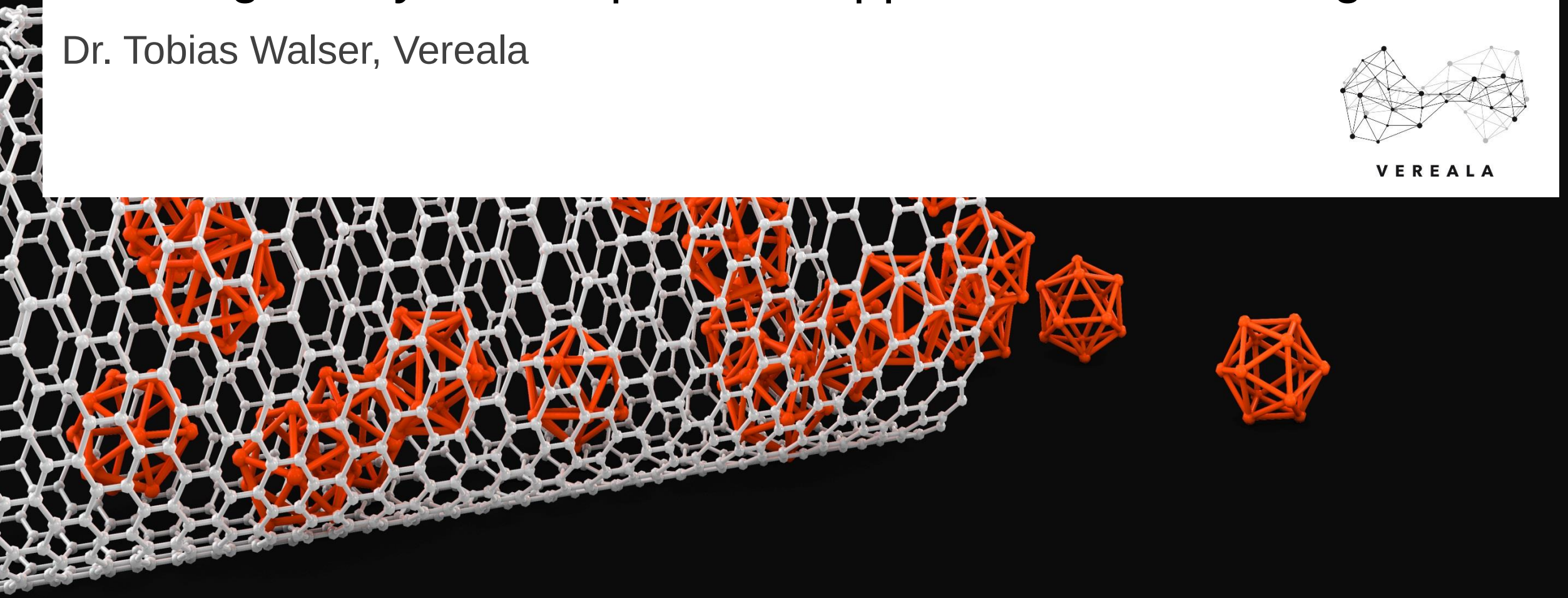
Contact Point Nano, December 7, 2018

New regulatory rules – practical approach and challenges

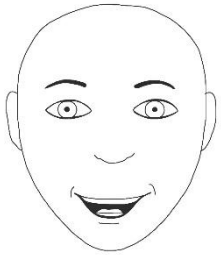
Dr. Tobias Walser, Vereala

VEREALA



Varnish for the bathroom

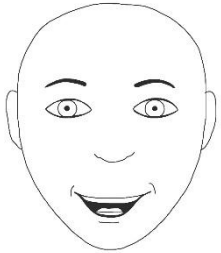
The story – The nanomaterial from idea to market



Tony Shell, NanoPerform AG (SME)

Innovation to Market

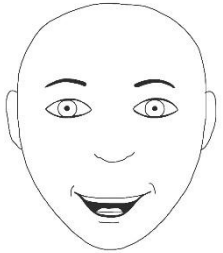
The story – The nanomaterial from idea to market



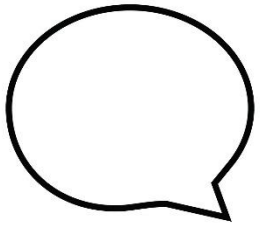
Tony Shell, Nanoperform AG (SME)
Innovation for Market

Superb protection against stains, water, detergents, it even changes colour if mold is present – **if nanomaterials are added**

The dialogue – The nanomaterial from idea to market

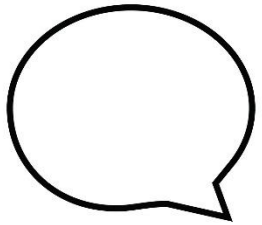


Tony Shell, Nanoperform AG (SME)
Innovation for Market



Regulatory agencies / Consultants
Safe products on the market

Let’s support Tony!

