Methodology and implementation of the Step 1 of the EC SSbD framework for the development of Safe and Sustainable by Design Graphene/Mxenes hybrids

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INTRODUCTION

The SAFARI EU project focuses on the development of Mxenes, 2D materials derived from MAXphases that present exceptional physico-chemical properties such as high electrical conductivity, mechanical strength, and chemical stability, making them excellent candidates for industrial applications like conductive inks, glucose and lactate biosensors, and electromagnetic shielding paints. Nevertheless, despite their significant potential, existing production methods frequently depend on hazardous chemicals, which present environmental and safety challenges.

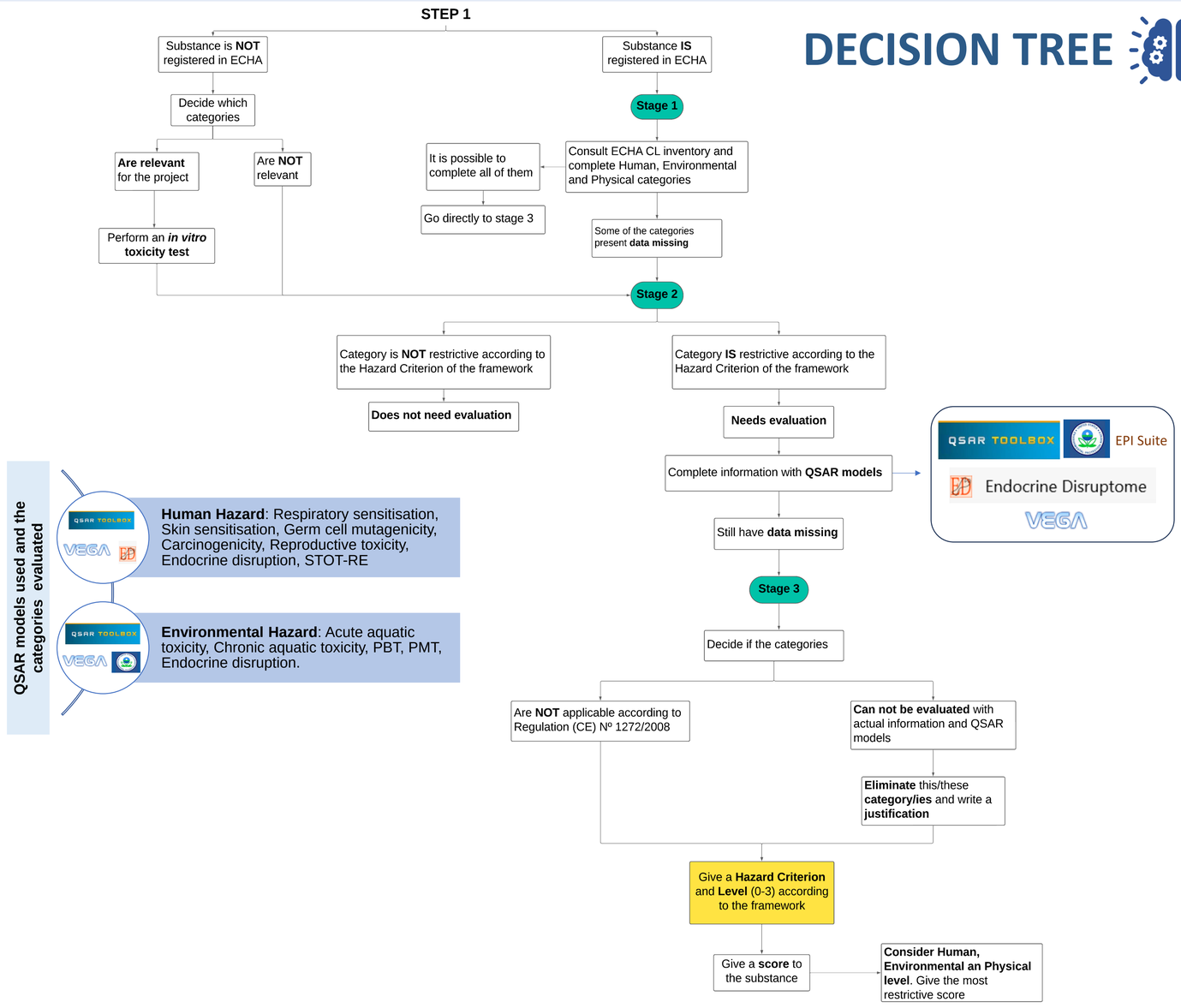
OBJECTIVES

- Implement Safe and Sustainable by Design (SSbD) principles.
- Integrate REACH-compliant chemicals.
- Perform a comprehensive human, environmental and occupational safety and sustainability assessment both in the development and application of the 2D material Mxenes and hybrid Mxenes with graphene.

