

**Request for Renewal of the Authorization of the genetically modified  
insect resistant and herbicide tolerant cotton LLCotton25 for food and  
feed uses, import and processing,  
in accordance with Articles 11 and 23 of Regulation (EC) No 1829/2003**

**EFSA-GMO-RX-010**

## General Information

On 29 October 2008, Commission Decision 2008/873/EC<sup>1</sup> authorised the placing on the market of LLCotton25 (ACS-GHØØ1-3) cotton pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council. The following products are authorized for the purposes of Articles 4(2) and 16(2) of Regulation (EC) No 1829/2003:

- a) foods and food ingredients containing, consisting of, or produced from ACS-GHØØ1-3 cotton;
- b) feed containing, consisting of, or produced from ACS-GHØØ1-3 cotton;
- c) products other than food and feed containing or consisting of ACS-GHØØ1-3 cotton for the same uses as any other cotton with the exception of cultivation.

The Community register<sup>2</sup> of genetically modified food and feed has been accessed on the 14<sup>th</sup> of July, as provided for in Article 28 of Regulation (EC) No 1829/2003 for the mentioned Commission Decision 2008/873/EC capturing the information set out in the Annex to the initial decision. There general product information are as follow:

(d) Method for detection:

- event specific real-time PCR-based method for the quantification of ACS-GHØØ1-3 cotton,
- validated on seeds by the Community reference laboratory established under Regulation (EC) No 1829/2003, published at <http://gmo-crl.jrc.it/statusofdoss.htm>

— reference material AOCS 0306-A and AOCS 0306-E accessible via the American Oil Chemists Society at [http://www.aocs.org/tech/crm/bayer\\_cotton.cfm](http://www.aocs.org/tech/crm/bayer_cotton.cfm)

The reference material provider AOCS provided the following updated links as the above mentioned ones are outdated.

Updated links for the reference material:

<https://www.aocs.org/crm>

<https://www.aocs.org/crm#n0306e2-LLCotton25-leaf-tissue-dna-10-µg>

Herewith we request the renewal of the mentioned authorization in accordance with Articles 11 and 23 of Regulation (EC) N° 1829/2003 and present the information accompanying the application.

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<sup>1</sup> Commission Decision 2008/837/EC authorising the placing on the market of products containing, consisting of, or produced from genetically modified LL cotton25 (ACS-GMØØ5-3) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council (*notified under document number C(2008) 6204*), <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:299:0036:0039:EN:PDF>, accessed July 10, 2017.

<sup>2</sup> [http://ec.europa.eu/food/dyna/gm\\_register/gm\\_register\\_auth.cfm?pr\\_id=30](http://ec.europa.eu/food/dyna/gm_register/gm_register_auth.cfm?pr_id=30)

**Information required under Articles 11 and 23 of Regulation (EC) N° 1829/2003 to accompany the application for renewal of LLCotton25 (ACS-GHØØ1-3) cotton**

The application is accompanied by the following:

- (a) a copy of the authorization for placing the product on the market;
- (b) a report on the results of the monitoring,
- (c) any other new information which has become available with regard to the evaluation of the safety in use of the food and feed and risks of the food and feed to animals, humans or the environment;
- (d) where appropriate, a proposal for amending or complementing the conditions of the original authorisation, *inter alia* the conditions concerning future monitoring.

Furthermore the renewal application for LLCotton25 cotton is following the requirements laid out in the EFSA Guidance for the authorization renewal of GM food and feed (EFSA, 2015).

In accordance with Articles 9 and 21 of Regulation (EC) No 1829/2003, Bayer provided updated sequence data for the cotton LLCotton25 event together with updated bioinformatics analyses to the European Commission on the 27<sup>th</sup> of September 2017.

In addition, the renewal application has been supplemented with a summary of the information previously provided in frame of applications EFSA-GMO-NL-2005-13, where applicable.

