bit more explanation why this is the case should be given.	The GMO Panel has assessed the compositional differences mentioned by Belgium as part of the overall comparative analysis. The mentioned differences are considered to be very small and therefore not biologically and nutritionally relevant.
Belgium	Belgian Biosafety Advisory Council	D, 07.04 Agronomic traits	Units of characteristics measurements should be included in the tables (ex: tables 29 and 30).	The GMO Panel agrees with Belgium that in general units should be given in the tables. The GMO Panel also acknowledged the fact that for reasons of simplification, parameters are explained in detail in the annex (see Freyssinet and Trolinder-Wright, 2006).
Belgium	Belgian Biosafety Advisory Council	D, 07.08 Toxicology	Please provide data based on dry weight. No range is mentioned. Please provide. A standard deviation of 0.00 for the pollen content seems to be rather small (data provided in the technical dossier). In Van der Klis and De Pestel, 2006, a SD of 0.01 is given. Please correct.	The GMO Panel is not sure about the data the comment refers to. Concerning agronomic studies, the applicant was requested by the GMO Panel to provide consistent data throughout the application.

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Belgium	Belgian Biosafety Advisory Council	D, 07.09 Allergenicity	The applicant did not evaluate the potential allergenicity of cottonseeds GHB 614, compared to their natural counterpart. The reviewer acknowledges that cottonseed allergy is not a major issue and that no major allergen of cottonseed has been described. In addition, the major destined use of cottonseed is to prepare refined oil that contain very low levels of proteins, hence with very low allergenic impact. However, because the introduction of new traits might influence the expression levels of other proteins of the host plant and because trace amounts of proteins can be found in refined oil, it is requested that the applicant evaluate the content of 2S storage protein and of vicillin, two known common and potent seed allergens, in the GHB614 cottonseed, compared with the natural counterpart.	This comment does not appear relevant to the GMO Panel since cotton is not considered to be a common allergenic food. Furthermore, the main cottonseed product in human food, cottonseed oil, is highly purified and contains negligible levels of proteins, if any. The assessment of allergenicity of the whole GM plant is addressed in section 4.2.5.2 of the scientific opinion.
Belgium	Belgian Biosafety Advisory Council	D, 10.02 Selective advantage or disadvantage	Feral populations can grow along roadsides for several years (see section B.3). Populations in Hofs et al (2006 and 2007) were all GM (RR and Bt) cultivars. Similar cases might occur in Southern Europe. Selective advantage can occur if glyphosate is used in roadside vegetation control.	The issue raised by Belgium has been considered in the scientific opinion of the GMO Panel.

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Belgium	Belgian Biosafety Advisory Council	D, 10.02 Selective advantage or disadvantage	In this chapter it is mentioned that the agronomic performance of GHB614 shows no disadvantage. Furthermore we note that "the likelihood that some escaped seed would germinate is very low because most of the imported seed is non-viable." Our question is: Is the germination power of the imported seed analysed?	Comparison of agronomic parameters with the non-GM counterpart did not reveal an increased survivability, persistence or invasiveness of cotton GHB614 in the absence of glyphosate-based herbicides. In addition, a seed germination study performed by the applicant on F ₁ seed did not show significant differences in germination rate between cotton GHB614 and its conventional counterpart, Coker 312, among tested treatments. Moreover, please note that according to the applicant, cotton GHB614 will be imported as mostly non-viable seed, in turn decreasing its probability of establishment.

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Belgium	Belgian Biosafety Advisory Council	D, 10.03 Potential for gene transfer	<p>The risk of seed spillage and seed germination with a further set-up of a feral population exists in Southern Europe. At this stage, there is no evidence that it constitutes an important risk of gene flow. It should be, however, included in a monitoring plan. Cotton doesn't need an arable surface to grow. In the case of seed spillage some seeds can germinate on the top of decomposing seeds, which act as a growth substrate (see picture in annex). When the cotton root system is developing in that cotton compost is strong enough it can pass through a harder surface (road coating). Comment related to seed germination at page 93 of the report: There is no need to treat fuzzy seeds to make it germinate. Fuzzy seeds can reach a germination rate of 80-85% and healthy seed germination rates are generally up to 60% (Lançon and Klassou, 1988). Delinted seeds do not need less moisture (or water) to start germination but need other additional moisture to achieve the process and reach the seedling stage. In contrast, in the case of fuzzy seeds, the seed doesn't germinate below a certain cumulated moisture level. If this level is attained, the germination process goes on until seedling development. It means that delinted seeds are more susceptible to drought periods during the germination process. Fuzzy seeds CAN germinate and present a risk as well.</p>	<p>The GMO Panel is aware that, due to the physical characteristics of cotton seeds and methods of transportation, accidental spillage is unavoidable. Therefore the GMO Panel recommends that, within general surveillance, specific measures are introduced to actively monitor the occurrence of feral cotton plants in areas where seed spillage is likely to occur. In addition, the applicant noted that cotton GHB614 will be imported as mostly non-viable seed. Therefore, the likelihood that some imported seed could escape and germinate is very low.</p> <p>Please note that in relation to the monitoring plan, the GMO Panel gives its opinion on the scientific quality of post-market environmental monitoring (PMEM) activities proposed by applicants. The definitive and final endorsement of PMEM activities is under the responsibility of risk managers.</p>