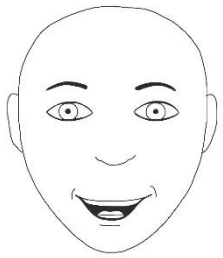


On which market would you like to sell your product?

- Globally
- European Union
- Switzerland only

The first two questions

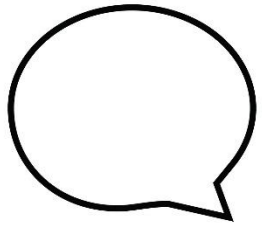
Switzerland and European Union



Switzerland is the principal market, but I also want to explore opportunities on the European market.

Focus on the European Regulation. Regulation in **Switzerland**, with a few particularities**, is compatible with the EU regulation**.

Choose the correct legislation, Tony!

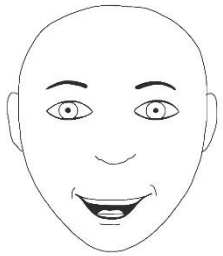


Into which type of product you would like to add your nanomaterials?

- Cosmetic?
- Pharmaceutical?
- Medical device?
- Chemical substance?
- Biocide?
- Novel food?

….A specific piece of legislation can cover nanomaterials only within its scope.

There is not just one regulation for nanomaterials



I need to know which regulation applies!

Crucial for the further procedure. Make sure you receive advice.

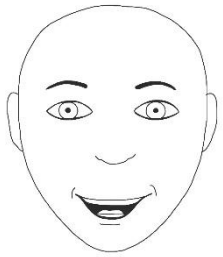
Different regulatory requirements

Nanomaterials in different jurisdictions

Regulatory Framework	Definition	Approval Procedure	Safety Assessment	Labeling
REACH (chemicals)	(A)		Tonnage triggered	CLP
Biocidal products	A	X	X	CLP
Cosmetic products	B	X	X	X
Food (5 different regulations)	C	(X)	X	(X)
Medical devices	A	X	X	X

Tony’s first thought

Medical devices

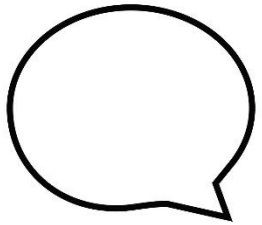


The paint changes its colour as soon as there is too much humidity and consequently a risk for mold in the bathroom. Is the product **maybe a Medical Device because it alerts for a potential health concern?**

No, the nanomaterials in the paint (or the nanoenabled paint) are not medical devices as there is no medical use and medical efficacy. However, for products potentially considered as “medical devices”, the borderline to other product groups is important to consider.

Short digression

Medical devices - new regulation



Since May 2017 the two new EU Regulations on medical devices were adopted by the European Parliament: Regulation on Medical Devices (MDR) and Regulation on in-vitro diagnostic medical devices (IVDR). Transitional period 2020 (MDR), 2022 (IVDR). **Switzerland adopted the changes (Medizinalprodukteverordnung).**

- **Classical Medical Devices (MD)** Data and proof of safety and performance.
- **In vitro diagnostic medical devices (IVD)** Depending on the purpose of applications, **the device is classified as IVD, Class 1 – 3, or AIMD**
- **Active implantable MD (AIMD)**

Short Digression

Medical devices - nanomaterials

!

The new Regulation on medical devices lays down a **dedicated classification rule for devices incorporating or consisting of nanomaterials**.

The **critical factor is the potential for nanomaterials to be in contact with membranes inside the body**.

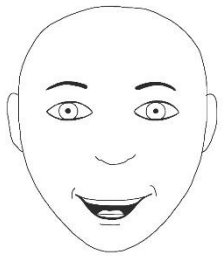
Those devices presenting a **high or medium potential for such contact will fall under the highest risk class** and thus be subject to the most stringent conformity assessment procedures.

Tony – It's a chemical! And this is the applicable definition

The definition concerns natural, incidental, and manufactured particulate material, refers to constituent (primary) particles and **uses size as the most important defining parameter**.

[excerpt] The material is a nanomaterial if 50 % or more of the constituent particles (by number) **have one or more external dimensions in the size range 1 – 100 nm**. A material can also be considered as nanomaterial if its volume-specific surface area is larger than 60 m^2cm^{-3} (recommendation by REACH).

