B. Summary

Dow AgroSciences LLC (herein referred to as "DAS") and M.S. Technologies LLC (herein referred to as "MS Tech") are submitting an application to amend the Food Standards Code Standard 1.5.2 to approve the use of DAS-444Ø6-6 Soybean; a new food produced using gene technology.

Dow AgroSciences considers this to be a major procedure under the FSANZ assessment procedures. This application is expected to confer and Exclusive Capturable Commercial Benefit.

This submission includes a dossier which addresses all the items identified by FSANZ as necessary to establish food safety and the supporting reports (as per section 3.5.1 of the FSANZ Application Handbook, 1st August, 2011). Only reports produced by Dow Agrosciences or The Dow Chemical Company are provided. All other citations are available but since these are from published literature have not been copied. Any or all of these citations will be forwarded if requested.

The references provided (Attachment 1) are proprietary information which is owned by and has value to Dow Chemical and their subsidiary Companies. These reports may not be used or referenced by any other company or person without our express agreement.

DAS-444Ø6-6 soybean is a transgenic soybean product that provides tolerance to the herbicides 2,4-dichlorophenoxyacetic acid (2,4-D), glyphosate and glufosinate. This herbicide-tolerant soybean will provide growers with greater flexibility in selection of herbicides for the improved control of economically important weeds; allow an increased application window for effective weed control; and provide an effective weed resistance management solution to the increased incidence of glyphosate resistant weeds.

DAS-444Ø6-6 soybean plants have been genetically modified to express the aryloxyalkanoate dioxygenase-12 (AAD-12), double mutant 5-enolpyruvylshikimate-3-phosphate synthase (2mEPSPS), and phosphinothricin acetyltransferase (PAT) proteins. The AAD-12 protein is an enzyme with an alpha ketoglutarate-dependent dioxygenase activity which results in metabolic inactivation of the herbicides of the aryloxyalkanoate family. The *aad-12* gene, which expresses the AAD-12 protein, was derived from *Delftia acidovorans*, a gram-negative soil bacterium. The 2mEPSPS protein has a decreased sensitivity to the herbicide glyphosate, allowing the enzyme to function in the presence of the herbicide and thereby making the plant tolerant to glyphosate. The 2mEPSPS protein is encoded by a modified version of the *epsps* gene from corn (*Zea mays*). The PAT enzyme acetylates the primary amino group of phosphinothricin rendering it inactive. The *pat* gene expressing the PAT protein was derived from *Streptomyces viridochromogenes*.

The *aad-12, 2mepsps* and *pat* genes were introduced into DAS-444Ø6-6 soybean using *Agrobacterium*-mediated transformation. Molecular characterization by Southern blot analyses of DAS-444Ø6-6 soybean confirmed that a single, intact DNA insert containing the *aad-12, 2mepsps* and *pat* gene expression cassettes was stably integrated into the soybean genome. Southern blot analyses also confirmed the absence of the plasmid backbone DNA in DAS-444Ø6-6 soybean. The integrity of the inserted DNA was demonstrated in five different breeding generations. Data from segregating generations confirmed the predicted Mendelian inheritance pattern. These data confirmed the stability of DAS-444Ø6-6 soybean during traditional breeding procedures.

The AAD-12, 2mEPSPS and PAT proteins in DAS-444Ø6-6 soybean were characterized biochemically and measured using protein-specific enzyme linked immunosorbent assays (ELISA). Protein expression was analysed in leaf, root, whole-plant and grain tissues collected throughout the growing season from DAS-444Ø6-6 soybean plants treated with 2,4-D, glyphosate, glufosinate, all three herbicides in combination, or not treated with any of these herbicides. The results showed a low level of expression of the AAD-12, 2mEPSPS, and PAT proteins across herbicide treatments and environments, indicating a low exposure to humans and animals.

