ANALYTICAL CHARACTERISATION OF WELL DEFINED SUBSTANCES FOR REACH

PART ONE: ORGANIC SUBSTANCES

WHITE PAPER

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Every registrant of a substance under REACH, be they a lead registrant or a joint registrant, must include characterisation of the substance as part of their submitted dossier.

INTRODUCTION

Characterisation presents evidence that the substance manufactured or imported by the registrant is the same as the substance being described in the registration dossier. A substance may be classified as:

- Well-defined – Has a defined qualitative and quantitative composition.
- UVCB – Substance of unknown or variable composition

Although there is no precise definition of an "organic substance", all organic substances will contain carbon in their molecular formula. This document describes the analytical methodology appropriate for the characterisation of a well-defined organic substance.

CHARACTERISATION OF WELL DEFINED ORGANIC SUBSTANCES

A well-defined substance may be further divided into two categories:

- Mono-constituent substance – *"a substance, defined by its quantitative composition, in which the main constituent is present to at least 80 % (w/w)".*
- Multi-constituent substance – *"a substance, defined by its quantitative composition, in which more than one main constituent is present in a concentration ≥ 10% (w/w) and < 80% (w/w)".*

The substance is defined by the identity and relative quantity of both its main component AND its impurities. Characterisation must provide evidence that the substance being manufactured can be described by the identity shown in the registration dossier. The main difference between mono- and multi-component substances surrounds the naming of the substance. Both categories require the same analytical burden of proof to identify the substance. There is no defined set of tests which must be used for characterisation. Rather, enough analysis should be performed to unequivocally identify and quantify all components in the substance at ≥ 1% (w/w) (or SVHCs at ≥ 0.1 %). Therefore, it is advisable to use a set of orthogonal analytical techniques that can identify and quantify different characteristics of the components.

IDENTIFICATION

Organic compounds as an entirety cannot be described as complex or simple, covalent or ionic, but most will contain one or more covalent bonds between carbon and another element (including carbon). Therefore spectroscopic techniques are powerful tools to identify both the main component(s) and impurities in a substance.

- Magnetic resonance spectroscopy – ^{1}HNMR, ^{13}CNMR
- Vibrational spectroscopy – IR, raman
- Electronic spectroscopy – uv-vis, fluorescence
- Mass spectrometry - FAB, ICP-MS

Only relevant methods need to be used to identify the substance, but justification for waiving these methods should be included in the dossier. For example, if none of the components in a substance contain an unsaturated bond, uv-vis spectroscopy would be irrelevant. Non-spectroscopic tools may also be essential to identify components in the substance:

- XRD – Crystal structure and polymorphs
- Microscopy – Particle size

QUANTIFICATION

Chromatographic separation techniques are potent methods to quantify the amounts of each component in the substance:

- Liquid chromatography
- Gas chromatography
- Capillary electrophoresis
- Gel permeation chromatography

The choice of which chromatographic technique to use is dependent on the physical and chemical characteristics displayed by the substance. Some techniques can be combined to both identify and quantify the components in a substance (e.g. GC-MS, LC-NMR). Non-chromatographic tools may also be appropriate for some substances:

- Titration – acids, bases, oxidising substances
- DSC – polymorphs
- Elemental Analysis – organometallic substances

INTERPRETATION AND PRESENTATION OF ANALYTICAL DATA

Simply attaching a copy of the spectra or other raw analytical data to the registration is not adequate for characterisation. Sufficient information on the experiment should be included, so that a competent person might be able to repeat the work. This information will be dependent on the analytical technique, but as a general guide it should provide detail on:

- Equipment
- Sample preparation
- Analyst
- Experimental conditions
- Data processing
- Calibration

An interpretation of the results must also be included, highlighting the features of the data that support the identification of the analysed sample as the substance to be registered. For example, a ^{1}HNMR spectrum should include a table assigning each peak to an identified proton in the chemical structure.

CONCLUSIONS

- A registration dossier needs to contain a characterisation section that proves that the substance manufactured or imported is the substance being registered.
- The requirements for proof of identity and quantity are the same for mono- and multi-component organic substances.
- A range of analytical techniques for both identification and quantification are necessary to reach a justified conclusion. The techniques will vary from substance to substance based on their structure and physical characteristics. Justification for waiving some techniques should be included.
- The results should be supplied with sufficient details for the analysis to be repeated by a competent person. Interpretation of the analysis must accompany the raw data.

GLOSSARY OF TERMS	
DSC	Differential Scanning Calorimetry
FAB	Fast Atom Bombardment
ICP-MS	Inductively Coupled Plasma with Mass Spectrometry
IR	Infra-Red spectrometry
NMR	Nuclear Magnetic Resonance
SVHC	Substance of Very High Concern
UVCB	Substance of Unknown or Variable composition, Complex reaction products or Biological materials
w/w	Weight/weight
XRD	X-Ray Diffraction

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