OBSTACLES

ECHA Database	QSAR models	Newer categories
• Some materials are not registered in the ECHA database, which makes the implementation of Step 1 more difficult. • Some of the registered materials still have data lacking in many categories.	• Limited capabilities. • Low reliability in certain cases. • More than one QSAR is needed to complete all the hazard classes involved in the Step 1.	• Endocrine Disruption (ED), Persistent Bioaccumulative and Toxic (PBT) and Persistent Mobilie and Toxic (PMT), suffer from a lack of robust data, making accurate classification more challenging.

DECISION TREE



IMPLEMENTATION

Step 1 SSbD- **Stage 1**

METRO		Human Health Hazards													
		Acute Toxicity-Oral	Acute Toxicity-Dermal	Acute Toxicity-Inhalation	Skin Corrosion/ Irritation	Serious Eye Damage/ Eye irritation	Respiratory Sensitation	Skin Sensitisation	Aspiration Hazard	Germ Cell Mutagenicity	Carcinogenicity	Reproductive Toxicity	Endocrine disruption	STOT SE	STOT RE
Glucose oxidase	9001-37-0	NC	NC	NC	NC	NC	1	NC	NC	NC	NC	NC	MISS	NC	NC
Lactate oxidase	9028-72-2	MISS	MISS	MISS	MISS	MISS	1	MISS	MISS	MISS	MISS	MISS	MISS	MISS	MISS
Potassium Ferricyanide	13746-66-2	NC	NC	MISS	NC	2	MISS	NC	MISS	NC	NC	NC	MISS	NC	NC
Nitric acid	7697-37-2	MISS	MISS	1	1	1	MISS	MISS	NC	MISS	NC	MISS	MISS	NC	NC
TRIZMA	77-86-1	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	MISS	NC	NC
Glucose	50-99-7	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	MISS	NC	NC
Lactate	867-56-1	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	MISS	NC	NC
Gluconic acid	526-95-4	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	MISS	NC	NC
Lactic acid	50-21-5	NC	NC	NC	1	1	NC	NC	NC	NC	NC	NC	MISS	NC	NC

METRO		Environmental Hazards					
		Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Ozone layer	PBT/VPvB	PMT/vPvM	Endocrine disruption (environment)
Glucose oxidase	9001-37-0	NC	NC	NC	MISS	MISS	MISS
Lactate oxidase	9028-72-2	MISS	MISS	MISS	MISS	MISS	MISS
Potassium Ferricyanide	13746-66-2	NC	2	MISS	MISS	MISS	MISS
Nitric acid	7697-37-2	NC	NC	NC	MISS	MISS	MISS
TRIZMA	77-86-1	NC	NC	NC	MISS	MISS	MISS
Glucose	50-99-7	NC	NC	NC	MISS	MISS	MISS
Lactate	867-56-1	NC	NC	NC	MISS	MISS	MISS
Gluconic acid	526-95-4	NC	NC	NC	MISS	MISS	MISS
Lactic acid	50-21-5	NC	NC	NC	MISS	MISS	MISS

NC	Not classified
MISS	Data lacking
NP	Not classified according to QSAR models
POS	Hazard class positive
Number	
NE	Not evaluated
NA	Hazard class not applicable
IN	Hazard class inconclusive

Step 1 SSbD- **Stage 2**

METRO		Human Health Hazards						
		Respiratory Sensitisation	Skin Sensitisation	Germ Cell Mutagenicity	Carcinogenicity	Reproductive Toxicity	Endocrine disruption	STOT RE
Glucose oxidase	9001-37-0	1	NC	NC	NC	NC	NT	NC
Lactate oxidase	9028-72-2	1	IN	NP	NP	NP	NT	NP
Potassium ferricyanide	13746-66-2	NP	NC	NC	NC	NC	NP	NC
Nitric acid	7697-37-2	NP	NP	NP	NC	NP	NP	NC
TRIZMA	77-86-1	NC	NC	NC	NC	NC	2	NC
Glucose	50-99-7	NC	NC	NC	NC	NC	NT	NC
Lactate	867-56-1	NC	NC	NC	NC	NC	NT	NC
Gluconic acid	526-95-4	NC	NC	NC	NC	NC	NT	NC
Lactic acid	50-21-5	NC	NC	NC	NC	NC	NT	NC

METRO		Environmental Hazards				
		Acute Aquatic Toxicity	Chronic Aquatic Toxicity	PBT/VPvB	PMT/vPvM	Endocrine disruption (environment)
Glucose oxidase	9001-37-0	NC	NC	NT	NT	NT
Lactate oxidase	9028-72-2	NP	NP	NT	NT	NT
Potassium Ferricyanide	13746-66-2	NC	2	POS	NA	NP
Nitric acid	7697-37-2	NC	NC	NP	NA	NP
TRIZMA	77-86-1	NC	NC	POS	POS	2
Glucose	50-99-7	NC	NC	NT	NT	NT
Lactate	867-56-1	NC	NC	NT	NT	NT
Gluconic acid	526-95-4	NC	NC	NT	NT	NT
Lactic acid	50-21-5	NC	NC	NT	NT	NT

① Complete the missing data for those categories that are considered restrictive according to the Hazard Criterion of the Framework, using QSAR models.

