*This single cover page is to be included; applicant is not to apply additional formatting to this document or insert new headers/footers, table of contents, extraneous information etc. Sample/guidance text for all data requirements is in red and is to be amended as appropriate.*

**Active Substance / Ingredient**

Product Chemistry Evaluation

(based on OECD Dossier Numbering)

Identity, Physical and Chemical Properties, Analytical Methods, Confidential Information

Prepared by: Applicant

Reviewed/edited by: Primary chemistry reviewer, Regulatory Authority

Secondary chemistry reviewer, Regulatory Authority

Approved by: Approving manager, Regulatory Authority responsible for primary review

Approving manager, Regulatory Authority responsible for secondary review

*Placeholder page for Agency-specific administrative information*

* *PMRA will capture submission number, source code, registration number, submission history, introduction, summary of findings, conclusion, chemical equivalence assessment as applicable (appended after CBI portion), peer review and signature blocks*
* *EPA will capture DP barcode, registration/file symbol number, product code, decision number, introduction, summary of findings, conclusions, chemical equivalence assessment as applicable (appended after CBI portion), peer review and signature blocks*

TABLE OF CONTENTS

[IIA 1.0 IDENTITY OF THE ACTIVE SUBSTANCE/INGREDIENT 4](#_Toc425324975)

[IIA 1.1 Applicant 4](#_Toc425324976)

[IIA 1.3 Common name 4](#_Toc425324977)

[IIA 1.4 Chemical name 4](#_Toc425324978)

[IIA 1.5 Manufacturer’s codes and names 4](#_Toc425324979)

[IIA 1.6 CAS and CIPAC numbers 4](#_Toc425324980)

[IIA 1.7 Molecular and structural formula, molecular mass 4](#_Toc425324981)

[IIA 1.9.1 Guarantee of active ingredient (excluding inactive isomers) 4](#_Toc425324982)

[IIA 1.12 Other/special studies 4](#_Toc425324983)

[IIA 2.0 PHYSICAL AND CHEMICAL PROPERTIES OF THE ACTIVE SUBSTANCE / INGREDIENT 5](#_Toc425324984)

[IIA 4.0 ANALYTICAL METHODS AND VALIDATION 12](#_Toc425324985)

[IIA 4.1 Analytical standards and samples 12](#_Toc425324986)

[IIA 4.2 Method for the analysis of the active substance as manufactured 12](#_Toc425324987)

[CONFIDENTIAL BUSINESS INFORMATION (CBI) 14](#_Toc425324988)

[IIA 1.2 Manufacturer 14](#_Toc425324989)

[IIA 1.8 Method of manufacture of the active ingredient 14](#_Toc425324990)

[IIA 1.10 Identity and structural formula of isomers, impurities, and additives 14](#_Toc425324991)

[IIA 1.9 Specification of purity of the active ingredient 15](#_Toc425324992)

[IIA 1.11 Batch analysis data 16](#_Toc425324993)

[REFERENCES RELIED ON 18](#_Toc425324994)

# IIA 1.0 IDENTITY OF THE ACTIVE SUBSTANCE/INGREDIENT

## IIA 1.1 Applicant

DACO 2.1 / OPPTS 830.1550

**In the United States of America**:  
Company A (the proposed owner of the registration in the U.S.) including address

**In Canada**:  
Company B (the proposed owner of the registration in Canada) including address

**Contacts:**

Global Name, address, telephone, e-mail, fax

USA As above

Canada As above

|  |  |
| --- | --- |
| IIA 1.3 Common name DACO 2.4 / OPPTS 830.1550 | As proposed or approved by ISO; otherwise, industry standard |
| IIA 1.4 Chemical name DACO 2.5 / OPPTS 830.1550 | **IUPAC:** As approved by ISO (may be multiple versions including Preferred IUPAC Name [PIN])  **CAS:** As approved by ISO |
| IIA 1.5 Manufacturer’s codes and namesIIA 1.5.1 Manufacturer’s development code number(s) DACO 2.3.1 / OPPTS 830.1550 | Development code number(s) |
| IIA 1.5.2 Trade names DACO 2.3 / OPPTS 830.1550 | Proposed trade name in each country |
| IIA 1.6 CAS and CIPAC numbers DACO 2.6 / OPPTS 830.1550 | CAS number:  CIPAC number: If assigned |
| IIA 1.7 Molecular and structural formula, molecular mass DACO 2.7, 2.8, 2.9 / OPPTS 830.1550 | Molecular formula: |
| Structural formula: |
| Molecular mass: g/mol |
| IIA 1.9.1 Guarantee of active ingredient (excluding inactive isomers) DACO 2.12.1 / OPPTS 830.1550 | Nominal guarantee (or minimum if applicable) of active ingredient in % |