### **1. A copy of the authorisation for placing the food/feed on the market;**

A copy of the Commission Decision 2008/837/EC authorising the placing on the market of products containing, consisting of, or produced from genetically modified cotton LLCotton25 (ACS-GHØØ1-3) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council is provided in [Annex 1](#) accompanying this request.

### **2. A report on the results of the monitoring, if so specified in the authorisation;**

The Annual Post Market Monitoring reports for the genetically modified cotton LLCotton25 covering the authorization period from September 2008 until June 2016 are provided in [Annex 2](#). The general surveillance considering the placing on the market of LLCotton25 cotton in the EU indicates that there have been no adverse health or environmental effects associated with the importation or use of LLCotton25 cotton.

There is, to the best of our knowledge, no information available that questions the conclusion that LLCotton25 cotton does not pose any greater risk to health or the environment than conventional cotton.

### **3. Any other new information, which has become available, with regard to the evaluation of the safety of the food/feed and the risks of the food/feed to humans, animals or the environment;**

Bayer has developed the LLCotton25 cotton LibertyLink (OECD identifier is ACS-GHØØ1-3) was developed through *Agrobacterium*-mediated transformation using the vector pGSV71 containing the *bar* expression cassette. LLCotton25 cotton produces phosphinothricin acetyl transferase (PAT) protein, which confers tolerance to glufosinate-ammonium herbicides.

To confirm the sequence identity for the LLCotton25 cotton event and to meet EFSA's recommendation to provide at least 1 kb of flanking sequence on either side of the insert the sequence of the cotton LLCotton25 transgenic locus and the corresponding insertion locus was sequenced by Sanger sequencing ([M-585342-01-1](#)).

There were no sequence differences identified between the LLCotton25 cotton sequence reported by Peeters (2017 - [M-585342-01-1](#)) and the LLCotton25 cotton sequence reported by Berghman (2002 - [M-207874-01-1](#)) and Moens (2010 - [M-384916-01-1](#)) which were submitted in the frame of the application EFSA-GMO-NL-2010-77. There were however a number of sequence differences observed between the LLCotton25 cotton sequence reported by Peeters (2017 - [M-585342-01](#)) and the LLCotton25 cotton sequence reported by Aerts (2002 - [M-215510-01-1](#)) and Aerts (2003 - [M-232215-01-1](#)) which were previously submitted to the European Commission, EFSA or the EURL GMFF in the frame of the application EFSA-GMO-NL-2005-13. These sequence differences have no impact on the detection tools or the conclusions of bioinformatics analysis reports.

In accordance with Article 9 and 21 of Regulation (EC) No 1829/2003, Bayer provided the updated sequence data for the cotton LLCotton25 event to the European Commission on the 27<sup>th</sup> of September 2017, [M-585342-01-1](#) and compared these to previously submitted sequences [M-600013-01-1](#). Bayer would like to introduce the LLCotton25 cotton transgenic

locus and insertion locus sequence as reported in [M-384916-01-1](#) (Moens, 2010) and provided in frame of the application EFSA-GMO-NL-2010-77 as the reference sequence for future sequencing studies.

#### a. Systematic search and evaluation of literature

A scoping review ([M-600671-01-1](#)) was performed for LLCotton25 cotton and the newly expressed protein PAT/*bar* in order to identify any specific questions regarding food and feed safety, environmental safety, and molecular characterization that might require in-depth examination and to support decisions about the value of conducting more focused systematic literature reviews. A broad literature search was performed using a comprehensive collection of bibliographic databases, covering a database entry period from January 2007 to September 2014. Literature searches for the years Sept 2014 – Sept 2015 ([M-541500-01-1](#)), October 2015 to September 2016 ([M-571962-02-1](#)) were provided in the frame of the annual Post Market Environmental Monitoring activities. The overview of the different searches (Time window, databases and search terms used) in each study is provided in Table 1 below.

Additional sources of information, such as web pages of food safety, agriculture, and biotechnology-related authorities were searched for the period of January 2007 through August 2017, along with the bibliographies of relevant scientific opinions and reviews. The references identified were evaluated for potential relevance to the scoping review questions according to pre-defined criteria.

