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VIA EXPRESS COURIER

February 21, 2011

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Lee:

***** THE FOLLOWING CONTAINS CONFIDENTIAL BUSINESS INFORMATION *****

Danziger - Dan Flower Farm, one of Israel's leading floriculture companies, is developing genetically engineered varieties of *Gypsophila paniculata* (Baby's Breath) for the cut flower market and wishes to import cut flowers of its genetically engineered varieties into the United States for commercial distribution and sale. After consulting with the USDA-APHIS Biotechnology Regulatory Service, we prepared the enclosed document in support of a request for opinion on the regulatory status of cut flowers of genetically engineered *Gypsophila paniculata* under 7 CFR Part 340.

The Freedom of Information Act exempts federal agencies from releasing information that is trade secret and commercial or financial information that is privileged or confidential (5 U.S.C. 552(b)(4)). Danziger considers certain information in this document as trade secret or commercial information that is privileged and confidential. In particular, Danziger designates the following as Confidential Business Information:

1. Intended commercialization date,
2. Intended production locations.

Disclosure of this information would cause substantial competitive harm to Danziger by enabling other companies to unfairly compete with it or could raise the possibility of acts of vandalism or other business interruption against the company or its collaborators. This information has not previously been disclosed outside of the company except under the terms of a non-disclosure agreement. We enclose here one copy of a CBI version and one copy of a redacted version of the document.

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We respectfully request your review and opinion on our request so that we can proceed with confidence to advance this exciting new research and development program. Thank you for your assistance in this matter.

Very truly yours,

THENELL & ASSOCIATES LLC

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Enclosures (2)

January 20, 2012 CBI-DELETED

Submission to the U.S. Department of Agriculture Animal and Plant Health Inspection Service Concerning the Status of Genetically Engineered *Gypsophila paniculata* Cut Flowers Under 7 CFR Part 340

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Danziger "Dan" Flower Farm, one of Israel's leading floriculture companies, is developing genetically engineered varieties of *Gypsophila paniculata* (Baby's Breath) for the cut flower market. Danziger wishes to import cut flowers of its genetically engineered varieties into the United States for commercial distribution and sale. Danziger requests an opinion from the U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) on the status of cut flowers of genetically engineered *Gypsophila paniculata* under 7 CFR Part 340. In support of our request, the company herewith provides the enclosed information to USDA-APHIS.

This document contains confidential business information of Danziger Dan Flower Farm for which the company seeks all applicable protection from public disclosure under the Freedom of Information Act.

Product concept

Danziger is developing varieties of *Gypsophila paniculata* (Baby's Breath) that exhibit altered color phenotypes through expression of a gene introduced using recombinant DNA techniques. [ ] CBI-DELETED

Expression of the introduced gene results in a range of altered flower colors from dark purple and red to light pink.

Gypsophila is traditionally used as a filler flower to lend fullness and visual interest to ornamental bouquets and floral arrangements. To date, conventionally bred gypsophila is available in predominately one color, white, and in very limited varieties, light pink. Danziger intends to commercially produce its new gypsophila varieties in selected floriculture production areas including, but not limited to [ ]. CBI-DELETED Danziger wishes to import cut flowers of its new varieties into the United States for commercial distribution and sale through wholesale flower markets and retail flower vendors [ ]. Danziger does not intend to cultivate its genetically engineered gypsophila varieties in the United States, nor does the company intend to authorize any other party to cultivate these varieties in the United States, unless such cultivation is conducted in compliance with applicable U.S. environmental laws.

Danziger requests an opinion from USDA-APHIS on the status of cut flowers of genetically engineered *Gypsophila paniculata* under 7 CFR Part 340. In particular, Danziger seeks USDA-APHIS confirmation that cut flowers of genetically engineered *Gypsophila paniculata* are not regulated articles under 7 CFR Part 340 and may be legally imported into and distributed in the United States.