## IIA 1.12 Other/special studies

DACO 2.16

If applicable

# 

# IIA 2.0 PHYSICAL AND CHEMICAL PROPERTIES OF THE ACTIVE SUBSTANCE / INGREDIENT

| Annex IIA Point Test or property | Guideline and method | Test material purity and specification | Study findings and applicant comments | Reviewer conclusions | Data accepted 1 | GLP Y/N | Reference |
| --- | --- | --- | --- | --- | --- | --- | --- |
| IIA 2.1.1 Melting point / melting range | OECD 102, DACO 2.14.4, OPPTS 830.7200 | Lot number, purity | The melting point of the pure active ingredient (PAI) was determined to be …°C, using …  The melting point of the technical grade active ingredient (TGAI) was determined to be …°C, using … |  |  |  | Applicant report #  PMRA #  MRID # |
| IIA 2.1.2 Boiling point / boiling range | OECD 103, DACO 2.14.5, OPPTS 830.7220 |  | The boiling point of the PAI was determined to be …°C, using …  The boiling point of the TGAI was determined to be …°C, using … |  |  |  |  |
| IIA 2.1.3 Temperature of decomposition or sublimation | OECD 102 |  | The decomposition temperature of the PAI was determined to be …°C, using …  The decomposition temperature of the TGAI was determined to be …°C, using …  OR  Not required by PMRA or EPA |  |  |  |  |
| IIA 2.2 Relative density / density | OECD 109, DACO 2.14.6, OPPTS 830.7300 |  | The (relative) density of the PAI was determined to be … at …°C, using …  The (relative) density of the TGAI was determined to be … at …°C, using … |  |  |  |  |
| IIA 2.3.1 Vapour pressure | OECD 104, DACO 2.14.9, OPPTS 830.7950 |  | The vapour pressure of the PAI was determined using … The results are reported below:  temperature (°C) vapour pressure (Pa) |  |  |  |  |
| IIA 2.3.2 Henry’s law constant | Calculated using solubility and vapour pressure |  | Refer to the environmental fate review. |  |  | N/A |  |
| IIA 2.4.1 Appearance: colour | Visual assessment, DACO 2.14.1, OPPTS 830.6302 |  | The PAI is …  The TGAI is … |  |  |  |  |
| IIA 2.4.1 Appearance: physical state | Visual assessment, DACO 2.14.2**,** OPPTS 830.6303 |  | The PAI is a …  The TGAI is a … |  |  |  |  |
| IIA 2.4.2 Appearance: odour | Olfactory assessment, DACO 2.14.3, OPPTS 830.6304 |  | The odour of the PAI is …  The odour of the TGAI is … |  |  |  |  |
| IIA 2.5.1.1 + 2.5.1.5 UV/Vis spectrum of active substance / Molecular extinction coefficient of active substance | OECD 101, DACO 2.14.12, OPPTS 830.7050 |  | UV absorption of the PAI was measured using …  conditions λmax (nm) ε (L/mol.cm)  acidic  basic  neutral |  |  |  |  |
| IIA 2.5.1.2 IR spectrum of active substance | DACO 2.13.2 |  | The IR spectrum for the PAI was obtained using … The interpretation of the IR bands was reported in … and is consistent with the structure. |  |  |  |  |
| IIA 2.5.1.3 NMR spectrum of active substance | DACO 2.13.2 |  | The 13C-NMR and 1H-NMR spectra were obtained using …. Assignments of chemical shifts were reported in … and are consistent with the structure. |  |  |  |  |
| IIA 2.5.1.4 MS spectrum of active substance | DACO 2.13.2 |  | The mass spectrum for the PAI was obtained using … The interpretation of the signals was reported in … and is consistent with the structure. |  |  |  |  |
| IIA 2.5.1.6 Optical purity of active substance / optical isomer ratio |  |  | The ratio of the enantiomers in the TGAI was determined to be …, obtained using … |  |  |  |  |
| IIA 2.5.2 Spectra for relevant impurities (i.e. of toxicological concern) | DACO 2.13.2 |  | Refer to confidential section of this review |  |  |  |  |