Literature referenced in the reports [M-600671-01-1](#), [M-541500-01-1](#) and [M-571962-02-1](#) is provided in the folder references under [Annex 3\\_New information](#). These relevant articles did not constitute new data on molecular characterization of LLCotton25 cotton, or the PAT/*bar* protein, nor showed potential adverse effects on human and animal health or on the environment.

In conclusion, this literature search and review of the retrieved articles identified relevant references that support the existing safety assessment of LLCotton25 cotton.

**Table 1: Overview of the different database searches performed.**

STUDY REPORT	COMPONENT	TIME WINDOW	DATABASES	SEARCH TERMS
<a href="#">M-600671-01-1</a>	LLCotton25	Jan 2007 – Sept 2014	Agricola, Biosis, CAB Abstracts, Chemical Abstracts, DRUGU, EMBASE, ESBIODBASE, FSTA, IPA, Medline, PQSciTech, Scisearch, Toxcenter	((LIBERTYLINK25 OR LLCOTTON25 OR LL25 OR (LIBERTYLINK OR LL OR LIBERTY(W)LINK)(W)25) OR LIBERTYLINK OR LL OR LIBERTY(W)LINK) AND (COTTON? OR GOSSYP?) OR LL(W)COTTON OR LLCOTTON OR LIBERTYLINKTM25 OR LLTMCOTTON25 OR LLTM25 OR (LIBERTYLINKTM OR LLTM OR LIBERTY(W)LINKTM)(W)25 OR (LIBERTYLINK OR LL OR LIBERTY(W)LINK)(W)(TM OR RTM)(W)25 OR LIBERTYLINKRTM25 OR LLRTMCOTTON25 OR LLRTM25 OR (LIBERTYLINKRTM OR LLRTM OR LIBERTY(W)LINKRTM)(W)25 OR (LIBERTYLINK OR LL OR LIBERTY(W)LINK OR LIBERTYLINKTM OR LIBERTYLINKRTM OR

STUDY REPORT	COMPONENT	TIME WINDOW	DATABASES	SEARCH TERMS
				LLTM OR LLRTM OR LIBERTY(W)(LINKTM OR LINKRTM)) AND (COTTON? OR GOSSYP?) OR ((LLTM OR LLRTM)(W)COTTON OR LLTMCOTTON OR LLRTMCOTTON) OR "ACS-GH001-3" OR "ACS- GH001-3" OR ACS(W)(GH001 OR GH001)(W)3) AND PY>2006 AND ED>=20070101 AND ED<=20140901 NOT P/DT
	PAT/ <i>bar</i>			(pat(2a)enzyme or phosphinothricin(2w)acetyltransferase or ppt(2w)acetyltransferase or pt(w)n(2w)acetyltransferase or phosphinothricin(2w)acetyl(w)transferase or ppt(2w)acetyl(w)transferase or pt(w)n(2w)acetyl(w)transferase) AND (BAR or (Bialaphos or BA)(w)(resistance or tolerance)(w)gene) AND PY>2006 AND ED>=20070101 AND ED<=20140901 NOT P/DT
<a href="#">M-541500-01-1</a>	LLCotton25	Sept 2014 – Nov 2015	More than 80 databases were used from the Scientific and Technical Information Network (STN), including: AGRICOLA, BIOSIS, CABA, EMBASE, HCAplus, Medline, PQSciTech, Scisearch, Toxcenter	s ((libertylink25 or LLCOTTON25 or ll25 or (libertylink or LL or liberty(W)link)(w)25) or libertylink or LL or liberty(W)link) and (cotton? or gossyp?) or ll(w)cotton or llcotton or libertylinkTM25 or LLTMCOTTON25 or llTM25 or (libertylinkTM or LLTM or liberty(W)linktm)(w)25 or (libertylink or LL or liberty(W)link)(w)(tm or rtm)(w)25 or libertylinkRTM25 or LLRTMCOTTON25 or llRTM25 or (libertylinkRTM or LLRTM or liberty(W)linkRtm)(w)25 or (libertylink or LL or liberty(W)link or libertylinktm or libertylinkrtm or LLtm or LLrtm or liberty(W)(linktm or linkrtm)) and (cotton? or gossyp?) or ((lltm or llrtm)(w)cotton or llrtmcotton) or "ACS-GH001-3" or "ACS-GH001-3" or ACS(w)(GH001 or GH001)(w)3) and ed>=20140901 not p/dt
	PAT/ <i>bar</i>			((pat (2a) enzyme or phosphinothricin (2w) acetyltransferase or ppt (2w)acetyltransferase or pt (w) n (2w) acetyltransferase or phosphinothricin (2w) acetyl (w) transferase or ppt (2w) acetyl (w) transferase or pt (w) n (2w) acetyl (w) transferase) not p/dt) and ed>=20140901 (bialaphos not p/dt) and ed>=20140901  Explanation: Truncation Symbol ? : 0 and more characters Proximity Operator (w): terms are searched in given order Proximity Operator (2w): 2 words are permitted between the terms in given order Proximity Operator (2a): 2 words are permitted between the terms in any order Abbreviation: ABB=ON Plural: PLU=ON