Production and distribution of *Gypsophila paniculata* cut flowers

The United States annually imports approximately 100 million gypsophila cut flower stems with an import value of about $20-24 million (USDA FAS 2010). Over 87% of all fresh cut gypsophila entering the United States are grown in Ecuador with another 11% from Colombia and lesser amounts from Peru, Mexico, and Costa Rica. Approximately two-thirds of all cut flowers consumed in the United States arrive through Miami International Airport and the nearly 75 fresh cut flower importers located there (AFIF 2010). On a daily basis, nearly 40,000 boxes of cut flowers of all types arrive at the Miami airport for inspection and redistribution throughout the United States.

Conventional gypsophila is currently grown on large commercial farms in Ecuador and Colombia, with additional production in Mexico and Peru. Stems are harvested when flowers are about 30% open, packed in sleeves, placed into cartons, and shipped by airfreight to the port of Miami, Florida. Upon arrival, shipments are inspected for pests and disease by plant protection authorities in compliance with quarantine regulations under 7 CFR Part 319. The flowers are then sold to flower wholesalers and buyers throughout the

United States and are transported by refrigerated trucks or air cargo to regional distribution centers. Wholesalers then sell the stems to flower retailers (florists, supermarkets) for use in bouquets and other floral arrangements. Cut flowers are a highly perishable commodity that requires rapid, but careful handling from harvest to the retail customer. Imported flowers remain fresh by employing a "cold-chain" of distribution, meaning the product is shipped in an unbroken refrigerated chain from grower to importer to wholesaler to retailer, providing the flowers with controlled temperature, humidity, and atmospheric conditions. The typical time from harvest to retail customer for cut flowers is 7–10 days, with a limited vase life of approximately 1 week. The total time from "harvest to house" is about 14–15 days. Danziger anticipates that commercial production, importation, distribution and use of its new gypsophila varieties will be the same as conventional gypsophila and sees potential for its new varieties to gain significant market share because of its extraordinary color.

Biology of *Gypsophila paniculata*

Gypsophila paniculata is a perennial herb that grows to 3 feet tall with widely branching stems. The stems are smooth, linear leaves are opposite, hairless, with a prominent mid vein and 3/4 to 4 inches long and sharp-pointed. The plants have a deep, penetrating root system. Leaves are reduced in the upper stem and are mostly gone by the time the plant is in flower. Flowers are 1/16 to 1/8 inch wide, with a 5-lobed calyx. Calyx lobes are green and in some cases purple and the petals are typically white. The fruit is a small capsule containing 2 to 5 seeds (Douglas et al. 1988, Royer and Dickinson 1999, Whitson et al. 2000).

Gypsophila is a member of the Caryophyllaceae (Shillo 1985). The genus consists of 12 species (USDA NRCS 2010) of which *Gypsophila paniculata* is the only species used as a cut flower (Shillo 1985, [ ]).

Kingdom	*Plantae* – Plants
Subkingdom	*Tracheobionta* – Vascular plants
Superdivision	*Spermatophyta* – Seed plants
Division	*Magnoliophyta* – Flowering plants
Class	*Magnoliopsida* – Dicotyledons
Subclass	*Caryophyllidae*
Order	*Caryophyllales*
Family	*Caryophyllaceae* – Pink family
Genus	*Gypsophila* L. – baby's-breath

Species *Gypsophila paniculata* L. – baby's breath

Gypsophila paniculata originated in Europe and temperate Asia and the eastern Mediterranean. It was first introduced into the United States as a garden ornamental in the late 1800's. It is often cultivated in gardens and flower beds, and has escaped cultivation to pastures and rangelands (Rutledge and McLendon 1996, Whitson et al. 2000). It is now widespread across the northern United States and Canada (MAFF 2010, Royer and Dickinson 1999, USDA NRCS 2010).

Gypsophila paniculata can invade natural habitats and out-compete native perennial plants (MAFF 2010, Rutledge and McLendon 1996, Wisconsin DNR 2010). It is not uncommon in partially disturbed pastures, rangelands, and stabilized sand dunes. It is considered a weed in California and Washington (USDA NRCS 2010), which makes it illegal to plant in these states. But, it is not listed as a U.S. federal noxious weed and millions of cut stems are annually imported into the United States as ornamentals.