| IIA 2.6 Solubility in water | OECD 105, DACO 2.14.7, OPPTS 830.7840, OPPTS 830.7860 |  | The water solubility of the active ingredient was determined using … The results are reported below:  pH solubility (units) at …°C |  |  |  |  |
| IIA 2.7 Solubility in organic solvents | OECD 105, DACO 2.14.8, OPPTS 830.1000, CIPAC MT 181 |  | The solubility of the active ingredient in various organic solvents was determined using … The results are reported below:  solvent solubility (units) at …°C |  |  |  |  |
| IIA 2.8 Partition coefficient n-octanol / water including effect of pH (4 to 10) | OECD 107, DACO 2.14.11, OPPTS 830.7550, 830.7560, 830.7570 |  | The Kow of the active ingredient was determined to be … using … The log Kow was calculated to be …  If applicable:  pH Kow log Kow |  |  |  |  |
| IIA 2.9.1 Hydrolysis rate at pH 4, 7, and 9 under sterile conditions in the absence of light |  |  | Refer to the environmental fate review. |  |  |  |  |
| IIA 2.9.2 Direct photo-transformation |  |  | Refer to the environmental fate review. |  |  |  |  |
| IIA 2.9.3 Quantum yield of direct photo-transformation |  |  | Refer to the environmental fate review. |  |  |  |  |
| IIA 2.9.4 Calculated theoretical lifetime in the top layer of aqueous systems and the real lifetime of the active substance |  |  | Refer to the environmental fate review. |  |  |  |  |
| IIA 2.9.5 Dissociation constant | OECD 112, DACO 2.14.10, OPPTS 830.7370 |  | The dissociation constant (pKa) for the active ingredient was determined in … (state medium) using … and was found to be … |  |  |  |  |
| IIA 2.10 Estimated photochemical oxidative degradation |  |  | Refer to the environmental fate review. |  |  |  |  |
| IIA 2.11.1 Flammability (solids) | EC A.10 |  | Not required by PMRA or EPA |  |  |  |  |
| IIA 2.11.2 Auto-flammability | EC A.16 |  | Not required by PMRA or EPA |  |  |  |  |
| IIA 2.12 Flash point (liquids) | EC A.9, OPPTS 830.6315 |  | Not required by PMRA for technical materials; may be required by EPA |  |  |  |  |
| IIA 2.13 Explosive properties | EC A.14, OPPTS 830.6316 |  | Not required by PMRA for technical materials; may be required by EPA |  |  |  |  |
| IIA 2.14 Surface tension | EC A.5, OECD 115 |  | Not required by PMRA or EPA |  |  |  |  |
| IIA 2.15 Oxidising and reducing properties / chemical incompatibility | EC A.17, OPPTS 830.6314 |  | Not required by PMRA for technical materials; required by EPA |  |  |  |  |
| IIA 2.16 pH | DACO 2.14.15, OPPTS 830.7000, CIPAC MT 75 |  | The pH of (a 1% dilution of) the PAI was determined as …  The pH of (a 1% dilution of) the TGAI was determined as … |  |  |  |  |
| IIA 2.17.1 Storage stability | DACO 2.14.14, OPPTS 830.6317 |  | The TGAI was stored for … (state conditions / duration) in … (state container material). Results at regular intervals (…) demonstrated that …  Required by PMRA only for ISPs. |  |  |  |  |
| IIA 2.17.2 Stability (temperature, metals) | DACO 2.14.13, OPPTS 830.6313, CIPAC MT 46 |  | The TGAI is stable upon exposure to … |  |  |  |  |
| IIA 2.18 Other/special studies  PMRA: Nanomaterial characteristics  EPA: Particle size, fiber length, & diameter distribution  EPA: Corrosion Characteristics | DACO 2.14.16  OPPTS 830.7520  OPPTS 830.6320 |  | Required by PMRA if the technical product is a nanomaterial  Required by EPA. For nanomaterials, please contact appropriate product manager.  Required by EPA. |  |  |  |  |
| 1 A = acceptable, N = not acceptable, NR = not required, NA = not applicable, G = data gap, U = requires upgrading, W = waived | | | | | | | |

# IIA 4.0 ANALYTICAL METHODS AND VALIDATION

## IIA 4.1 Analytical standards and samples

DACO 2.15 / OPPTS 830.1900

Submittal of sample and analytical standard (PMRA requires only the standard).