STUDY REPORT	COMPONENT	TIME WINDOW	DATABASES	SEARCH TERMS
<a href="#">M-571962-02-1</a>	LLCotton25	Oct 2015 – Sept 2016	Agricola, Biosis, CAB Abstracts, Chemical Abstracts, Derwent Drug File, EMBASE, ESBIODBASE, IPA Medline, Pascal, PQSciTech, CAS Registry, Scisearch, Toxcenter	((((LIBERTYLINK25 OR LLCOTTON25 OR LL25 OR (LIBERTYLINK OR LL OR LIBERTY(W)LINK)(W)25) OR LIBERTYLINK OR LL OR LIBERTY(W)LINK) AND (COTTON? OR GOSSYP?) OR LL(W)COTTON OR LLCOTTON OR LIBERTYLINKTM25 OR LLTMCOTTON25 OR LLTM25 OR (LIBERTYLINKTM OR LLTM OR LIBERTY(W)LINKTM)(W)25 OR (LIBERTYLINK OR LL OR LIBERTY(W)LINK)(W)(TM OR RTM)(W)25 OR LIBERTYLINKRTM25 OR LLRTMCOTTON25 OR LLRTM25 OR (LIBERTYLINKRTM OR LLRTM OR LIBERTY(W)LINKRTM)(W)25 OR (LIBERTYLINK OR LL OR LIBERTY(W)LINK OR LIBERTYLINKTM OR LIBERTYLINKRTM OR LLTM OR LLRTM OR LIBERTY(W)(LINKTM OR LINKRTM)) AND (COTTON? OR GOSSYP?) OR ((LLTM OR LLRTM)(W)COTTON OR LLTMCOTTON OR LLRTMCOTTON) OR "ACSGH001-3" OR "ACS-GH001-3" OR ACS(W)(GH001 OR GH001)(W)3) AND ED>20150930 NOT P/DT
	PAT/bar			(pat(2a)enzyme or phosphinothricin(2w)acetyltransferase or ppt(2w)acetyltransferase or pt(w)n(2w)acetyltransferase or phosphinothricin(2w)acetyl(w)transferase or ppt(2w)acetyl(w)transferase or pt(w)n(2w)acetyl(w)transferase) AND (BAR or (Bialaphos or BA)(w)(resistance or tolerance)(w)gene) AND ED>20150930 AND ED<20161001 NOT P/DT

### b. Updated bioinformatics

Following the requirement as laid out in the EFSA Guidance for renewal applications of genetically modified food and feed authorised under Regulation (EC) No 1829/2003, the updated bioinformatics analyses were conducted using the newly generated sequence information. The overview of the bioinformatic algorithms and databases used in these analyses is provided in Table 2 below.