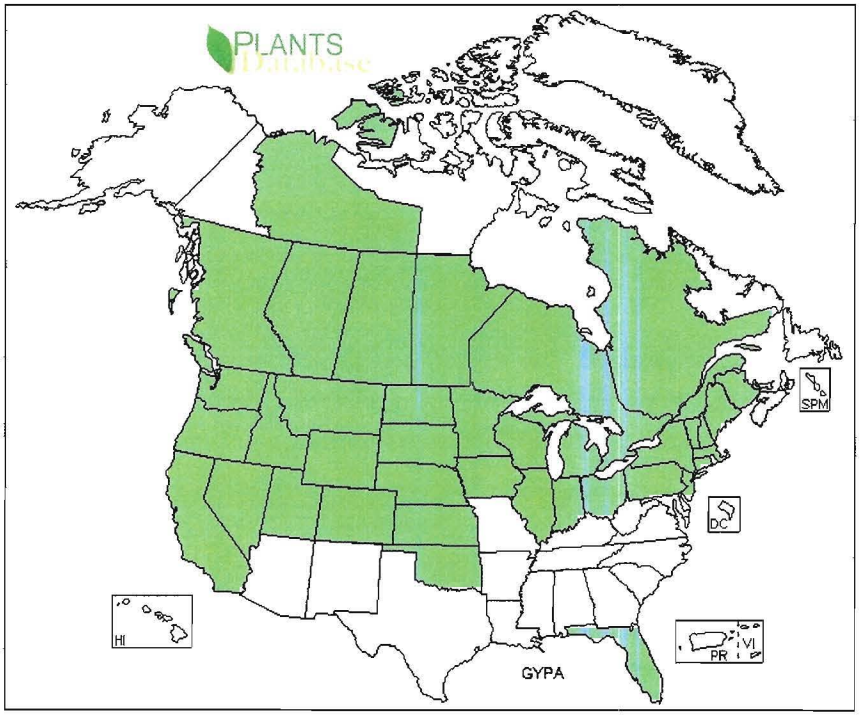

Figure 1: Distribution of naturalized *Gypsophila paniculata* in the U.S. and Canada

Gypsophila paniculata is attractive to numerous species of pollinating bees and flies (Darwent and Coupland 1966) and is considered to be predominately insect-pollinated. Seed is the only mechanism for natural reproduction with an average plant producing 13,700 seeds. Most seeds drop close to the plant; however some can be dispersed to remote locations by wind. Seeds show little or no dormancy (MAFF 2010).

It should be noted that there is a significant difference in male fertility between gypsophila that has escaped cultivation and become naturalized in the United States and the ornamental gypsophila that is grown for cut flowers marketed in auctions all over the world. Ornamental gypsophila varieties exhibit very low pollen production, which has hampered classical breeding efforts and resulted in few varieties sold worldwide (Shillo 1985, [CBI-DELETED], Rady and Hanafy 2004). The near male sterility of ornamental gypsophila diminishes the possibility of pollen dispersal to sexually compatible relatives that exist in the United States.

Cultivation methods for production of cut flowers differ by country; in some areas they are grown outdoors, while in others they are grown in heated or unheated greenhouses. The main method of propagation for cut flower production is vegetative propagation of mother plants followed by cultivation as described above. We found no reports to indicate that vegetative cuttings of *Gypsophila paniculata* (such as cut flower stems) are capable of establishing in the environment without significant human intervention required for vegetative propagation in commercial production. Additionally, Danziger has extensive experience with large-scale cultivation of gypsophila in Israel, Colombia and Ecuador and has never found gypsophila growing wild, even in the immediate vicinity of growing areas where waste material has been discarded or has been left for composting.

Production and distribution of genetically engineered *Gypsophila paniculata* cut flowers for importation

Danziger plans to conduct variety development field trials of its new gypsophila varieties in [ ]. The field trials will take place at major gypsophila production farms, which are expert in the cultivation and export of conventional CBI-DELETED gypsophila flowers. Following sufficient variety development, Danziger anticipates the first commercial sale of its new gypsophila cut flowers in the United States [ ].