Implicit and explicit guidance for nanomaterials under REACH



Specific requirements for nanomaterials under REACH?

No, not until 2020.

In principle, **nanomaterials, and especially potential risks associated with them, are covered by existing legislation under REACH**, **even if nanomaterials are not explicitly mentioned.** The same holds true for Switzerland (ChemV, ChemG).

Procedure for the safety assessment of chemicals (short)

How does the substance look like, is it a nanomaterial?

→ Physical characterization, *new data*

What is it made from?

→ Chemical characterization, *new data*

How does it interact with the surrounding environment? → Tonnage, Uses of the substance and conditions of use in the whole supply chain, exposure and toxicity*, ideally existing data*

How does the material look like?

Characterization in the registration dossier: Parameters

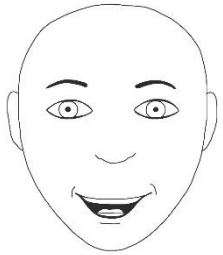
- **Chemical composition (incl. crystalline structure)**

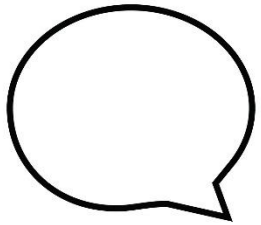
- **Surface chemistry**
- **Size**
- **Shape**
- **Surface area**
- **Dustiness**

- **If useful for hazard and exposure profile:** Rigidity for fibers Impurities, solubility (rate), dispersibility, dustiness, biological reactivity (e.g. ROS formation), photoreactivity, stability in storage

How does the material look like?

Characterization in the registration dossier: Parameters





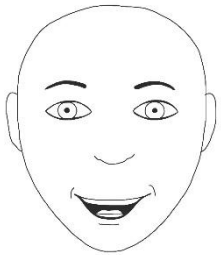
There is the **basic set of parameter and the additional (vorluntary) set of parameters** I need to provide as a registrant. How to deal with it?

The variation of morphological parameters (e.g. size, shape) and surface chemistry should be considered, in particular if **relevant for the hazard profile**.

Challenges: Validated measurement devices, predictive tools to prioritize measurement efforts, access to other dossiers

How does the material look like?