H1	Most harmful substances, should be replaced.
H2	Substances of concern, can be used but require special safety measures.
H3	Substances safer than H2 but also need special safety measures.
NC	No Hazard class identified, safe to use.

Decide which categories are not applicable or can not be evaluated ②

Step 1 SSbD- **Stage 3**

METRO		Human Health Hazards															
		Acute Toxicity-Oral	Acute Toxicity-Dermal	Acute Toxicity-Inhalation	Skin Corrosion/ Irritation	Serious Eye Damage/ Eye irritation	Respiratory Sensitisation	Skin Sensitisation	Aspiration Hazard	Germ Cell Mutagenicity	Carcinogenicity	Reproductive Toxicity	Endocrine disruption	STOT SE	STOT RE	Human Hazard	LEVEL
Glucose oxidase	9001-37-0	NC	NC	NC	NC	NC	1	NC	NC	NC	NC	NC	NT	NC	NC	H1	Level 0
Lactate oxidase	9028-72-2	NE	NE	NE	NP	NE	1	IN	NE	NP	NP	NP	NT	NE	NP	H1	Level 0
Potassium ferricyanide	13746-66-2	NC	NC	NE	NC	2	NP	NC	NE	NC	NC	NC	NP	NC	NC	H3	Level 2
c acid	7697-37-2	NE	NE	1	1	1	NP	NP	NC	NP	NC	NP	NP	NC	NC	H3	Level 2
MA	77-86-1	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	2	NC	NC	H2	Level 1
:ose	50-99-7	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NT	NC	NC	NC	Level 3
:ate	867-56-1	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NT	NC	NC	NC	Level 3
Gluconic acid	526-95-4	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NT	NC	NC	NC	Level 3
:ic acid	50-21-5	NC	NC	NC	1	1	NC	NC	NC	NC	NC	NC	NT	NC	NC	H3	Level 2

METRO		Environmental Hazards							
		Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Ozone layer	PBT/VPvB	PMT/vPvM	Endocrine disruption (environment)	Environmental Hazard	LEVEL
Glucose oxidase	9001-37-0	NC	NC	NC	NT	NT	NT	NC	Level 3
Lactate oxidase	9028-72-2	NP	NP	NA	NT	NT	NT	NC	Level 3
Potassium Ferricyanide	13746-66-2	NC	2	NA	POS	NA	NP	H1	Level 0
Nitric acid	7697-37-2	NC	NC	NC	NP	NA	NP	NC	Level 3
TRIZMA	77-86-1	NC	NC	NC	POS	POS	2	H1	Level 0
Glucose	50-99-7	NC	NC	NC	NT	NT	NT	NC	Level 3
Lactate	867-56-1	NC	NC	NC	NT	NT	NT	NC	Level 3
Gluconic acid	526-95-4	NC	NC	NC	NT	NT	NT	NC	Level 3
Lactic acid	50-21-5	NC	NC	NC	NT	NT	NT	NC	Level 3

③ Calculate the score of the Step 1

Materials score

0	Substances should be replaced.
1	Substances can be used with special safety measures.
2	Substances safer tan ones with level 1 but also need special safety measures.
3	Substances safe to use.

If there is not an alternative available, they can be used with special safety and recycling measures.

METRO	SCORE HUMAN HAZARD		SCORE ENVIRONMENTAL HAZARD		SCORE PHYSICAL HAZARD	SCORE STEP 1	SCORE WITHOUT PBT, PMT AND ED CATEGORIES
	ALL CATEGORIES	WITHOUT ED CATEGORY	ALL CATEGORIES	WITHOUT PBT, PMT AND ED CATEGORIES			
Glucose oxidase	0	0	3	3	3	0	0
Lactate oxidase	0	0	3	3	3	0	0
Potassium Ferricyanide	2	2	0	1	3	0	1
Nitric acid	2	2	3	3	2	2	2
TRIZMA	1	3	0	3	3	0	3
Glucose	3	3	3	3	3	3	3
Lactate	3	3	3	3	3	3	3
Gluconic acid	3	3	3	3	3	3	3
Lactic acid	2	2	2	3	2	2	2

Our **recommendation** is to consider the s**core without PBT, PMT and Endocrine disruption (ED)** categories because all of them have been calculated with QSAR models and the reliability in most cases is low.

CONCLUSIONS

The developed decision tree and strategies for addressing data gaps helped and supported Step 1 implementation in the different alternatives proposed in SAFARI Project.

The application of this Step has helped to identify chemicals that require special attention, and appropriate measures have been taken to ensure the safety of the final product from the production stage onward.

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