Genotype and phenotype of genetically engineered *Gypsophila paniculata*

Danziger's new gypsophila varieties are genetically engineered for constitutive expression of the [

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The introduced [ ] gene results in the accumulation of anthocyanin pigments in various plant tissues, including anthers, pistils, ovaries, petals, sepals, stems, and leaves. During subsequent crosses and selections, Danziger has produced hybrids with different pigment expression patterns and intensities in various flower organs such as green stem, green foliage (leaves), red flowers; dark stem, dark foliage (leaves), red flowers; and dark stem, dark foliage (leaves), white flowers.

Danziger has confirmed the genetic stability of transformed lines by selection on [ ] media and by PCR analysis for the presence of the [ ] CBI-
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genes. Danziger has selected new varieties for advancement and commercialization based on plant phenotype and agronomic performance, which includes the level and pattern of pigment expression, as well as the fulfillment of commercial criteria such as plant architecture, flower morphology, agronomic performance, and economic yield. To date, Danziger has observed no evidence that the expression of the [ ] gene has altered the reproductive biology of these new gypsophila varieties in any manner that would compromise environmental safety. CBI-DELETED

Environmental safety

Danziger cut flowers will be imported into the United States from farms in South and Central America. The flowers pose no greater risk to the environment in the United States than any other gypsophila variety grown for cut flower production. This is because there are only three theoretical avenues of gene dispersal, none of which are possible for imported gypsophila cut flowers.

- Vegetative spread of the imported cut flowers leading to the formation of wild populations.
- Formation and dispersal of seed from the imported cut flower as a result of self fertilization or fertilization with pollen from an external source.
- Formation of seed by a recipient gypsophila plant fertilized by pollen dispersed from the imported cut flower.

The improbability of these theoretical occurrences of gene dispersal involving the new gypsophila varieties are discussed below.

Vegetative spread

Gypsophila does not spread vegetatively; it does not produce stolons, rhizomes, root-borne shoots, tubers, bulbs, corms or runners and roots will not form on discarded or old cut flowers. Danziger has experience with large scale production of gypsophila in Israel, Colombia and Ecuador and has never found gypsophila growing wild, even in the immediate vicinity of gypsophila growing areas where waste material has been discarded or has been left for composting. Even if imported cut flowers are discarded onto disturbed soil, there is no evidence to suggest that they are capable of rooting and establishing in the environment.

Formation of seed on a cut flower

For gene dispersal by seed formation to occur from a cut gypsophila flower, the following events would all need to occur successfully: arrival of viable pollen on the stigma of the gypsophila, pollen germination, pollen tube growth to the ovule of the gypsophila, fertilization, seed formation and seed dispersal. Notwithstanding that successful pollination of a gypsophila flower in a vase is highly unlikely, no seed set could occur. This is because the process of seed development takes four to six weeks during which the growth of any developing embryo must be sustained. A cut flower will survive for less time than this, ordinarily only two weeks. Additionally, gypsophila flowers are picked from the mother plant when about 30% of the flowers are open. Therefore, the probability of seed set is further limited to only those flowers that might have been fertilized prior to harvest.

Pollen dispersal from a cut flower leading to a successful hybridization event

There are several mutually exclusive facts that, in combination, indicate that potential pollen spread is not a feasible avenue for gene dispersal.

- First, the potential for pollen spread from a cut flower is only theoretically possible. In general, production of viable pollen by cultivated gypsophila is much lower than that of wild or naturalized gypsophila. Additionally, gypsophila pollen is viable for approximately 12–24 hours during which time the cut flower is physically isolated in commercial distribution channels and not in proximity to receptive native populations.
- Hybridization of gypsophila in nature is facilitated by insect pollination and is only effectively achieved by Hymenoptera and Diptera (pollinating bees, flies). Pollen is not spread by wind. Gypsophila flowers are numerous, but relatively small, which would appear to diminish their relative attractiveness to pollinators.
- Cut flowers are distributed and marketed in contained structures (vehicles, buildings, retail stores). The only point in the distribution chain where insects could be reasonably expected to access flowers is when the flowers are on display or in the hands of the consumer.
- The existence of so very few commercial gypsophila varieties in worldwide commercial production is further evidence of the difficulties with successful pollination and seed production even in the hands of knowledgeable and skilled breeders.