New Substance, Nanoform, Set of Nanoforms, …

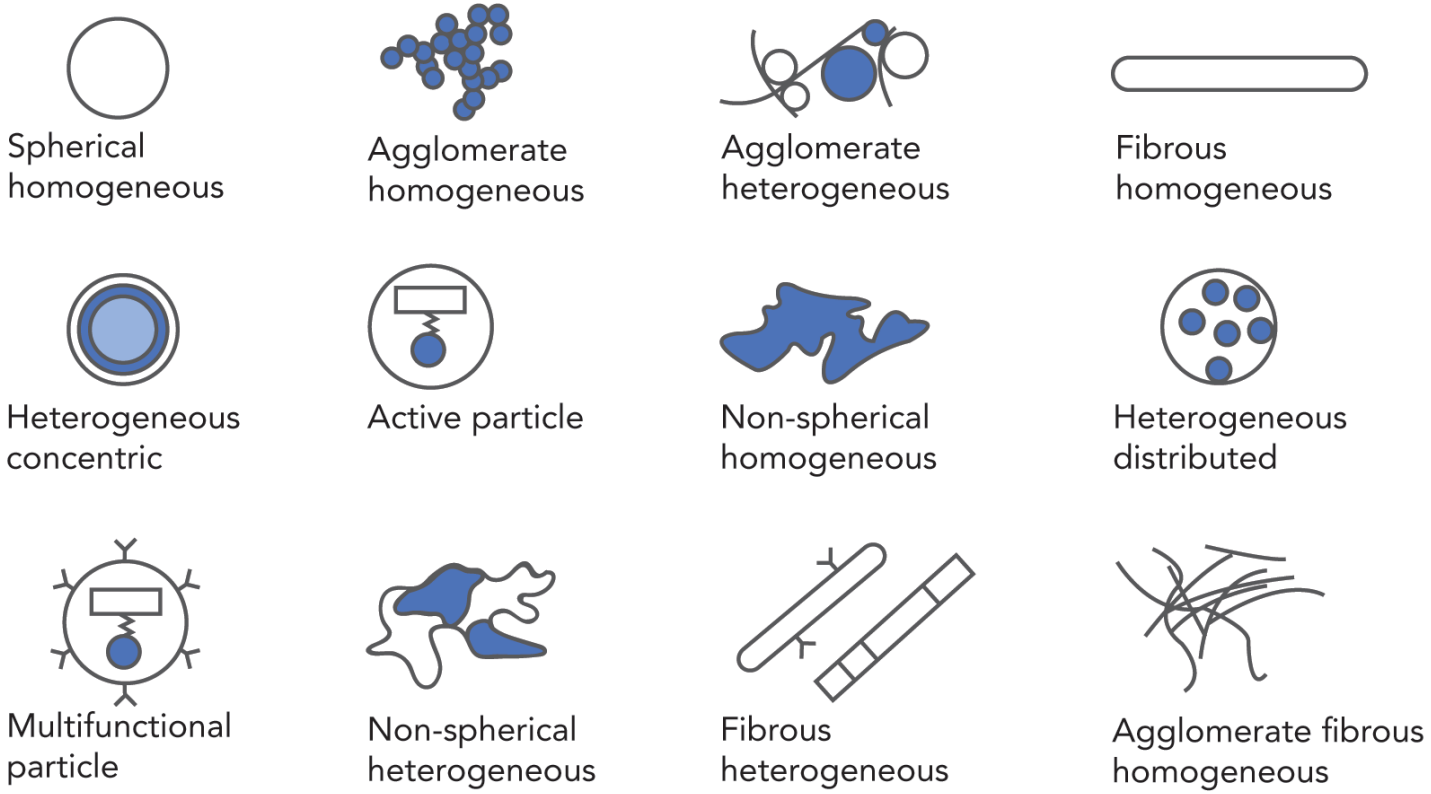


Yes, based on my measurements, the produced substances are indeed nanomaterials. But I am confused, the nanomaterials are **not homogeneous in size – are they still considered as just one substance to be registered**?

How does the nanomaterial look like?

New Substance, Nanoform, Set of Nanoforms, …

Tony makes a valid point.

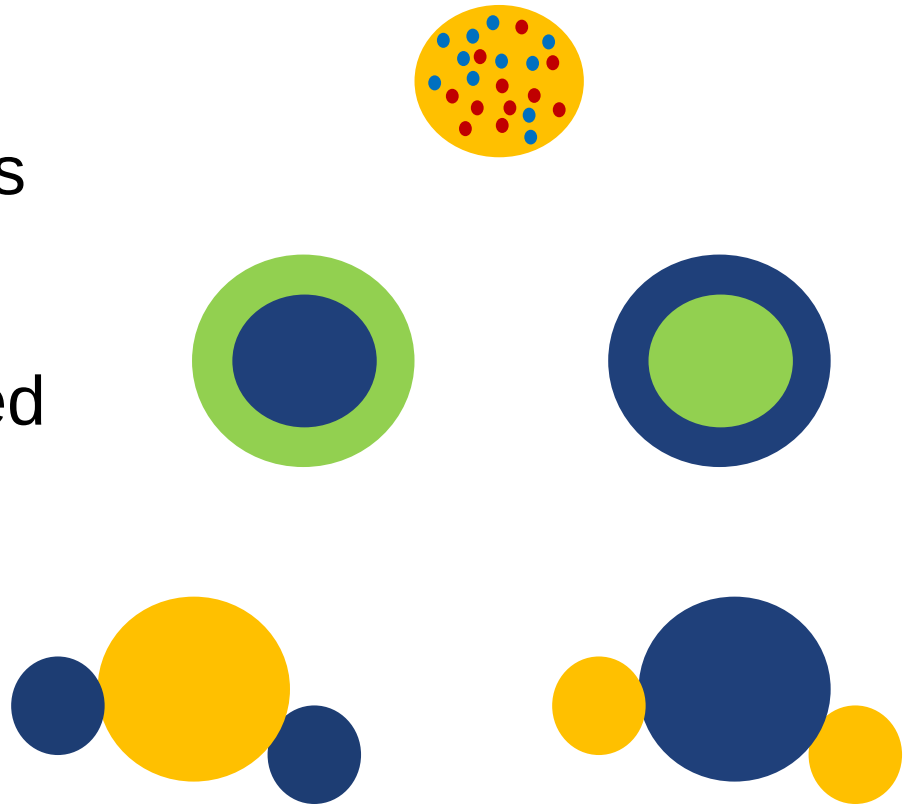


US EPA 2012

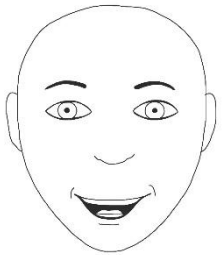
How does the nanomaterial look like?