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Belgium	Belgian Biosafety Advisory Council	D, 10.09 Impacts of the specific cultivation, management and harvesting ...	The applicant should report on the presence of the glyphosate, their metabolites and related surfactant residues in seed products. Their (medium or long term) impacts on animal and human health should be discussed. Reference of pesticide (glyphosate) risk assessment and EU regulatory measures would be valuable.	Outside the remit of the GMO Panel.
Belgium	Belgian Biosafety Advisory Council	D, 11 Potential interactions with the abiotic environment	It is said that GHB614 varieties showed the same susceptibility as the conventional counterparts to abiotic stress (Freysinet & Trolinder-Wright, 2006). But what is the reaction of GHB614 2mEPSPS protein concentration in the plant to environmental stress? In other words, is the GHB614 cultivar less tolerant to glyphosate under abiotic stress? The 2004-2005 field experimentation was obviously not designed to answer these questions.	The GMO Panel is of the opinion that changed expression levels of mEPSPS have limited environmental concerns due to the scope of the application.
Belgium	Belgian Biosafety Advisory Council	D, 12.03 General Surveillance of the impact of the GM plant	Baselines must consider the strengthening of the control of herbicide residues in seeds and other processed products. The GS plan is not clear and there is confusion between monitoring plan and general information to the agribusiness sector. The detailed GS protocols (to detect potential unanticipated adverse effects) should be presented. These protocols are not provided through the mentioned websites (Europabio etc.).	Outside the remit of the GMO Panel.

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Finland	Board for Gene Technology	General comments	The Board for Gene Technology wants to emphasize that high quality of general surveillance plan should be taken into consideration when the plan is adopted in a specific country. The general surveillance plan should indicate that the monitoring will be carried out in an active manner.	<p>The GMO Panel comments on the scientific quality of the monitoring plan. EFSA has published guidance and scientific opinion on PMEM (EFSA, 2006a,b) following a broad consultation with stakeholder, including national competent authorities. The information supplied by the applicant is in line with this guidance.</p> <p>See section 5.2 of the PMEM opinion (EFSA, 2006b): <i>Details of the specific plans and methods of monitoring in each country should not be included in the original application. The GMO Panel advises that the application should describe the general approaches and methods that the applicant would apply in different commercialisation sites, including the type of dialogue that would be established with risk managers in each Member State. (...) Thus detailed local arrangements will be developed by the applicant after the application has been accepted (...).</i></p> <p>See section 5.2.2 of the scientific opinion.</p>

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Germany	Federal Agency for Nature Conservation (BfN)	B, 02 (b) Sexual compatibility with other cultivated or wild plant species	The dossier states that "G. hirsutum is readily cross-compatible only with other tetraploid members of the tribe Gossypium" and that "in Australia, three individual 'naturally' produced hybrid plants between G. sturtianum and a primitive G. hirsutum cultivar have been observed". Therefore, for the environmental risk assessment, it has to be considered that cultivated cotton species may hybridise with sexually compatible feral or wild species of Gossypium occurring in certain regions of Europe. This potential exists e.g. in Greece, Spain and Italy since feral or wild species of Gossypium have been reported from these countries in Southern Europe: (1) G. herbaceum is reported as having escaped from cultivation (also stated in the dossier under B.5.) and having subsequently turned into a naturalized species of several Southern European floras occurring on disturbed ground (e.g. arable land and waste land) e.g. in Greece, Italy and Spain (Zangheri 1976, Pignatti 1982, Tutin et al. 1992, Polunin 1997), (2) G. hirsutum is reported as having escaped from cultivation and having subsequently turned into a naturalized species of several Southern European floras e.g. in Greece and Italy (Zangheri 1976, Pignatti 1982, Polunin 1997). The term naturalized means that feral cotton populations live outside cultivation and do not depend on repeated input of seeds	The scope of application EFSA-GMO-NL-2008-51 includes import and processing for food/feed uses of cotton GHB614. Considering the proposed uses of cotton GHB614, excluding cultivation purposes, the environmental risk assessment is concerned with indirect exposure through manure and faeces from gastrointestinal tracts mainly of animals fed on cotton GHB614 and with the unintentional release into the environment of cotton GHB614 seeds during transportation and processing. Since cotton GHB614 will be imported as mostly non-viable seed, there is only a very low probability that that feral cotton GHB614 would establish and produce pollen.

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			<p>from cultivated cotton plants. Cultivated and feral <i>G. hirsutum</i> belong to the same species and show the same level of ploidy. <i>G. herbaceum</i> is a diploid species, but there is field evidence from Australia of the formation of triploid hybrids between <i>G. herbaceum</i> and another tetraploid species. The number of three observed triploid hybrid individuals is far too small to get a clear picture of the degree of sterility of these plants. Therefore, the applicant is requested to consider the sexual compatibility with wild and feral cotton species in Southern Europe and to revise the environmental risk assessment accordingly.</p> <p>Pignatti, S. (1982): Flora d'italia. Vol. 2. Edagricole, Bologna: p. 94. Polunin, O. (1997): Flowers of Greece and the Balkans. Oxford University Press, Oxford: p. 333. Tutin, T. G., Heywood, V. H. et al. (eds.) (1992): Flora Europaea. Vol. 2., 5th reprint. Cambridge University Press, Cambridge: p. 469. Zangheri, P. (1976): Flora Italica. CEDAM, Padova: p. 391.</p>	