Safety to human health

There are no potential harmful effects from handling the transgenic gypsophila flowers and the flower produce no wind borne pollen. Gypsophila has been used safely by humans for ornamental purposes for centuries. The increased production of anthocyanins is novel for gypsophila, but there are many flowers and other ornamental species that produce anthocyanins and such pigments are also present in many raw foods, such as grapes, blueberry and other edible foods. The introduced genes [ ] are derived from a well characterized plant species and a common intestinal microorganism, respectively. Neither gene is derived from a known allergenic source, nor do they share any significant homology to known human allergens using internationally accepted criteria for evaluating new proteins in genetically engineered crops (FARRP 2010). Incidental contact or consumption of the flowers should therefore pose no risk to human health.

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Summary

Danziger believes that the importation and commercial distribution of cut flowers of genetically engineered *Gypsophila paniculata* described above does not pose an unreasonable risk to the environment for the following reasons:

a. The introduced genes do not change the biology of *Gypsophila paniculata* in ways that compromise environmental or human safety;

b. The cut flowers are highly unlikely to become established or persist in the natural environment by any of the identified means; and

c. Gene dispersal from the cut flowers is highly unlikely to occur by any of the identified means.

Danziger respectfully requests USDA-APHIS to confirm that cut flowers of genetically engineered *Gypsophila paniculata* are not regulated articles under 7 CFR Part 340 and may be legally imported into and distributed in the United States.

References

AFIF. 2010. South Florida industry statistics. Association of Floral Importers of Florida, http://www.afifnet.org, September 30, 2010.

[CBI-DELETED]

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Darwent, A.L. and R.T. Coupland. 1966. Life history of *Gypsophila paniculata*. Weeds 14, 313-318.

Douglas, G.W., G.B. Straley, D. Meidinger and J. Pojar. 1998. Illustrated flora of British Columbia. British Columbia, Ministry of Environment, Lands and Parks, Ministry of Forest, v.1. 436 pp.

FARRP. 2010. AllergenOnline Database, version 10.0. http://www.allergenonline.org, September 29, 2010.

[CBI-DELETED]

MAFF 2010. Government of British Columbia, Ministry of Agriculture, Food and Fisheries. Pest management. Aggressive ornamentals. Baby's breath (*Gypsophila paniculata*), http://www.agf.gov.bc.ca/cropprot/index.htm, September 15, 2010.

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Rady, M.R. and M.S. Hanafy. 2004. Synthetic seed technology for encapsulation and regrowth of *in vitro*-derived *Gypsophila paniculata* L. shoot-tips. Arab J. Biotech. 7, 251-264.

Royer, F. and R. Dickinson. 1999. Weeds of the Northern U.S. and Canada. The University of Alberta press. 434 pp.

Rutledge, C.R. and T. McLendon. 1996. An assessment of exotic plant species of Rocky Mountain National Park. Department of Rangeland Ecosystem Science, Colorado State University. http://www.npwrc.usgs.gov/resource/plants/explant/gypspani.htm.

Shillo, R. 1985. *Gypsophila paniculata.* In: Halevy, A.H. (ed) Handbook of flowering. vol. 3. CRC Press Inc., Boca Raton. p. 83.

USDA FAS. 2010. Global agricultural statistics, http://www.fas.usda.gov/gats/default.aspx, September 30, 2010.

USDA NRCS. 2010. The PLANTS Database, http://plants.usda.gov, September 15, 2010. National Plant Data Center, Baton Rouge, LA 70874-4490 USA.

Whitson, T.D., L.C. Burrill, S.A. Dewey, D.W. Cudney, B.E. Nelson, R.D. Lee, and R. Parker. 2000. Weeds of the West. The Western Society of Weed Science in cooperation with the Western United States Land Grant Universities, Cooperative Extension Services. University of Wyoming. Laramie, Wyoming. 630 pp.

Wisconsin DNR. 2010. Invasive plants of the future: Baby's breath, http://dnr.wi.gov/invasives/fact/babys_breath.htm, September 15, 2010. WI Department of Natural Resources, Madison, WI 53707-7921 USA.

[CBI-DELETED]