Nanomaterial definitions: Beyond size and composition

- Uncoated nanomaterials consisting of different substances
- Coated nanomaterials with sealed or permeable surface
- Aggregates or agglomerates of different nanomaterials



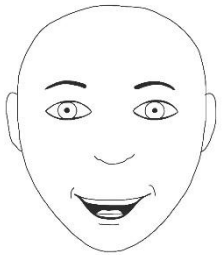
Nanoform, Set of Nanoforms, Substance, …



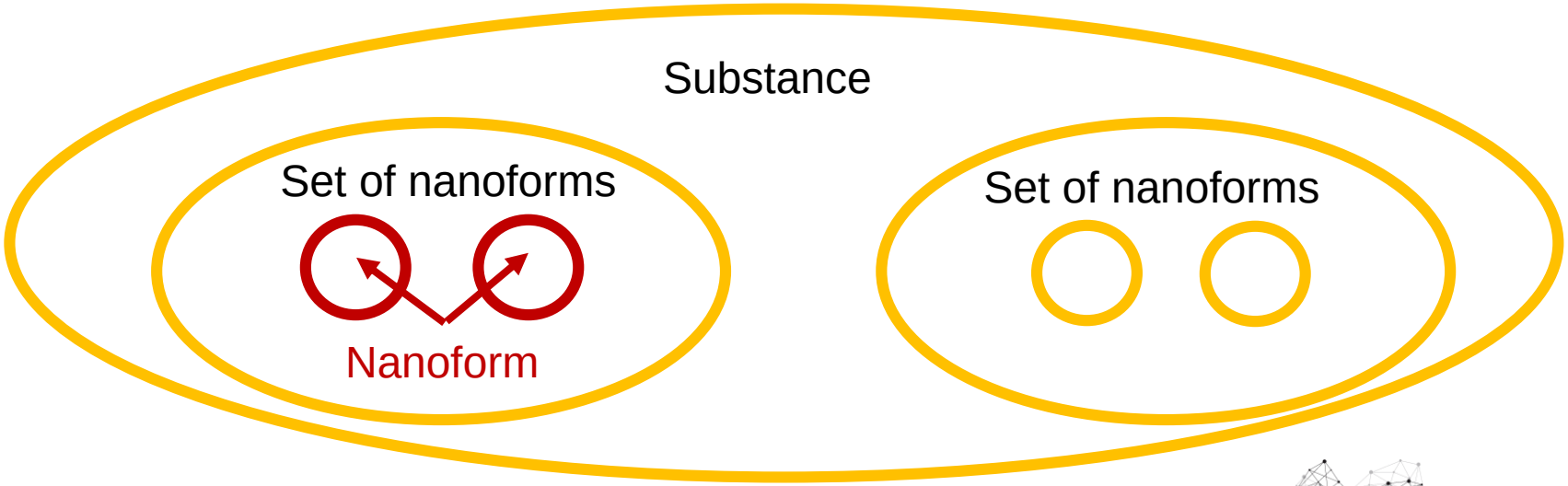
… But I am confused, the nanomaterials are **not homogeneous in size – are they still considered as just one substance to be registered**?

Nanomaterials are seldom identical to each other, therefore, **pragmatic approaches are there to group nanomaterials into "sets of nanoforms"** according to their properties.
Technical Term **"Nanoform": Form of a substance that meets the recommended definition and has a shape and a surface chemistry.**

Nanoform, Set of Nanoforms, Substance, …



I am confused, there are billions of different nanomaterials and it is not feasible to register all of them. My nanomaterials also look not always the same – are they still considered as one single nanoform of a substance?