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Germany	Federal Agency for Nature Conservation (BfN)	D, 07.04 Agronomic traits	We do not share the applicant's opinion that the performed agronomic trials and the compositional analysis can prove the absence of pleiotropic effects. The study by Freyssinet & Trolinder-Wright (2006) does not contain information about climate conditions during field trials or any statistical analysis for environmental interactions. Therefore the data give only insufficient evidence about gene-environment interactions, unintended or pleiotropic effects. A detailed description of the test design, the climatic conditions and the data of volunteers for GHB614 and Cocker312 in the Study "Census of Volunteers in subsequent seasons" are missing (Van Duyn, 2007). Therefore, it is not possible to evaluate these results.	<p>We are satisfied with the design of the compositional analysis. Weather conditions in the 2004 and 2005 agronomic trials were described in Freyssinet & Trolinder-Wright (2006).</p> <p>The scope of application EFSA-GMO-NL-2008-51 includes import and processing for food/feed uses of cotton GHB614. Considering the proposed uses of cotton GHB614, excluding cultivation purposes, the environmental risk assessment is concerned with indirect exposure through manure and faeces from gastrointestinal tracts mainly of animals fed on cotton GHB614 and with the unintentional release into the environment of cotton GHB614 seeds during transportation and processing. Since cotton GHB614 will be imported as mostly non-viable seed, there is only a very low probability that that feral cotton GHB614 would establish and produce pollen.</p>

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Germany	Federal Agency for Nature Conservation (BfN)	D, 07.08 Toxicology	Testing of the whole GM food/feed is crucial to obtain the necessary information about any adverse unintended effects of GHB614 cotton on human or animal health. One animal feeding study with the GMO (Stafford 2007) has been carried out. This feeding study was performed with male broiler chickens. The diets contained only 10% cotton meal. It must be stressed that chicken broiler studies are designed to test for effects on animal nutrition and are no model for toxicology. Therefore no valid toxicological study with the GHB614 cotton was carried out. The applicant should be requested to test for unintended acute and subchronic toxic effects of the GHB614 cotton by carrying out a 90 day rat study. In addition we advise to carry out supplemental studies with especially ruminants which differ with respect to their digestive system and will be substantially exposed by feed derived from processing residues of GHB614 cotton.	The comparative analysis has shown that cotton GHB614 is compositionally and agronomically equivalent to the non-GM counterpart and other conventional cotton, except for the introduced trait (see section 3.3 of the scientific opinion). Therefore, in accordance with the EFSA Guidance Document (EFSA, 2006a) additional animal safety studies or nutritional studies with livestock animals using the whole GM food/feed are not required.

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Germany	Federal Agency for Nature Conservation (BfN)	D, 07.10 Nutritional assessment of GM food/feed	We do not share the applicant's opinion that the performed agronomic trials and the compositional analysis can prove the absence of pleiotropic effects. The study by Oberdörfer (2007) do not contain information about climate conditions during field trials or any statistical analysis for environmental interactions. Therefore the data give only insufficient evidence about gene-environment interactions, unintended or pleiotropic effects. The statistic differences of Malvalic Acid, Sterculic Acid, Dihydrosterculic Acid, Pamittoleic Acid, Stearic Acid, Oleic Acid, Linoleic Acid to pleiotropic effects and have to be analysed further.	Field trials details including information on climate and weather conditions are given in the appendices 1 of the reports to studies DQ05B001 and DQ06B001 (Kowite, 2006a and Kowite, 2007). There is no evidence for unintended effects due to the genetic modification (see section 3.3 of the opinion)
Germany	Federal Agency for Nature Conservation (BfN)	D, 08 Post-market monitoring of GM food/feed	The data provided to show the human and animal safety of GHB614 cotton on the basis of its substantial equivalence to conventional cotton (except for the introduced traits) are not sufficient. Therefore, a post-market monitoring of the use of GHB614 cotton for food and feed is regarded obligatory and a post-market monitoring plan covering this issue is required.	The risk assessment concluded that no data have emerged to indicate that cotton GHB614 is any less safe than its non-GM comparator. In addition, cotton GHB614 is, from a nutritional point of view, equivalent to conventional cotton. Therefore, and in line with the Guidance document (EFSA, 2006a), the GMO Panel is of the opinion that post-market monitoring of the GM food/feed is not necessary.
Germany	Federal Agency for Nature Conservation (BfN)	D, 12.01 General	Interplay between environmental risk assessment and monitoring: Although the deliberate release into the environment of GHB614 cotton for cultivation is not within the scope of the application, GHB614 cotton might unintentionally enter the environment. The applicant states in the monitoring plan under 4.1 that "exposure to the environment will be	The GMO Panel comments on the scientific quality of the monitoring plan. EFSA has published guidance and scientific opinion on PMEM (EFSA, 2006a,b) following a broad consultation with stakeholder, including national competent authorities. The information supplied by the applicant is in line with this guidance. See section 5.2 of the PMEM opinion (EFSA, 2006b) and

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			<p>limited to unintended release of GHB614 cotton, which could occur for example via substantial losses during loading/unloading of the viable commodity including GHB614 cotton destined for processing into animal feed or human food products". Furthermore, the dossier states under B.5. that "occasional feral plants of G. hirsutum have been reported in Southern Europe". Since it can not be excluded that GHB614 cotton is spilled in cotton growing areas of Southern Europe during transport and might survive, gene flow through out-crossing from GHB614 cotton into non-transgenic wild (feral / naturalized) cotton or non-transgenic cultivated cotton may occur (see also our comments in section B.2.). Since no information was given by the applicant whether transport routes lie within the cotton growing areas, spillage of GHB614 cotton in these areas during transport has to be addressed in the environmental risk assessment. The data provided with the application are not sufficient to complete the environmental risk assessment (see comments in sections B.2. and D.7.). Depending on the results of an updated environmental risk assessment, the conclusions concerning a case-specific post-market monitoring may need to be revised.</p>	<p>section 5.2.2 of the scientific opinion.</p>