**Table 2: Overview table on bioinformatics analyses.**

Flanking sequences (both against DNA and protein databases)			
<b>LLCotton25</b>			
EST Database	Date of latest release version	Algorithms	Appendix
NCBI Expressed sequence tags (est)	22 July 2017	BLASTn	M-384904-06-1
<b>General Database</b>			
NCBI Non-redundant protein sequences (nr)	17 July 2017	BLASTx	M-384904-06-1
NCBI nucleotide collection (nr/nt)	22 July 2017	BLASTn	
CottonGen NBI <i>Gossypium hirsutum</i> genome	30 Apr 2015		
<b>ORF analyses <input checked="" type="checkbox"/> insert-plant (a) / <input type="checkbox"/> insert-insert (b) / <input checked="" type="checkbox"/> whole insert (c)</b>			
<b>LLCotton25</b>			
Allergen database	Date	Algorithms	Reference
COMPARE	3 Feb 2017	SeqMatchAll FASTA	M-412814-05-1
<b>General Database</b>			
Bayer Toxin Database	13 Feb 2017	FASTA	M-412814-05-1
Newly expressed proteins			
<b>PAT/bar</b>			
Allergen database	Date	Algorithms	
COMPARE	03 Feb 2017	SeqMatchAll FASTA	M-266641-12-2
<b>General or toxin database</b>			
NCBI non-redundant protein database	02 Nov 2016	FASTA	M-266641-12-2
Bayer Toxin database	13 Feb 2017		

**i. Bioinformatic analyses to assess any interruption of plant genes by the insert(s) in the GM food and feed**

A bioinformatics analysis was performed on the LLCotton25 insertion locus sequence to identify the position of the insertion locus in the genome and to determine whether endogenous cotton genes were interrupted upon the insertion of T-DNA sequences ([M-384904-06-1](#)). Therefore, similarity searches using BLASTn against a *Gossypium hirsutum* genome database, nucleotide and EST databases and BLASTx against the NCBI non redundant protein database were performed on the LLCotton25 insertion locus as a query sequence. The bioinformatics analysis demonstrated that the LLCotton25 insertion locus originates from *Gossypium hirsutum* chromosome D06. The results indicate that it is unlikely that the insertion of T-DNA sequences in the LLCotton25 insertion locus interrupts endogenous cotton genes.

**ii. Bioinformatic analyses to identify whether the newly expressed proteins show similarity with known toxic and/or allergenic proteins**



**PAT/*bar***

The objective of the bioinformatic analysis ([M-266641-12-2](#)) was to evaluate the potential amino acid sequence homology of the phosphinothricin acetyltransferase protein from the *bar* gene (PAT/*bar*) with known allergens and known toxins by using several *in silico* approaches.

This search evaluated the potential amino acid sequence identity of the query protein with known allergens by using two *in silico* approaches.

- An 80-mer sliding window search was carried out to compare the query sequence, subdivided into 80 amino acid blocks, with all known allergens present in the public allergen database COMPARE ([www.comparedatabase.org](http://www.comparedatabase.org)). The FASTA algorithm was used, with the BLOSUM50 scoring matrix, and an E-value threshold of 100. The criterion indicating potential allergenicity was a 35 % identity with an allergenic protein. For alignment lengths shorter than 80 amino acids, the percentage of identity was recalculated over a hypothetical 80 amino acid window, with gaps treated as mismatch. From this calculation, only the matches of >35% identity were considered potentially relevant.
- An overall identity search was carried out to compare the complete query sequence with all protein sequences present in the COMPARE database. The FASTA algorithm was used, with the BLOSUM50 scoring matrix and an E-value threshold of 10. The criterion indicating potential allergenicity was ≥35% identity over at least 80 consecutive amino acids with an allergenic protein.

Furthermore, this study considered the potential N-glycosylation sites by searching their known consensus sequences, potentially found in allergenic proteins.