## IIA 4.2 Method for the analysis of the active substance as manufactured

### IIA 4.2.1 Method for the determination of pure active substance as manufactured

DACO 2.13.1 / OPPTS 830.1800

Reference: Author, year, title, company, report number, GLP Y/N

PMRA #, MRID #

| **Table 4.2.1-1. Details of the analytical method used to determine the active** | |
| --- | --- |
| Method ID | Company A Method 1.1 |
| Analyte | Active ingredient |
| Sample preparation | 100 mg of technical product is dissolved in 10 mL of solvent… |
| Instrument | HPLC |
| Detector | MS-MS *OR* UV at … nm |
| Column | Company B tradename, dimensions |
| Mobile phase (for LC) or oven temperature gradient (for GC) |  |
| Quantitation | e.g. By external standard (lot #, purity) obtained from Commercial Source C *OR* synthesized/characterized by the applicant – see IIA 4.2.3 |
| Total run time |  |
| *footnotes as applicable; table to be tailored to suit method if needed (e.g. titration)* | |

Specificity was evaluated by … (state method). The remaining validation data are summarized below.

| **Table 4.2.1-2. Method validation data** | | | | | |
| --- | --- | --- | --- | --- | --- |
| Component  Method type / ID | Linearity (w %) / Correlation coefficient | Retention time (min) | Accuracy as recovery (%) | Precision as RSD (%) | LOD and / or LOQ (%) 1 |
| Active  HPLC-MS/MS / Method 1.1 |  |  |  |  |  |
| 1 For instrument or method (select appropriate)  *other footnotes as applicable – e.g. details of accuracy or precision determination* | | | | | |

A validated analytical method was provided for determination of the active in five batches of the technical product and was assessed to be … for this purpose.

### IIA 4.2.2 + 6 + 7 Applicability of existing CIPAC methods / Inter-laboratory analytical methodology validation / Storage stability of working solutions in analytical method

Not required by PMRA or EPA

### IIA 4.2.5 Enforcement analytical methodology

OPPTS 830.1800

### Not required by PMRA. Required by EPA but may be referenced to method reviewed under IIA 4.2.1.

# CONFIDENTIAL BUSINESS INFORMATION (CBI)

## IIA 1.2 Manufacturer

DACO 2.2 / OPPTS 830.1550

Manufacturer of the technical grade of active ingredient, including name and physical address of plant

## IIA 1.8 Method of manufacture of the active ingredient

### IIA 1.8.2 Description of starting materials

DACO 2.11.2 / OPPTS 830.1600

Reference: Author, year, title, company, report number, GLP Y/N

PMRA #, MRID #

### IIA 1.8.1 Method of manufacture ~~(~~synthesis pathway) of the active ingredient

DACO 2.11.3 / OPPTS 830.1620

Reference: Author, year, title, company, report number, GLP Y/N

PMRA #, MRID #

Synthetic pathway to manufacture the technical grade of active ingredient, including reaction conditions, detailed text description, chemical reactions and full chemical names

## IIA 1.10 Identity and structural formula of isomers, impurities, and additives

### IIA 1.10.1+2 Inactive isomers / Impurities and additives

DACO 2.11.4 / OPPTS 830.1670

Reference: Author, year, title, company, report number, GLP Y/N

PMRA #, MRID #

Include origin of impurities with reference to manufacturing process.

| **Table 1.10.2-1. Chemical names, company codes, possible origins and chemical structures of impurities** | | | |
| --- | --- | --- | --- |
| Chemical name | Code | Possible origin | Structure |
|  | Isomer A |  |  |
|  | Impurity A |  |  |

**DACO 2.13.4 Impurities of human health or environmental (toxicological) concern**

Reference: Author, year, title, company, report number, GLP Y/N

PMRA #, MRID #

Impurities of human health or environmental concern are not expected to be present in the technical product (PMRA would use specific standard text here) *OR* The applicant has provided data for the following impurities of concern found in the technical product.

| **Table 1.10.2-2. Analytical data for impurities of concern in technical product** | | | |
| --- | --- | --- | --- |
| Impurity of concern | Analytical method used to obtain data (see IIA 4.2.3 for details) | Range in five batches (units) | LOQ and / or LOD |
| e.g. Polychlorinated dibenzodioxins and furans (list individually as analyzed)  PMRA: TSMP Track 1 substance |  | ND at 0.1 ppm - 11 ppm |  |
| e.g. Tetra- to hexachlorobenzene (list individually as analyzed)  PMRA: TSMP Track 1 substance |  |  |  |
| e.g. Heavy metals (list individually as analyzed) |  |  |  |
| *footnotes as applicable*  ND = not detected | | | |