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Germany	Federal Agency for Nature Conservation (BfN)	D, 12.01 General	As stated by the applicant, the scope of the application of GHB614 cotton is for import and processing and all uses for food and feed. The applicant's proposal for an environmental monitoring plan does not fully meet the requirements according to Annex VII of Directive 2001/18/EC and Council Decision 2002/811/EC. Therefore, a plan suitable to meet the objectives is requested. Both parts of the monitoring plan, the case-specific monitoring and the general surveillance have to meet the following requirements: <ul style="list-style-type: none"> • Provision of a fully specified list of monitoring parameters: The applicant is requested to present for each parameter a detailed statement of the parameter definition, the observation methods (collection and analysis of samples with references), the frequencies of observations (time and number of visits to collect data) and the monitoring locations including number and size. Furthermore, an operating schedule giving full details of points in time is requested. • Determination of the baseline status of the receiving environment with respect to the monitoring parameters if applicable. • Elaboration of a sampling concept: Particularly, it must be explained how the necessary representativeness of the collected data in space and time is ascertained. The applicant is requested to indicate how the monitoring plan is 	<p>The GMO Panel comments on the scientific quality of the monitoring plan. EFSA has published guidance and scientific opinion on PMEM (EFSA, 2006a,b) following a broad consultation with stakeholder, including national competent authorities. The information supplied by the applicant is in line with this guidance.</p> <p>See section 5.2 of the PMEM opinion (EFSA, 2006b) and section 5.2.2 of the scientific opinion.</p>

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			<p>adapted to different local conditions where appropriate.</p> <ul style="list-style-type: none"> • Characterisation of reference areas. • In case of monitoring data being collected by external persons or institutions other than the applicant, binding agreements/contracts with third parties are requested which clearly determine what data are provided and how these data are made available. • Elaboration of the methods of data analysis including the statistical methods. The monitoring should be run in regions, where GHB614 cotton will be transported, processed or used. In case of substantial losses and spread of GHB614 cotton, all receiving environments need to be monitored. The time-period of monitoring needs to be sufficient to detect delayed or long-term adverse effects. Therefore, it may be necessary to extend the monitoring of certain parameters beyond the period of the consent. 	

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Germany	Federal Agency for Nature Conservation (BfN)	D, 12.02 Case-specific GM plant monitoring	We do not share the opinion of the applicant that a case-specific monitoring is not necessary. During transport, storage, package or processing incidental spillage of GHB614 cotton can occur. Therefore, case-specific monitoring has to focus on pathways, how GHB614 cotton can get via spillage into the environment. The applicant is requested to provide a case-specific monitoring plan including information • how spillage of GHB614 cotton during transport, storage, package, processing and use will be monitored, • how gene transfer from spilled viable GHB614 cotton seed to cultivated or wild (feral / naturalized) Gossypium species via cross-pollination will be monitored in relevant regions of Southern Europe. If spread, persistence and accumulation of GHB614 cotton in the receiving environment occur, further observations of possible impacts on organisms, food chains and habitats in the specific environment are required.	<p>The GMO Panel comments on the scientific quality of the monitoring plan. EFSA has published guidance and scientific opinion on PMEM (EFSA, 2006a,b) following a broad consultation with stakeholder, including national competent authorities. The information supplied by the applicant is in line with this guidance.</p> <p>See section 5.2 of the PMEM opinion (EFSA, 2006b) and section 5.2.2 of the scientific opinion.</p>
Germany	Federal Agency for Nature Conservation (BfN)	D, 12.03 General Surveillance of the impact of the GM plant	According to Directive 2001/18/EC general surveillance is a compulsory part of the monitoring. The objective of general surveillance is to monitor potential cumulative long-term impacts on human health and the environment and to identify the occurrence of adverse effects of the GMO on human health and the environment which were not anticipated in the environmental risk assessment. The general	<p>The GMO Panel comments on the scientific quality of the monitoring plan. EFSA has published guidance and scientific opinion on PMEM (EFSA, 2006a,b) following a broad consultation with stakeholder, including national competent authorities. The information supplied by the applicant is in line with this guidance.</p> <p>See section 5.2 of the PMEM opinion (EFSA, 2006b) and section 5.2.2 of the scientific opinion.</p>

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			<p>surveillance plan has to focus on possible pathways how GHB614 cotton can get into the broader environment and how unforeseen adverse effects on human health and the environment can be linked to the dispersal of GHB614 cotton. During transport, storage, packaging or processing incidental spillage of GHB614 cotton including viable GHB614 cotton seed can occur. Therefore, the applicant is requested to provide an appropriate general surveillance plan. The general surveillance plan has to comprise at least the following elements:</p> <ul style="list-style-type: none"> • exposure of the environment to GHB614 cotton e.g. via spillage during transport, storage, packaging, processing and use, • spread and persistence of GHB614 cotton if spillage or loss during transport, storage, packaging, processing and use occurs, • gene transfer from spilled viable GHB614 cotton seed to cultivated or wild (feral / naturalized) <i>Gossypium</i> species via cross-pollination in relevant regions of Southern Europe. If spread and persistence of GHB614 cotton or out-crossing of GHB614 cotton occur, further observations of possible impacts on organisms, food chains and habitats are required.