In addition, two *in silico* approaches based on the FASTA algorithm associated with the BLOSUM50 scoring matrix were used to evaluate the potential amino acid sequence identity of the query protein with known toxins:

- An overall identity search with all protein sequences present in the NCBI non-redundant database. An E-value threshold of 0.1 was used for pre-selecting the most similar proteins. The biological relevance of the matches was further assessed. Biologically relevant matches provide insight on the familiarity and potential toxic properties of the query protein.
- An overall identity search with all protein sequences present in the in-house Bayer toxin database. An E-value threshold of 10 was used for pre-selecting the most identical toxins. The biological relevance of the matches was further assessed. Biologically relevant matches provide insight on the potential toxic properties of the query protein.

The 80-mer sliding window search as well as the overall identity search against the allergen database showed no biologically relevant identities between the query sequence and known allergenic proteins. No potential N-glycosylation sites were identified on the amino acid sequence of the query protein. As expected, the results of the overall homology search against the general protein database showed that most of the matches corresponded to acetyltransferases sequences from various origins. Furthermore, no biologically relevant identities were found with any toxic proteins from the Bayer toxin database. In conclusion, there are neither allergenic nor toxicological *in silico* findings associated with the PAT/*bar* protein.

**iii. Bioinformatic analyses to identify whether open reading frames present within the insert and spanning the junctions between the inserts and the flanking genomic DNA, potentially encode peptides with similarity to known allergenic or toxic proteins**

A bioinformatics analysis ([M-412814-05-1](#)) was performed on the transgenic locus sequence of the LLCotton25 cotton to identify open reading frames (ORF).

The LLCotton25 transgenic locus, containing the inserted DNA together with the 5' and 3' flanking sequences was used as query sequence. The GetORF search program was used to identify all ORF crossing a junction or overlapping the inserted DNA, between two translation stop codons, with a minimum size coding for 3 amino acids. This search identified 161 ORF.

In the next step, the translated amino acid sequences from the identified ORF with a minimum size of 8 amino acids were used as query sequences in homology searches to known allergens and toxins. After elimination of duplicates, they represented 117 unique sequences.

Three *in silico* approaches were used to evaluate the potential amino acid sequence identity with known allergens contained in the public allergen database COMPARE ([www.comparedatabase.org](http://www.comparedatabase.org)):

- An 80-mer sliding window search was carried out to compare the ORF query sequences of  $\geq 80$  amino acid length, subdivided into 80 amino acid blocks, with all known allergens present in the allergen database. The FASTA algorithm was used, with the BLOSUM50 scoring matrix, and an E-value threshold of 100. The criterion indicating potential allergenicity was a  $>35\%$  identity with an allergenic protein. For alignment lengths shorter than 80 amino acids, the percentage of identity was recalculated over a hypothetical 80 amino acid window, with gaps treated as mismatch. From this calculation, only the matches of  $>35\%$  identity were considered potentially relevant.
- An 8-mer search was carried out to identify any short sequences of 8 amino acids or longer that share 100% identity to an allergenic protein. This search was performed using SeqMatchAll from the EMBOSS suite, which compared each ORF sequence with all known allergens present in the allergen database.
- An overall identity search was carried out by using FASTA algorithm, which compared each complete query sequence with all protein sequences present in the allergen database. The scoring matrix was BLOSUM50. An E-value threshold of 1 was used. The criterion indicating potential relevant identity to an allergen was  $\geq 35\%$  identity over at least 80 amino acids for sequences of  $\geq 80$  amino acids, or  $\geq 35\%$  recalculated over a hypothetical 80 amino acid window for sequences of  $< 80$  amino acids.

In addition, each query sequence was evaluated for potential identity with known toxins. An overall identity search was carried out by using FASTA algorithm with all protein sequences present in the in-house Bayer toxin database, using the BLOSUM50 scoring matrix. An E-value threshold of 10 was used for pre-selecting the most identical toxins. The biological relevance of the matches was further assessed. Biologically relevant matches provide insight on the potential toxic properties of the potential polypeptide.

