Ministry of Infrastructure
and Water Management

> RIVM/SEC/BGGO, PO box 1, 3720 BA Bilthoven, The Netherlands.

Contact

Our ref.
C/NL/06/01_001.ar.1

Your ref

Cc

Encl.

ASSESSMENT REPORT OF THE NETHERLANDS COMPETENT AUTHORITY IN ACCORDANCE WITH DIRECTIVE 2001/18/EC

RENEWAL OF NOTIFICATION C/NL/06/01

1. THE NOTIFICATION

The notification, submitted by Suntory Flowers Limited, Tokyo, Japan (formerly: Florigene), concerns renewal of placing on the market of imported cut flowers derived from genetically modified carnation (*Dianthus caryophyllus*) line 123.8.12 (FLO-40689-6) in accordance with Directive 2001/18/EC. The flowers of the carnation line have been modified with the *dfr* gene from petunia (*Petunia x hybrida*) and the *f3'5'h* gene from viola (*Viola* sp.), resulting in a modified flower colour (violet). Line 123.8.12 also contains a herbicide tolerance gene (s*uRB*) from *Nicotiana tabacum*, used to facilitate selection *in vitro*. The commercial name of the product is Florigene®Moonaqa™.

2. SCOPE OF THE NOTIFICATION

This notification for renewal concerns import, distribution and retailing of line 123.8.12 in the cut flower market in the same way as any other carnation. This notification does not include cultivation or the use as feed or as food of line 123.8.12.

3. PROCEDURE

The original decision of the Netherlands competent authority to Florigene for import of line 123.8.12, under dossier number C/NL/06/01, was issued on July 20, 2009.
According to article 17 of Directive 2001/18/EC the notifier shall submit a notification to the competent authority which received the original notification at the latest nine months before the expiry of the consent.
The dossier for renewal was received by the Netherlands competent authority on May 3, 2018. This dossier, under number C/NL/06/01_001, has been assessed with reference to Article 17 (2) of Directive 2001/18.

Scientific advice
Based on the dossier for renewal of May 3, 2018, the Dutch scientific advisory committee (COGEM) gave its advice on June 13, 2018 (CGM/180613-02) and concluded that the risks for human health and the European environment associated with import, distribution and retail of cut flowers of line 123.8.12 are negligible.

Confidentiality
The notification does not contain any information which the applicant regards as Confidential Business Information.

4. LIST OF DOCUMENTS

Based on article 17 (2) of Directive 2001/18/EC the following is required for a renewal of an existing market approval:

a) A copy of the consent to the placing on the market of the GMO
b) A report of the results from monitoring
c) Any new information which has become available with regards to the risks of the product to human health and/or the environment
d) As appropriate, a proposal for amending or complementing the conditions of the original consent, inter alia the conditions concerning future monitoring

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(a) A copy of the consent to the placing on the market of the GMO

A copy of the consent, issued by the Netherlands on July 20, 2009, is provided in *Appendix 1* of the application for renewal.

(b) A report of the results from monitoring

Reports of monitoring during 8 years are supplied (2010-2017) in *supplementary file 1*. The reports contain:

✓ Questionnaire feedback from the importer

These questionnaires have been provided by the importer each year. The importer has reported every year that he was not aware of any illegal growing and that neither the staff nor consumers have reported any adverse effects of handling the flowers.

✓ Expert monitoring group

Since 2010 members of an expert group of breeders and research have been asked on a yearly basis to report on whether they have become aware of any illegal propagation of transgenic carnation in Europe, or of the incidence of any wild carnation populations. There were no reports on the establishment of transgenic carnation in the wild, or of introgression to wild *Dianthus* species in any survey, in any year. No reports of illegal propagation were made.

✓ Mailing list

Herbaria, European botanical and plant conservation groups, national plant protection authorities, Italian phytosanitary agencies, national botanic survey networks, plant protection services, botanical gardens and individual scientists have been contacted by mail and email to request information on any reports of the identification of wild populations of carnation. Some responses identified recent wild populations of *Dianthus caryophyllus*. In all cases where it was possible to confirm the nature of the samples, collections were of the 5-petal unimproved *Dianthus caryophyllus*, and not carnation.

✓ Literature review

From 2010 a literature search was undertaken on an annual basis to identify any new, or previously unidentified, scientific reports on any aspects of *Dianthus* biology or distribution in Europe. All literature cited in the annual monitoring reports is compiled in *supplementary file 2.* Details of the literature searches, including the keywords used, are indicated in the application. None of these reports identified carnation in the wild or evidence of introgression to wild *Dianthus* species.

✓ Database review

From 2011, annual database and website review was added to the general monitoring process. None of these reports identified carnation populations in the wild.

✓ Website

The Florigene website has been in place continuously since 2007 (http://www.florigene.com). No information on possible wild populations of Florigene®Moonaqua™ has been conveyed through the website by the public, distributors or retailers.

The results from monitoring do not indicate any risk for human health and the environment of the import of cut flowers of line 123.8.12.

(c) Any new information which has become available with regards to the risks of the product to human health and/or the environment

A summary of all new information that was generated or found since the consent was issued in 2009, is described below.

Resequencing of the event
In February 2017 the applicant provided, on request of the European Commission, the results of resequencing of FLO-40689-6. Only for locus 1 correction was required, by addition of one nucleotide to the sequence at base 12996 of the original sequence. The correction was in a linker sequence component of the transformation vector. The exact location of the correction is shown in *supplementary file 3*. The correction in the sequence in locus 1 had no effect on the validated unique identification protocol.