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Germany	Federal Agency for Nature Conservation (BfN)	D, 12.06 Reporting the results of monitoring	The monitoring results including case-specific monitoring and general surveillance have to be reported on an annual basis. All raw data have to be provided upon request. The applicant is requested to state, how the monitoring results will be published.	<p>The GMO Panel comments on the scientific quality of the monitoring plan. EFSA has published guidance and scientific opinion on PMEM (EFSA, 2006a,b) following a broad consultation with stakeholder, including national competent authorities. The information supplied by the applicant is in line with this guidance.</p> <p>See section 5.2 of the PMEM opinion (EFSA, 2006b) and section 5.2.2 of the scientific opinion.</p>
Germany	Federal Office of Consumer Protection and Food Safety (BVL)	General comments	The German CA is of the opinion, that the data provided with the application EFSA/GMO/NL/2008/51 support the conclusion that cotton GHB614 is unlikely to have adverse effects on human and animal health or on the environment in the context of its intended use. However, clarification on some points of the dossier is demanded. Specification of the plan for general surveillance is requested as the objectives defined in Annex VII of Directive 2001/18/EC and Council Decision 2002/811/EC are not fully met.	<p>The GMO Panel comments on the scientific quality of the monitoring plan. EFSA has published guidance and scientific opinion on PMEM (EFSA, 2006a,b) following a broad consultation with stakeholder, including national competent authorities. The information supplied by the applicant is in line with this guidance.</p> <p>See section 5.2 of the PMEM opinion (EFSA, 2006b) and section 5.2.2 of the scientific opinion.</p>
Germany	Federal Office of Consumer Protection and Food Safety (BVL)	A, 07 Where appropriate, the conditions for placing on the market the	The import documents should indicate that cotton GHB614 has not been approved for cultivation by the EC. Appropriate measures have to be taken during transport, storage and processing to avoid unintended release into the environment.	The GMO Panel is aware that, due to the physical characteristics of cotton seeds and methods of transportation, accidental spillage is unavoidable. Therefore the GMO Panel recommends that, within general surveillance, specific measures are introduced to actively monitor the occurrence of feral cotton plants in areas where seed spillage is likely to occur. In addition, the applicant noted that cotton GHB614 will be imported as mostly non-viable seed. Therefore, the likelihood that some imported seed could escape and

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		food(s) or...		germinate is very low. Please note that in relation to the monitoring plan, the GMO Panel gives its opinion on the scientific quality of post-market environmental monitoring (PMEM) activities proposed by applicants. The definitive and final endorsement of PMEM activities is under the responsibility of risk managers.
Germany	Federal Office of Consumer Protection and Food Safety (BVL)	D, 04 Information on how the GM plant differs from the recipient plant in: ...	On page 42 of the technical dossier, the applicant states, that "post-trial monitoring of the field trials during the seasons 2002-2005 found some volunteers". Van Duyn (2007) is cited as a reference. Neither in the technical dossier nor in the reference information is given on whether the number of volunteers of cotton GHB614 and the non-genetically modified counterpart were comparable. The respective data should be provided by the applicant.	Based on the volunteer monitoring data performed in the US, no evidence of change in characteristics that would enhance survival and/or weediness of cotton GHR614 has been observed as compared to the non-GM counterpart. The GMO Panel wishes to remind that the scope of the application excludes cultivation. Moreover, the GMO Panel is not aware of any scientific report of increased fecundity, volunteerism or fertility of GM cotton in regions where it is cultivated. Finally, there is no evidence that the herbicide tolerance trait introduced by the genetic modification results in increased persistence and invasiveness of any crop species, except in the presence of glyphosate-based herbicides. Thus shed seed remaining on the soil after harvest and consequent volunteers will be no different from conventional counterparts and would not create additional agronomic or environmental impacts in regions of cultivation.
Germany	Federal Office of Consumer Protection and Food Safety (BVL)	D, 07.04 Agronomic traits	The production of material for the comparative assessment is described on pp. 55-59 of the technical dossier. To assess agronomic performance, the applicant performed field trials at 17 locations during the 2004 and 2005 growing season. In 2005, trials were performed, amongst others, with a descendant of GHB614 in the background of FiberMax9740 (BC2F3). On	On the request of the Panel the applicant provided additional information on the identity and the breeding scheme of the non-GM comparators used in the agronomic / compositional and feeding studies. It was confirmed by the applicant that non-GM comparators with a similar genetic background were used in the agronomic and compositional analyses.


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			p. 56 of the technical dossier, it is stated that the recurrent parent variety counterpart was used as a comparator for GHB614 in FiberMax9740 background. However, considering Fig. 11 on p. 43 of the technical dossier, the non-transgenic BC2F3 which is said to have been used for equivalence field trials seems to be a negative segregant of BC2F2 (bottom of Fig. 11). In addition, it is not unambiguously clear from Fig. 11 which BC2F3 has been used for replicated agronomic field tests. The applicant should be asked to clarify on these points.	
Germany	Federal Office of Consumer Protection and Food Safety (BVL)	D, 07.06 Effect of the production and processing	In the study of Currier (2007), the study DQ06B005 is referred to for information on field trials. This reference has not been provided as part of the application and should therefore be asked for from the applicant.	The GMO Panel is of the opinion that this study report is not required. In the study of Currier (2007) information is given on the "Content of mEPSPS protein in Processed Fractions of Transgenic Cotton Event GHB614".
Germany	Federal Office of Consumer Protection and Food Safety (BVL)	D, 07.08 Toxicology	The applicant performed an animal feeding study with male broiler chickens (Stafford, 2007). GHB614 was used as test substance and the "non-transgenic counterpart" is said to have been used as a control. Neither the technical dossier nor Stafford (2007) state clearly whether the "non-transgenic counterpart" was made up of Coker 312. The applicant should be asked to clarify.	On request of the GMO Panel the applicant indicated that Coker312 was used as the non-GM counterpart in the 42-day broiler feeding study.


