

## Outcome of step 2 of the call for data on E 140(i) chlorophylls, E 140(ii) chlorophyllins, E 141(i) copper complexes of chlorophylls and E 141(ii) copper complexes of chlorophyllins

### Chlorophylls (E 140(i))

The Natural Food Colours Association (NATCOL) has committed to submitting the data requested in the call for scientific and technical data on the permitted food additive chlorophylls E 140(i). The deadlines for data submission are indicated below.

- Data on the definition and identity of the food additive E 140(i) including data on components with biological activity (e.g. phytoestrogens, phytotoxins and allergens): November 2018
- Data on actual levels of ethanol and methanol in E 140(i): November 2018
- Data on the lowest achievable limits for the impurities of toxic elements (arsenic, lead, mercury and cadmium): November 2018

### Copper complexes of chlorophyllins (E 141(ii))

The business operator FMC Corporation has committed to submitting the data requested in the call for scientific and technical data on the permitted food additive copper complexes of chlorophyllins (E 141(ii)). The milestones and deadlines for data submission are indicated below.

- Data on the definition and identity of the food additive E 141(ii): April 2018
- Toxicological data

For E141(ii) Copper complexes of chlorophyllins		
Preliminary investigations	In Vitro Intestinal absorption (CACO-2) In vitro ADME investigations: Metabolic stability Hepatobiliary disposition Enzyme induction/inhibition Detection of glucuronide Heme oxygenase inhibition Oxidative stress	In progress Completion: Oct 2017
Phase 1	In vitro genotoxicity testing: Ames test Micronucleus assay	Completed: September 2017
	Follow-up in vivo genotoxicity study bioanalytical method development/validation & Study execution	Study start Q1/2 2018 Completion expected Q3 2018
Review	Review of in vitro data and design & planning of Phase 2 studies (including bioanalytical method validation)	Start Q3 2017 Complete Q2 2018

Phase 2	In vivo ADME study	Start Q2 2018 Complete Q4 2018
	28 day range finding study	Start Q3 2018; complete Q1 2019
	90 day study	Start Q1 2019 Finish Q1 2020
Phase 3	Possible Chronic toxicity & carcinogenicity study, reproductive and developmental toxicity study, teratology study  To be determined after evaluation of data from Phase 2	up to 3 years depending on study requirements  completion by mid 2023
<p>The studies are being phased based on the EFSA guidance and also in order to be able to use data in earlier studies in order to better design the later studies. For instance, data generated in the ADME study will be useful in the design of the 90 day study.</p>		

- Data on the lowest achievable limits for the impurities of toxic elements (arsenic, lead, mercury and cadmium): April 2018

### **Chlorophyllins (E 140(ii))**

The business operator FMC Corporation has committed to submitting the data requested in the call for scientific and technical data on the permitted food additive chlorophyllins E 140(ii). The milestones and deadlines for data submission are indicated below.

- Data on the definition and identity of the food additive E 140(ii): April 2018
- Toxicological data:

For E140(ii) Chlorophyllins		
Phase 1	In vitro genotoxicity testing: Ames test Micronucleus assay  In vitro Intestinal absorption (CACO-2)  In vitro ADME investigations: Metabolic stability Hepatobiliary disposition Enzyme induction/inhibition Detection of glucuronide Heme oxygenase inhibition Oxidative stress	In progress Completion: October 2017
Phase 1	In vitro genotoxicity testing: Ames test Micronucleus assay	Completed: September 2017

	Follow-up in vivo genotoxicity study (including bioanalytical method validation)	Study start Q1/2 2018 Completion expected Q3 2018
Phase 2	90 day study	Already completed
E140(ii) Chlorophyllins are present in the coppered chlorophyllin and therefore it is anticipated that the above data combined with the studies on E141(ii) will provide an adequate toxicological database		

- Data on the lowest achievable limits for the impurities of toxic elements (arsenic, lead, mercury and cadmium): April 2018

### **Copper complexes of chlorophylls (E 141(i))**

The business operator FMC Corporation has committed to submitting the data requested in the call for scientific and technical data on the permitted food additive copper complexes of chlorophylls (E 141(i)). The milestones and deadlines for data submission are indicated below.

- Data on the definition and identity of the food additive E 141(i): January 2019
- Toxicological data:

For E141(i) Copper complexes of chlorophylls		
Phase 1	In vitro genotoxicity testing: Ames test Micronucleus assay Intestinal absorption (CACO) In vitro ADME investigations: Metabolic stability Hepatobiliary disposition Enzyme induction/inhibition Detection of glucuronide Heme oxygenase inhibition Oxidative stress	In progress Completion: November 2017
Review	Review of in vitro data and determination whether bridging is possible or additional studies are required	Start November 2017 Complete April 2018

- Data on the lowest achievable limits for the impurities of toxic elements (arsenic, lead, mercury and cadmium): April 2018