The 80-mer sliding window search showed no biologically relevant identities between the query sequences of  $\geq 80$  amino acid length and known allergenic proteins. The 8-mer search showed no 100% identity with known allergenic proteins. The overall search showed no biologically relevant identity between the query sequences and any known allergenic proteins. In addition,

no biologically relevant identities were found with any toxic protein from the Bayer toxin database. In conclusion, there are neither allergenic nor toxicological *in silico* findings associated with the potential ORF polypeptides.

#### iv. Bioinformatic analyses to assess the potential for homology-facilitated horizontal gene transfer from plant transgenic DNA to microorganisms

A bioinformatics analysis was performed ([M-535606-02-1](#)) to identify LLCotton25 cotton sequences with identity to microbial DNA sequences that might contribute to double homologous recombination (HR) events and homology-facilitated horizontal gene transfer (HGT) of plant transgenic DNA to microorganisms.

BLASTN searches identified sequence identities of the *bar* gene and the 3'nos terminator sequence present in LLCotton25 cotton with sequences present in Bacteria & *Archaea* and Plasmids datasets. None of the obtained BLASTN results using the Bacteria & *Archaea* or the Plasmids datasets contain at least two alignments of at least 200 bp in length and 95% identity, indicating that double HR into homologous microorganism recipient sequences is highly unlikely.

The genetic elements present in LLCotton25 cotton are ubiquitous in nature and are not expected to provide a selective advantage of the potential receiving microorganisms. In addition, HGT between homologous sequences from LLCotton25 cotton and microbial genomes is highly unlikely due to the multiple steps needed for the process to occur and the low probability of each of them. In conclusion, HGT between LLCotton25 cotton and microorganisms leading to harm to humans, animals or the environment is unlikely to occur.

#### c. Additional documents or studies performed by or on behalf of the applicant

The overview of global approvals of LLCotton25 cotton is provided in Table 3 below. Cultivation approvals are present in Brazil, Colombia, Mexico and the USA. All other approvals are for import scope only. None of the competent authorities has prohibited or revoked the authorization for LLCotton25 cotton for neither import nor cultivation purposes.

**Table 3: Global Approval Overview for LLCotton25 cotton**

Country	Agency	Status
<b>United States</b>	FDA	Completed (2-Apr-03)
	USDA	Completed (10-Mar-03)
<b>Colombia</b>	INVIMA (Food)	Completed (10-May-16)
	ICA (Feed)	Completed (11-Feb-08)
	ICA (cultivation)	Completed (19-Jul-10)
<b>Mexico</b>	COFEPRIS	Completed (9-Aug-06)
<b>Korea</b>	MFDS	Completed (26-Aug-15)†
	RDA	Completed (7-Jan-08)

<b>Japan</b>	MHLW	Completed (28-Jun-04)
	MAFF	Completed (26-Feb-06)
	MAFF & MoE	Completed (10-Feb-06)
<b>Canada</b>	HC	Completed (3-Sep-04)
	CFIA	Completed (31-Aug-04)
<b>Australia/New Zealand</b>	FSANZ	Completed (10-Feb-06)
	OGTR	Completed (8-Aug-06)
<b>Argentina</b>	SENASA	Completed (6-Mar-14)
<b>Brazil</b>	CTNBio	Completed (4-Sep-08)
<b>Taiwan</b>	TFDA	Completed (19-Apr-15)
	CoA	Completed ( 2/3/2017)
<b>Singapore</b>	GMAC	Submitted (27-Jun-16)
<b>South Africa</b>	DAFF	Completed (23-Sep-11)
<b>Philippines</b>	DOA	Submitted (17-Mar-15)
<b>China</b>	MOA	Completed (12/31/2015 )†
<b>Malaysia</b>	MNRE	Completed (30-Mar-17)
<b>Vietnam</b>	BPI	Submitted (14-Jan-15)

Bayer reviewed studies not previously submitted produced, controlled or sponsored by the applicant or provided to the applicant by a third party during the authorization period in a summary and provided as [M-592130-02-1](#). Studies part of the present renewal submission are not included in the summary report. The collected information has been identified and assessed in terms of potential effect on molecular characterization, human and animal safety, and the environment. The information obtained from the studies listed in the summary report ([M-592130-02-1](#)) is consistent with the information provided in the LLCotton25 application submitted to EFSA. The detailed review did not identify any studies that would constitute any new data relevant for the risk assessment of LLCotton25 cotton for the scope of the application or the newly expressed protein (PAT/bar) or which challenge or change in any way the conclusions of the original risk assessment.