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Germany	Federal Office of Consumer Protection and Food Safety (BVL)	D, 12 Environmental Monitoring Plan	The monitoring plan proposed by the applicant provides a general strategy following the outlines in the Guidance Document of EFSA. The general surveillance plan is basically acceptable, but needs some modifications. Therefore, we suggest that the applicant shall detail the monitoring plan according to the following comments and present an elaborated monitoring plan with a first report after one year for further evaluation. In the risk assessment no relevant risks were identified. Therefore, there is no necessity for a case-specific monitoring. As part of the "active surveillance", it is planned to inform traders and processors as well as to gather information from different communication networks. However, a sufficient strategy is not explained by the applicant. According to the EFSA Guidance Document, an important task within general surveillance is to link monitoring to protection goals. The applicant neither sufficiently defines protection goals nor describes methods or parameters to address them. General relevant issues or protection goals that should be addressed by monitoring have been listed in chapter 2 of this plan. They are not equally relevant for imported GHB614 cotton (see EFSA Guidelines). Predominantly, the impact on human health during handling and on cattle due to feeding should be considered in relation to the likely	<p>The GMO Panel comments on the scientific quality of the monitoring plan. EFSA has published guidance and scientific opinion on PMEM (EFSA, 2006a,b) following a broad consultation with stakeholder, including national competent authorities. The information supplied by the applicant is in line with this guidance.</p> <p>See section 5.2 of the PMEM opinion (EFSA, 2006b) and section 5.2.2 of the scientific opinion.</p>


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			<p>exposure. Spillage of seeds as such may not represent an adverse effect by itself, but it nevertheless may be a key factor for further environmental exposure. Therefore, spillage may be considered for a proportionate monitoring focus that may guide further measures. Further, it is requested that the applicant specifies in detail, how and which information will be pro-actively queried and gathered. However, "any unanticipated adverse effect" is solely not an appropriate parameter, because it already anticipates an evaluation made on the spot. As the general surveillance shall especially detect cumulative, indirect and long-term effects, it is highly unlikely that such effects can be detected ad hoc by a single record or campaign. Appropriate parameters, the kind of data, its analysis and collation, as well as a thorough strategy of analysis must be sufficiently described. The role and interplay of all actors responsible for recording, analysis and evaluation of monitoring data should be clarified. An additional issue may be considered along a set of parameters from different sources (data on specific parameters supplied from networks, reviews of literature, reports, etc.), as it is partly sketched by the applicant. It might be useful to integrate food and feed surveillance in coordination with the competent authorities. Information about the use of the product in food</p>	

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			and feed could deliver supplementary helpful data (of exposure to consumers and animals) for general surveillance. Furthermore, the applicant should specify monitoring activities in the field of human and animal health. Therefore, it should be described in more detail how animal and human health surveillance is integrated in the monitoring plan. A report on GS activities on an annual basis is sufficient. However, the monitoring reports should not only consist of general information from participating networks, but should also be analysed by the consent holder in more detail. In particular, indirect, long-term or cumulative effects could be detected after consideration of data from different networks and overall analysis over several years. Possibly, single participating networks will not be able to take this aspect into consideration.	
Greece	Hellenic Food Authority (EFET)	D, 07.08 Toxicology	Despite the fact that a 42-day feeding study in broiler chickens was conducted, an additional 90-day feeding study should be carried out to further complete its safety assessment	The comparative analysis has shown that cotton GHB614 is compositionally and agronomically equivalent to the non-GM counterpart and other conventional cotton, except for the introduced trait (see section 3.3 of the scientific opinion). Therefore, in accordance with the EFSA Guidance Document (EFSA, 2006a) additional animal safety studies using the whole GM food/feed are not required.

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Malta	Malta Environment and Planning Authority	General comments	The way the results are presented in certain sections does not facilitate comprehension. For example, the specific detection method (annex 2 of Part 5 of the Detection method) only states that a 117bp ?? fragment is amplified 'at the 3'end across the insert and the plant junction' which is presumably spanning across the specific GM event (?). This is critical information as the mepsps insert is the same as that in maize GA21. A simple diagram in an easily accessible site in the Detection Method dossier to illustrate where the amplified region spans and therefore where the primers would attach would help.	Outside the remit of the GMO Panel.
Malta	Malta Environment and Planning Authority	General comments	On page 38 2d of the Technical Dossier a 17bp fragment is present in the wild type target locus but is missing from the transgene locus. Section 2b states that there are no deletions are these statements compatible	In section 2b, the company refers to the structure of the insert and not to the pre-insertion site. The 17 bp deletion identified at the target site raises no safety issue.

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Malta	Malta Standards Authority	General comments	Despite the fact that cotton will be mainly used in processed form, the following comments should be made: - Absence of toxicity is based on proof that the single isolated component protein "mepsps" is not toxic, however could one rule out chronic long-term effects of consumption? - The study by Rouqie 2006d to show that there is no homology with known toxins or allergens could not be accessed. - The study by Stafford 2007 which was supposed to show evidence that an animal feeding study with transgenic cotton on male broiler chickens did not have any effects on the health or behaviour of the chickens <u>could not be accessed</u> .	<p>The GMO Panel was able to access all studies provided by the applicant.</p> <p>The comparative analysis has shown that cotton GHB614 is compositionally and agronomically equivalent to the non-GM counterpart and other conventional cotton except for the introduced trait (see section 3.3 of the scientific opinion). Therefore, in accordance with the EFSA Guidance Document (EFSA, 2006a) additional animal safety studies or nutritional studies with livestock animals using the whole GM food/feed are not required. Details of the risk assessment of the food/feed safety of cotton GHB614 and derived products are provided in section 4 of the scientific opinion.</p> <p>Stafford 2007.pdf </p> <p style="text-align: right;">1628 0 KB</p> <p>Part I technical dossier appendices From EFSA it is downloadable. No request/complaint has been done (SHV)</p>
Malta	Malta Environment and Planning Authority	D, 02 Information on the sequences actually inserted or deleted	The fragments of approximately 13,000bp and a fragment of about 1500bp found in figure 9 cannot be explained since pTEM2 should give rise to smaller fragment sizes, the largest being that of the undigested pTEM2 at 3978bp. Can the applicant explain the fragments obtained?	Both fragments are correctly explained by the plasmid map shown in figure 3 (page 23) of the Technical dossier. 3978 bp is not the size of the pTEM2 plasmid but that of the T-DNA contained in the plasmid.