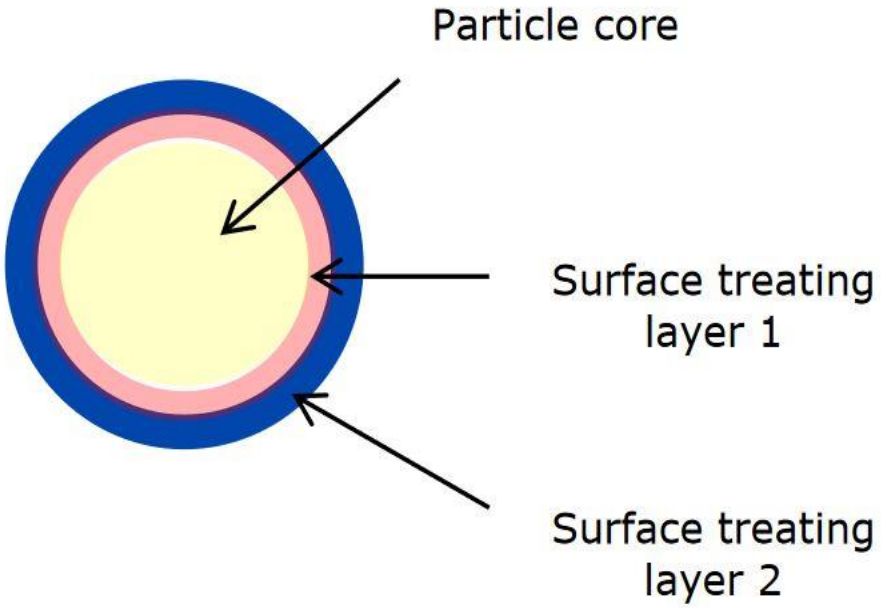


Recommendation by ECHA

Pragmatic approach, applicable for a small set of NM

Substance identity is based on the identity of the **particle core substance (minimum of 80% w/w).**

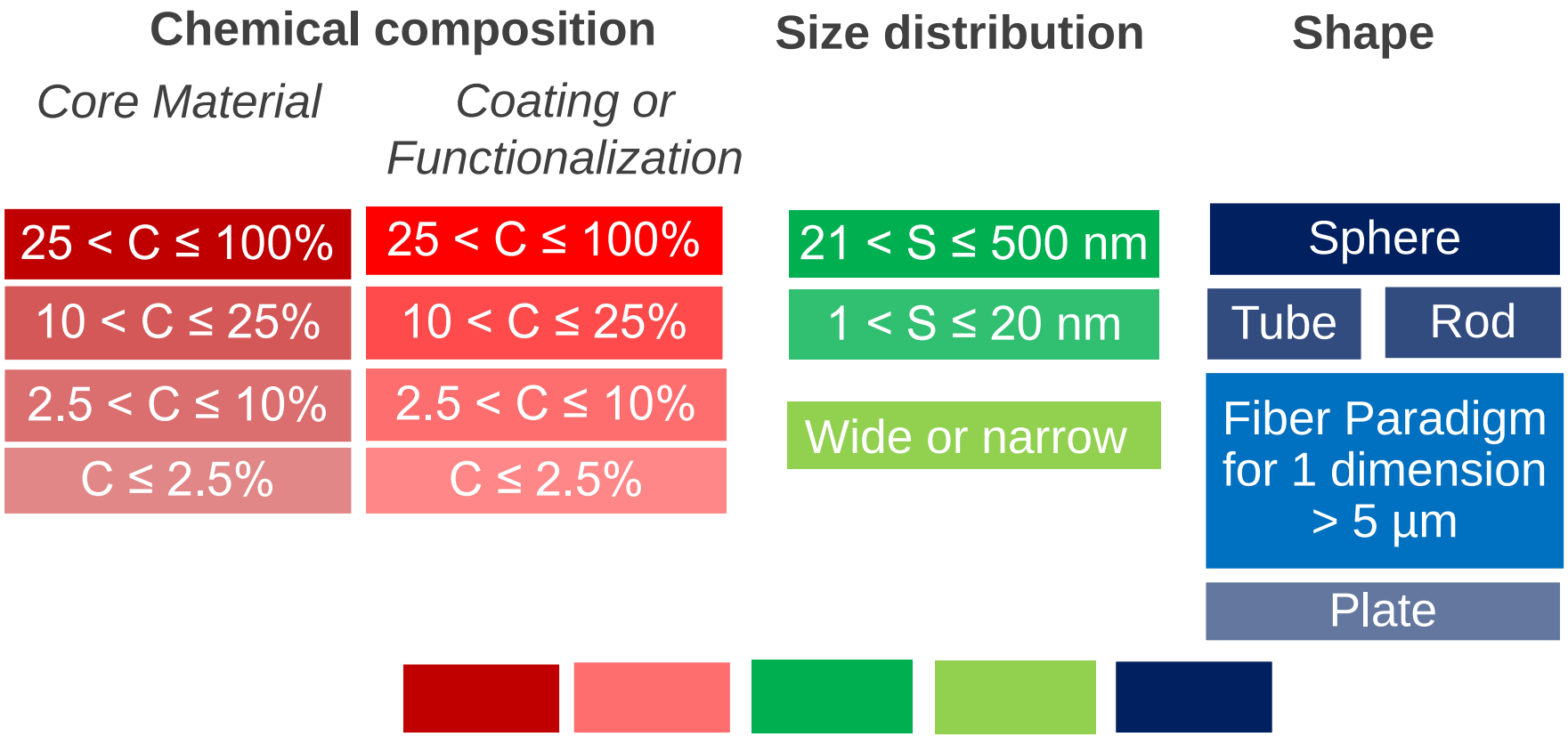
Pitfall: If surface is a major determinant of the properties, **how to find a nanomaterial in the registry with a different core but the same (similar) safety profile?**