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Bioinformatics analyses
Because of the introduction of an additional base in the sequence of locus 1 the applicant carried out new bioinformatic analyses of the inserts and flanking regions in FLO-40689-6. A full copy of the information which was provided to the European Commission in April 2017 is included as *supplementary file 4*.
Results of these analyses are summarized below:

- ✓ Disruption of endogenous genes

Blastn and blastx results indicated that the insertions in loci 1 and 2 may be in protein encoding regions, though the function of the hypothetical proteins could not be identified from the information available in databases. Loci 3 was shown to be in a non-coding region of the carnation genome.

- ✓ Novel ORFS in junction regions

2,186 putative open reading frames (ORFs) were identified, 31 of which were generated across the genomic DNA/T-DNA junctions. Analysis of the sequences of all ORFs indicated no biologically significant homology to known toxins or allergens.

- ✓ Inserted genes and expressed proteins

Analysis of the sequences of the three newly expressed proteins in FLO-40689-6 indicated no biologically significant homology to known toxins or allergens. The three newly expressed proteins are ubiquitous, well characterized proteins and are not known to be allergens *(supplementary file 5).*

Botanical surveys at the production site
The two main sites of production, Colombia and Ecuador respectively, have been inspected regularly from 2009 to 2018. Composting areas were considered the most likely places in which a wild population might establish. On none of the inspections sites a wild population of carnation has been identified.

Viable anther number and style length
From 2012 to 2017 anther number and style length was measured in flowers grown in Colombia. As was noted in the initial application, FLO-40689-6 produced a low number of intact anthers when grown in Colombia. Average length is variable, but is consistent within a range of 1.6-2.2 cm, indicating no change in potential gene flow.

Comparison to parental variety
A comparative trial was performed in Colombia in 2015. Several significant differences were observed, but did not indicate an environmental risk according to the applicant, since the characters were considered to be not of biologically relevant *(supplementary file 6).*

Literature review
In addition to the publications as described under 'literature review', three literature reviews have been carried out for other transgenic carnation lines with a similar phenotype *(supplementary file 7)*. These reviews were updated on 13 March 2018. None of the publications identified since the approval was issued in 2007 suggests that FLO-40689-6 poses a risk to human health and the environment.

Off-types
From 2011, it was noted in both Ecuador and Colombia production that line FLO-40689-6 contained plants which produced purple flowers (off-types). Since early 2017, approximately 2.5 % of this production consisted of this off-types. These off-types are not exported to the EU. Experiments demonstrated these off-types to exhibit a changed anthocyanin profile and a changed flower morphology. The unique identification test validated by JRC was positive for both FLO-40689-6 and its off-types and thus shows the off-type to be transgenic.

(d) As appropriate, a proposal for amending or complementing the conditions of the original consent, inter alia the conditions concerning future monitoring
The following information is supplied:

Changes to the conditions of the original consent:

- ✓ Change of company name
  The consent for placing on the market for Florigene® Moonaqua™ as issued to Florigene Limited, Melbourne. This company has been purchased by Suntory Limited, Osaka, Japan. The company requests therefore that the consent for renewal will be in the name of Suntory Flowers Limited.

- ✓ A correction to the sequence that was made to locus 1. The correction has no effect on integrity or accuracy of the detection method (section 3.1).

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Future monitoring

- ✓ No changes are foreseen in the general monitoring scheme.
- ✓ The detection method validated by JRC is still applicable.

5. ADVICE OF THE NETHERLANDS COMPETENT AUTHORITY FOR DIRECTIVE 2001/18/EC

Based on the notification for renewal and the above mentioned considerations, the Netherlands competent authority concludes that no reasons have emerged on the basis of which consent to the proposed renewal of placing on the market should be withheld.

The Netherlands Competent Authority therefore proposes to consent to the renewal of placing on the market of the product as described below, for which a notification has been submitted on May 3, 2018, registered under number C/NL/06/01_001 under explicit specification of:

a) The consent will be granted to Suntory Flowers Ltd, Tokyo, Japan and concerns renewal of the placing on the market under part C of 2001/18/EC of the product consisting of carnation genetically modified with the *dfr, f3'5'h* and *SuRB* genes, with the unique identification code FLO-40689-6, for the purpose of import, distribution and retailing. The consent includes line 123.8.12, product name Florigene® Moonaqua™. This consent excludes cultivation and excludes the use as feed or as food of line 123.8.12.
b) The consent will be valid for a period of 10 years after approval.
c) The company should ensure that the following information is transmitted in writing to the importer receiving the product:
   - The statement that "These flowers are genetically modified to alter the flower colour and are only produced for use as an ornamental product";
   - The unique identifier of line 123.8.12 is FLO-40689-6.
d) The consent holder is required to supply reference material of line 123.8.12 for detection purposes at any time to the competent authority.
e) The consent holder should carry out monitoring according to the general surveillance plan of the notification and report on the results of the general surveillance every year, during the period the consent is valid.
f) The consent holder shall submit to the Commission and to the competent authorities of the Member States annual reports on the results of the monitoring activities.

03 juli 2018,
DE STAATSSECRETARIS VAN INFRASTRUCTUUR EN WATERSTAAT,
namens deze,
het afdelingshoofd Veiligheid en Risico's

dr. Dick Jung