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Malta	Malta Environment and Planning Authority	D, 03 Information on the expression of the insert	No information on the position of the insert could be located.	The nuclear location of the insert is established by the segregation analysis and by the molecular cloning and analysis of the inserted T-DNA. No more information is needed, according the EFSA guidelines (EFSA, 2006a).
Malta	Malta Environment and Planning Authority	D, 03 Information on the expression of the insert	The protein was expressed as always in E.coli and not in the parent plant. If there is any interaction between the locus outside the insert and the inserted construct the material derived from E.coli would not show it. Likewise the digestibility studies on mepsps protein were carried out on the purified protein from E.coli and not on the native protein.	The GMO Panel has not found indications for the interaction between 2mEPSs and plant proteins.
Malta	Malta Environment and Planning Authority	D, 07.08 Toxicology	The absence of toxicity is based on proof that the single isolated component protein mepsps is not toxic. Obviously the cotton is not acutely toxic but chronic long-term effects cannot be ruled out.	Please see the reply to the general comment.
Malta	Malta Environment and Planning Authority	D, 07.08 Toxicology	The study by Rouquie 2006d to show that there is no homology with known toxins or allergens <u>could not be downloaded from the EFSA website and opened</u>	The GMO Panel was able to access all studies provided by the applicant. Rouquie 2006d.pdf  21504 KB Part I technical dossier appendices From EFSA it is downloadable. No request/complaint has been done (SHV)

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Malta	Malta Environment and Planning Authority	D, 07.10 Nutritional assessment of GM food/feed	The study by Stafford 2007 which was supposed to show evidence that an animal feeding study with transgenic cotton on male broiler chickens did not have any effects on the health or behaviour of the chickens <u>could not be downloaded from the EFSA website.</u>	The GMO Panel was able to access all studies provided by the applicant. Stafford 2007.pdf  16280 KB
Malta	Malta Environment and Planning Authority	D, 07.10 Nutritional assessment of GM food/feed	The mice fed the transgenic diet showed a lower rate of growth between days 8-15 compared to those fed the non transgenic diet. No major changes were recorded in the organs but in the organisms fed the transgenic diet, very minor changes were seen in the kidney (n = 2) and the spleen (n=3). At what point should minor changes be taken to indicate that there is a raised chance of long-term effects? Again the Malta Environment and Planning Authority requests that EFSA issue guidance documents for applicant to abide to such as specific literature range limits etc.	No feeding study with mice fed a transgenic diet was provided by the applicant. In an acute oral toxicity study using mice the protein mEPSPS produced in <i>E. coli</i> was administered at a single dose of 2000 mg/kg bodyweight (bw). There were no deaths and no relevant differences in body weight compared with the control group. Regarding the findings in the macroscopic examinations at necropsy, i.e. 2 animals of 5 with enlarged spleen vs. 0 in the control group and 3 animals of 5 with pale livers (vs. 1 in the control group), the GMO Panel requested an explanation from the applicant. According to the applicant the spleen enlargement is attributable to congestion related to the Isoflurane anaesthesia used to kill the animals. Congestion and haemorrhage is a common finding in toxicity studies, which can be an agonal phenomenon related to the mode of death or method of euthanasia (Greaves, 2000). The finding of pale kidneys was regarded as incidental since it was also observed in one control animal. In addition, pale kidneys can be attributed to an exhaustive exsanguination at necropsy or to a higher fat content of the organ. The applicant provided an additional acute toxicity study in mice. Intravenous administration of 2mEPSPS protein induced no systemic effects up to the highest dose of 10 mg/kg bw (see section 4.2.3.1 of the Opinion). Furthermore, no spleen or kidney findings were noted in an acute oral toxicity study in

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				mice using the protein mEPSPS, which is identical to 2mEPSPS and expressed in maize GA21. Maize GA21 was previously evaluated by the GMO Panel. Taken account of these study results the Panel was of the opinion that the observed spleen and kidney findings are not related to administration of the protein 2mEPSPS.
Spain	Ministry of the Environment, and Rural and Marine Affairs	D, 07 Information on any toxic, allergenic or other harmful effects on human or... D, 07.08 Toxicology	EFSA/GMO/NL/2007/51: GHB614 Cotton Comments from the National Commission on Biosafety of Spain D.07. Information on any toxic, allergenic or other harmful effects on human or animal health arising from the GM food and feed D.07.08-Toxicology 1. Enterprise has conducted a study of acute toxicity in mice: - For several days, observations have not been recorded. This mistake has been considered unimportant; because enterprise assures that there were no noteworthy problems. - In 4 of the 5 control animals, they don't identify any macroscopic alteration. However, in the 5 animals who were administered the m2EPSPS protein, there have been identified macroscopic alterations in spleen and kidneys. But all this is seen by the enterprise as something normal in this kind of experimental animals, so they don't	The GMO Panel does not advocate this type of study. However, an acute oral toxicity study using the protein 2mEPSPS was provided. This study was conducted in accordance with the OECD Guideline 425. Regarding the findings in the macroscopic examinations at necropsy see the comment above. Details of the risk assessment of the food/feed safety of cotton GHB614 (including the 2mEPSPS protein) and derived products are provided in section 4 of the scientific opinion.