ECHA 2016

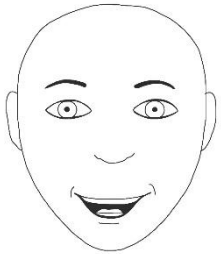
Recommendation by Walser, Studer, et al (2015)

Pragmatic approach, applicable for a broader set of NM



* Walser and Studer (2015): Sameness: The regulatory crux with nanomaterial identity and grouping schemes for hazard assessment. Reg.Tox.Pharm (72): 569–571

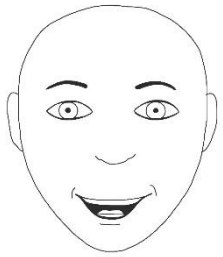
Characterization is done – what about the safety of the NM?



Do I need to evaluate the safety of my product, and if so, what are the principal criteria?

Yes. Most information requirements for the safety of a substance in REACH are triggered by the tonnage, i.e., the quantity of a substance produced or imported per year per manufacturer or importer. Substances that are marketed in the EU in volumes more than 1t per year have to be registered, and for more than 10t per year a chemical safety assessment is required. **Tonnage triggers for registration apply to the total tonnage of a substance, including the nano and the non-nanoform.**

Risk Assessment



Is my product safe?

Hazard identification and assessment

- incorporating the dose-response relationship

+

Exposure

- Environmental
- Human

→

Risk characterisation,

- integration of hazard and exposure assessments

Information sharing for (sub-)substances of a substance

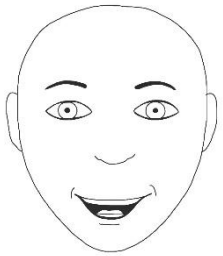
Goal

Meet the information requirements for a **sufficient safety evaluation with the least data generation effort possible**

Tools

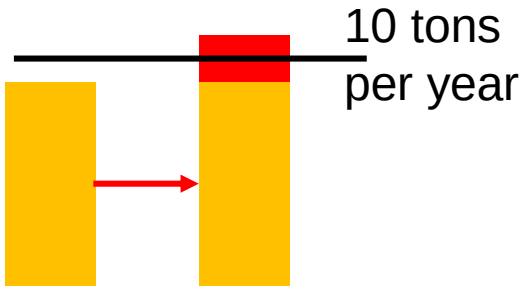
Weight of Evidence
Data Waiving
Read-across and Grouping
Avoid unnecessary testing
Use data from other registrants (access to dossier)

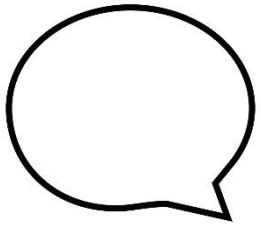
How about…?



1) **How do I find out about the dossiers** of the other registrants of the same substance?

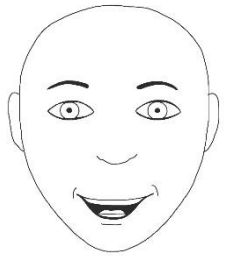
2) What happens if my additional amount of substance **triggers a shift in the total tonnage of all registrants/consortium?**





1) Substance information exchange forum (SIEF, pre-SIEF) and direct contact to ECHA (no duplicates of animal studies allowed). Double registration of similar nanoforms possible.

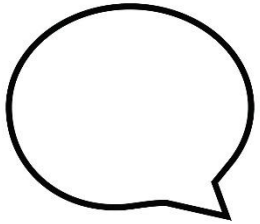
Principal questions before starting the registration process



- Is my Nanomaterial a **nano-form of an existing substance**?
- Does my Nanomaterial belong to a **set of nanoforms of a substance**?
- Is my nanomaterial a **nanoform of a substance which has not been registered before**?
- **What tonnage** am I aiming for?

Short summary

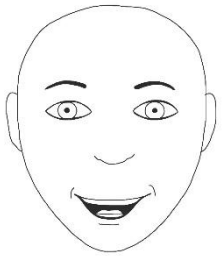
Read useful guidelines and listen to experts



- Federal Offices (e.g. Anmeldestelle Chemikalien)
- Precautionary Matrix (V2)
- Anleitung zur Selbstkontrolle (Entwurf)
- Contactpoint Nano

- ECHA Helpdesk

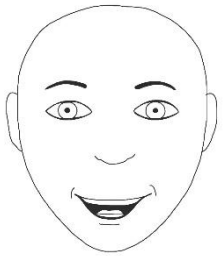
Tony proceeds with the registration



I found out that with a total **amount of 300 kg nanomaterials embedded safely in the varnish**, **I don’t need to carry out a chemical safety report on** my nanomaterial (less than 10t). However, I will include the **characterization information in a dossier, the information of the entire supply chain and I will make sure, that the labeling criteria are met** in order to ensure that the **entire supply chain handles my product in a responsible way.**
If my business grows and I trigger the tonnage criteria, I will check for other registrants, in order to develop the data in the most efficient way.