#### 4. Overall assessment

The EFSA previously concluded in 2006<sup>3</sup> that “the GM LLCotton25 is as safe as its non-genetically modified counterparts with respect to potential effects on human and animal health

<sup>3</sup> <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2006.429/epdf> (accessed, 31<sup>st</sup> of August)

*or the environment. Therefore the GMO Panel concludes that LLCotton25 is unlikely to have any adverse effect on human and animal health or on the environment in the context of its intended uses”.*

Considering the available information previously provided and positively concluded on by EFSA, and the information presented in this renewal application it can be concluded that the previous risk assessment conducted by EFSA for LLCotton25 cotton remains valid. Furthermore, in line with the conditions of the Commission Decision 2008/873/EC<sup>4</sup>, the general surveillance was performed and annually reported through the annual post market environmental monitoring. These activities did not identify any adverse effects for the LLCotton25 cotton event related to human and animal health or the environment.

There is, to the best of our knowledge, no information available that questions the previous conclusions regarding the safety of the LLCotton25 cotton event. Nor are there indications or literature known which would challenge the previously conducted risk assessment and EFSA’s conclusions that *“the GM LLCotton25 is as safe as its non-genetically modified counterparts with respect to potential effects on human and animal health or the environment”*.

## Reference Material

As elaborated in the general information part in this application the reference material is available and remains accessible throughout the authorization period at the reference laboratory mentioned in the authorization decision.

## Detection Method

As elaborated in the general information in this application the event-specific detection method for the quantification of cotton LLCotton25 has been validated by Institute for Health and Consumer Protection (DG Joint Research Centre, JRC). At the moment of the renewal request the method is fit-for-purpose. The updated sequence information as described in section 3 has no impact on the detection methods for the cotton LLCotton25 event.

## **5. where appropriate, a proposal for amending or complementing the conditions of the original authorization, inter alia the conditions concerning future monitoring.**

Based on the conclusions of the overall assessment of the here presented renewal application of GM cotton LLCotton25 for food and feed uses we do not consider the need to update the monitoring plan or propose changes to the existing restrictions and conditions of release/use as laid down in the initial authorization.

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<sup>4</sup> Commission Decision 2008/837/EC authorising the placing on the market of products containing, consisting of, or produced from genetically modified LL cotton25 (ACS-GMØØ5-3) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council (*notified under document number C(2008) 6204*), <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:299:0036:0039:EN:PDF>, accessed July 10, 2017.

The initial authorization which was issued on 29 October 2008, Commission Decision 2008/873/EC<sup>5</sup> authorised the placing on the market of LLCotton25 (ACS-GHØØ1-3) cotton pursuant to Regulation (EC) No 1829/2003 and lays out conditions in Article 4 and point (h) of the Annex of the authorization decision. These lay down the need for general monitoring and do not impose specific conditions or restrictions on the placing on the market, use or handling of the products. Considering that the annual EU Post market environmental monitoring activities for the years 2009-2016 did not identify adverse effects nor that there was literature identified changing previous risk assessment conclusions, presented here under 3.a. Systematic search and evaluation of literature, we do not consider revisions or changes necessary to the general surveillance measures needed.

## References

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<sup>5</sup> Commission Decision 2008/837/EC authorising the placing on the market of products containing, consisting of, or produced from genetically modified LL cotton25 (ACS-GMØØ5-3) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council (*notified under document number C(2008) 6204*), <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:299:0036:0039:EN:PDF>, accessed July 10, 2017.

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