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			investigate any of the findings. - The performed necropsies are quite superficial, or at least there are very few data about them. No additional samples are taken, no organs are weighed or studied (even those who appear macroscopically altered), no histological or blood analysis are made. Despite the almost absence of information, they conclude that it is highly unlikely that the protein m2EPSPS is a toxin. In fact this looks like a preconceived conclusion, rather than the result of the study itself. 2. There is no study of chronic or subchronic toxicity (the study with broilers can't be considered in that category). Since the mechanisms of acute and chronic toxicity are different, and that there is no reason to assume that the studied protein is only able to be toxic in an acute way, it can't be extrapolated the results of the acute toxicity study to chronic or subchronic toxicity.	

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The Netherlands	Ministry of Agriculture, Nature and Food Quality and Ministry of Health	D, 07.01 Comparative assessment	In the study on comparative analysis, the information on literature values of reference cotton in the studies is limited to the range of observed values by providing the lowest and highest value only. Provision of the mean levels and standard deviation of the given reference values in addition to the ranges, if available, should facilitate the interpretation of observed effects. As an interaction with year and location has been observed in many instances, the applicant should be required to provide additional analyses of the compositional data on a per-year and per-location basis. Furthermore, although the data provided on processed cottonseed products suggest that there are no major differences between GHB614-derived products and non-transgenic control-derived products, no standard deviation or range was given for the provided values. Moreover, for linters also no reference values are provided. Without these data, it is difficult to evaluate the compositional equivalence of these products.	The GMO Panel has carefully assessed the data provided by the applicant which included an analysis on a per year and per location basis (Rattemeyer-Matschurat, 2007). The Panel is of the opinion that the applicant provided sufficient information on the natural variability of cottonseed constituents (see Oberdörfer, 2007, Appendix A) The Panel concluded that the raw commodity, GHB614 cottonseed, is compositionally equivalent to conventional cottonseed except for the introduced trait. The GMO Panel further concluded that the characteristics of processed products derived from cotton GHB614 are not expected to be different compared to the respective products from conventional cottonseed. The data provided for GHB614 and conventional cottonseed products; support the conclusion that cotton GHB614 is compositionally equivalent to conventional cotton. Therefore, further comparative analyses on processed cottonseed products are not required by the Panel.

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The Netherlands	Ministry of Agriculture, Nature and Food Quality and Ministry of Health	D, 07.08 Toxicology D, 07.10 Nutritional assessment of GM food/feed	- As described under D, 07.05, cottonseed meal is derived after delinting, dehulling and extraction of oil from the cottonseed. Therefore, the cottonseed meal used in the broiler study is only relevant for the evaluation of the nutritional equivalence of feed. Since animal studies with GHB614 derived cotton products relevant for food were not performed, there are no data presented by the applicant that can be used for the nutritional equivalence and safety assessment of GHB614 derived food (based on effects from oil and/or linters). In addition, the comparative assessment revealed that GHB614 derived cottonseed has a slightly altered fatty acid and anti nutrient composition. Therefore, at this moment it can not be excluded that GHB614 derived food products induce changes in animals and or humans following repeated intake. Consequently, additional data should be provided that can be used for the nutritional equivalence and safety assessment of GHB614-derived food.	The comparative analysis has shown that cotton GHB614 is compositionally and agronomically equivalent to the non-GM counterpart and other conventional cotton, except for the introduced trait (see section 3.3 of the scientific opinion). Therefore, in accordance with the EFSA Guidance Document (EFSA, 2006a) additional animal safety studies using the whole GM food/feed are not required. In addition, for C16:1 (palmitoleic acid), C18:0 (stearic acid), C18:1 (oleic acid), C18:2 (linoleic acid) and C18:3 (linolenic acid) compositional differences were observed at 8, 11, 13, 12, 17 out of the seventeen field trial locations. However, differences were very small and are therefore not considered biologically relevant. In case of the anti-nutritional cyclopropenoid fatty acids (CPFAs), the t-tests at the majority of per-location analyses found significantly lower values for sprayed and unsprayed GHB614 cotton versus the non-GM control. The estimated differences between the CPFAs mean values for the control and the GHB614 groups were all very small and are therefore not considered biologically relevant.

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The Netherlands	Ministry of Agriculture, Nature and Food Quality and Ministry of Health	D, 07.10 Nutritional assessment of GM food/feed	- Feed conversion in male chickens was increased in the GHB614 group when compared to the non-transgenic counterpart group. Although feed conversion in male of the commercial control diet was even higher, only one commercial reference diet was included in the study, and no data on other commercial reference diets were provided. For a proper evaluation of the effects on feed conversion, data on more reference diets (including average, standard deviation and range), possibly from other studies, should be provided.	Since cotton GHB614 was found to be compositionally and agronomically equivalent to conventional cotton, specific nutritional studies in animals are not required. Therefore, the Panel accepts that the only one conventional cotton variety was included in the study.

List of References

- Eastick, R.J., Hearnden, M.N., 2006. Potential for weediness of Bt cotton in northern Australia. *Weed Science*, 54: 1142-1151.
- EFSA, 2006a. Guidance document for the risk assessment of genetically modified plants and derived food and feed, prepared by the Scientific Panel on Genetically Modified Organisms of the European Food Safety Authority, updated version May 2006, http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178620775747.htm.
- EFSA, 2006b. Opinion of the Scientific Panel on Genetically Modified Organisms on the Post-Market Environmental Monitoring (PMEM) of genetically modified plants. *EFSA Journal* 319, 1-27, http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178620769727.htm.