The AAD-12 protein was assessed for any potential adverse effects to humans or animals resulting from the environmental release of crops containing the AAD-12 protein. A step-wise, weight-of-evidence approach was used to assess the potential for toxic or allergenic effects from the AAD-12 protein. Bioinformatic analyses revealed no meaningful homologies with known or putative allergens or toxins for the AAD-12 amino acid sequence. The AAD-12 protein hydrolysed rapidly in simulated gastric fluid. There was no evidence of acute toxicity in mice at a dose of 2000 mg/kg body weight of AAD-12 protein. Glycosylation analysis revealed no detectable covalently linked carbohydrates in the AAD-12 protein expressed in DAS-444Ø6-6 soybean plants. The low level expression of the AAD-12 protein presents a low exposure risk to humans and animals, and the results of the overall safety assessment of the AAD-12 protein indicate that it is unlikely to cause allergenic or toxic effects in humans or animals.

The 2mEPSPS protein was assessed for any potential adverse effects to humans and animals resulting from the environmental release of crops containing the 2mEPSPS protein. A step-wise, weight-of-evidence approach was used to assess the potential for toxic or allergenic effects from the 2mEPSPS protein. Bioinformatic analyses revealed no meaningful homologies to known or putative allergens or toxins for the 2mEPSPS amino acid sequence. The 2mEPSPS protein hydrolysed rapidly in simulated gastric fluid. There was no evidence of acute toxicity in mice at a dose of 5000 mg/kg body weight of 2mEPSPS protein. Glycosylation analysis revealed no detectable covalently linked carbohydrates in the 2mEPSPS protein expressed in DAS-444Ø6-6 soybean plants. The low level expression of the 2mEPSPS protein presents a low exposure risk to humans and animals, and the results of the overall

safety assessment of the 2mEPSPS protein indicate that it is unlikely to cause allergenic or toxic effects in humans or animals. The safety of the 2mEPSPS protein has been assessed previously and it has been approved for use in corn and cotton.

The PAT protein was assessed for any potential adverse effects to humans and animals resulting from the environmental release of crops containing the PAT protein. A step-wise, weight-of-evidence approach was used to assess the potential for toxic or allergenic effects from the PAT protein. Bioinformatic analyses revealed no meaningful homologies to known or putative allergens or toxins for the PAT amino acid sequence. The PAT protein hydrolysed rapidly in simulated gastric fluid. There was no evidence of acute toxicity in mice at a dose of 5000 mg/kg body weight of PAT protein. The low level expression of the PAT protein presents a low exposure risk to humans and animals, and the results of the overall safety assessment of the PAT protein indicate that it is unlikely to cause allergenic or toxic effects in humans or animals. The safety of the PAT protein has been assessed previously and it has been approved for use in canola, corn, cotton, rice, soybeans, and sugar beets.

Nutrient composition analyses of forage and grain were conducted to compare the composition of DAS-444Ø6-6 soybean with the composition of a non-transgenic control. Compositional analyses were used to evaluate any changes in the levels of key nutrients and anti-nutrients in DAS-444Ø6-6 soybean which was treated with 2,4-D, glyphosate, glufosinate, all three herbicides in combination, or not treated with any herbicide. Along with the agronomic data, the compositional analyses indicate that DAS-444Ø6-6 soybean is substantially equivalent to conventional soybean and will not exhibit unexpected or unintended effects with respect to plant pest risk.

Since DAS-444Ø6-6 soybean is agronomically and nutritionally similar to conventional soybean, and the safety of the AAD-12, 2mEPSPS and PAT proteins has been demonstrated, no significant impact is expected on current crop production practices, non-target or endangered species, crop rotation, volunteer management, or commodity food and feed soybean products.

The availability of DAS-444Ø6-6 soybean is expected to have a beneficial impact on weed control practices by providing growers with another tool to address their weed-control needs. The use of DAS-444Ø6-6 soybean will allow growers to proactively manage weed populations while avoiding adverse population shifts of troublesome weeds or the development of resistance, particularly glyphosate-resistance in weeds.

In summary, Dow AgroSciences are seeking an amendment of Standard 1.5.2 by inserting: food derived from Herbicide Tolerant DAS-444Ø6-6 soybean line, into column 1 of the Table to clause 2, immediately after the last entry by means of this application.