## IIA 1.9 Specification of purity of the active ingredient

### IIA 1.9.3 Specification form + certified limits

DACO 2.12 + 2.12.1 / OPPTS 830.1700 + 830.1750

Reference: Specification form dated …

PMRA #, MRID #

| **Table IIA 1.9.3-1. Specifications and batch analytical data of technical product** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| Component | CAS # | Nominal % | Lower % | Upper % | Batch range % (n = 5) | Confirmation method |
|  |  |  |  |  | xx – xx%  = | LC-MS-MS |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| Material accountability | |  | | |  | |
|  | | | | | | |

## IIA 1.11 Batch analysis data

### IIA 1.11.1 Analytical profile of batches

DACO 2.13.3 / OPPTS 830.1700

Reference: Author, year, title, company, report number, GLP Y/N

PMRA #, MRID #

Include lot numbers, dates of manufacture, and scale (pilot or commercial) for each manufacturing site as applicable. For actual results, either leave only as summary in IIA 1.9.3 above or give details for each batch here as additional information.

### IIA 1.11.2 Results of analysis of batches produced in laboratory or pilot scale production systems and used in toxicological testing

Not required by EPA or PMRA HED.

### IIA 2.5.2 Spectra for impurities (confirmation of identity)

DACO 2.13.2 / OPPTS 830.1700

Reference: Author, year, title, company, report number, GLP Y/N

PMRA #, MRID #

The identity of the active ingredient was confirmed spectroscopically (see IIA 2.5.1). The identity of each impurity was confirmed by comparison of chromatographic retention time and UV spectrum between the sample and reference standard. Each standard was either obtained commercially or synthesized/characterized by the applicant using HPLC for purity and NMR for identity. The supporting characterization data were provided and were consistent with the stated structures.

### IIA 4.2.3 + 4 Methods of analysis for the determination of impurities / additives

DACO 2.13.1 / OPPTS 830.1700

Reference: Author, year, title, company, report number, GLP Y/N

PMRA #, MRID #

| **Table 4.2.3-1. Details of the analytical methods used to determine impurities in technical product.** | | |
| --- | --- | --- |
| Method ID | Company A Method 1.1 | Company A Method 2.1 |
| Analyte | Impurities A, B, C and D | Solvent E |
| Sample preparation | 100 mg of technical product is dissolved in 10 mL of solvent… |  |
| Instrument | HPLC | GC |
| Detector | MS-MS | FID |
| Column | Company B tradename, dimensions |  |
| Mobile phase (for LC) or oven temperature (for GC) | Gradient … | Isocratic … |
| Quantitation | By external standard (lot #, purity) obtained from Commercial Source C *OR* synthesized/characterized by the applicant – see IIA 2.5.2 |  |
| Total run time |  |  |
| *footnotes as applicable* | | |

Specificity was evaluated by … (state method). The remaining validation data are summarized below.

| **Table 4.2.3-2. Method validation data** | | | | | |
| --- | --- | --- | --- | --- | --- |
| Component / Method type | Linearity (w %) / Correlation coefficient | Retention time (min) | Accuracy as recovery (%) | Precision as RSD (%) | LOQ and / or LOD (%) 1 |
| Impurity A /  HPLC/MS-MS |  |  |  |  |  |
| Impurity B |  |  |  |  |  |
| Impurity C |  |  |  |  |  |
| Impurity D |  |  |  |  |  |
| Solvent E / GC-FID |  |  |  |  |  |
| 1 For instrument or method (select appropriate)  *other footnotes as applicable – e.g. details of accuracy or precision determination* | | | | | |

Validated analytical methods were provided for determination of the impurities in five batches of the technical product and were assessed to be … for this purpose.

# REFERENCES RELIED ON

| Annex No., OECD Data Requirement No. | Author(s) | Year | Title Source Company Report No. GLP or GEP Status (where relevant) Published or not | Data Protection Claimed (Y/N) | Owner |
| --- | --- | --- | --- | --- | --- |
| IIA, 1.8 | Smith, A.B. | 2013 | Technical grade: manufacturing process Company A Company A Report No. 1 GLP: No Published: No | Y | Company A |
| IIA, 1.9 | Jones, C.D. | 2014 | Technical grade: Identity, composition, and certified limits Company B Company B Report No. 1 GLP: No Published: No | Y | Company A |

PMRA and EPA will generate their respective reference lists electronically.