How does it interact with the surrounding environment?

Tony wants to use the safety data more holistically

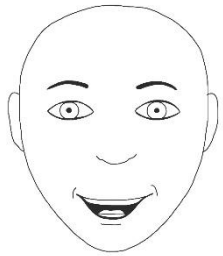


Why are the testing efforts only tonnage triggered and not by e.g. a precautionary approach or a more substance focused approach?

Over the long-term **it makes sense to investigate the life cycle of the nanomaterial with ist potential implications**, independent of the tonnage. Use the data not only for Risk Assessment, but also for Life Cycle Assessment.

Using the data for multiple purposes

Life Cycle Assessment



Is my product sustainable, how does it compare to other products?

Definition of Scope and System Boundaries

- Nanoenabled Varnish: Production, Performance and Use, and Disposal Scenario

Fate Assessment

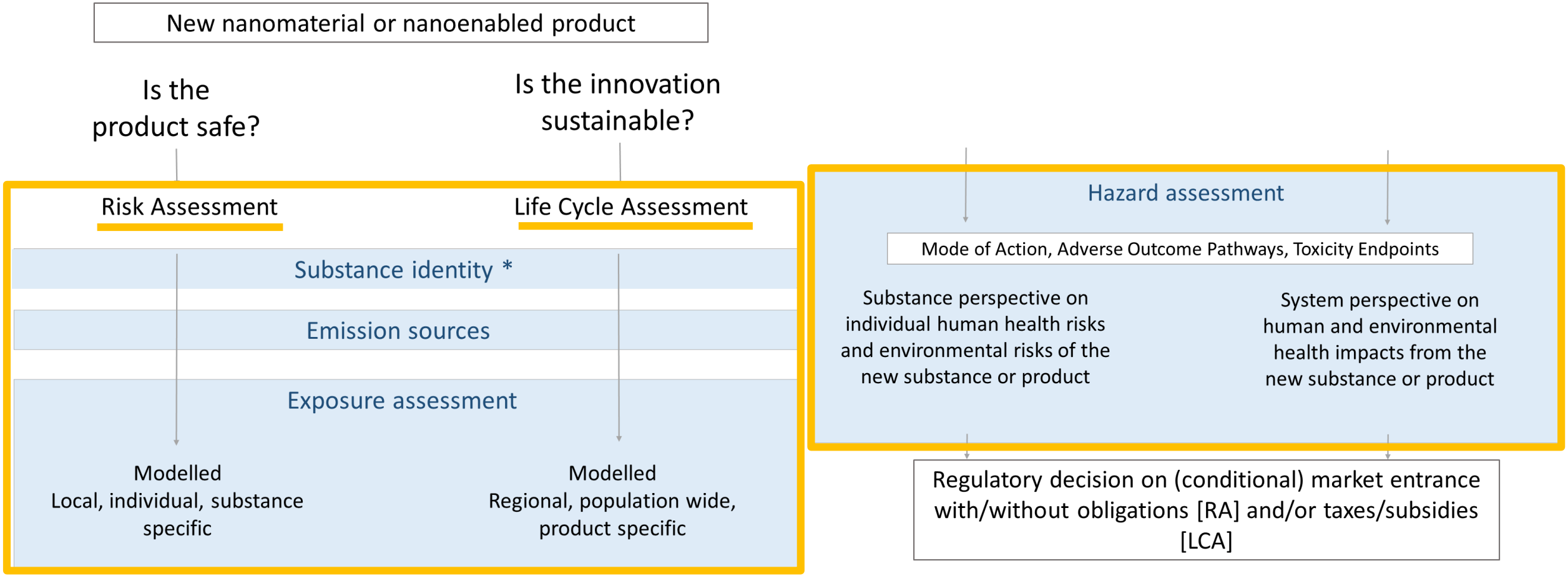
- Emission and exposure of all materials flows
- To humans
- To environment

Impact Assessment

- Quantification of the impact from human and environmental exposure and comparison to the current state

Life Cycle Assessment and Risk Assessment, two complementary methods

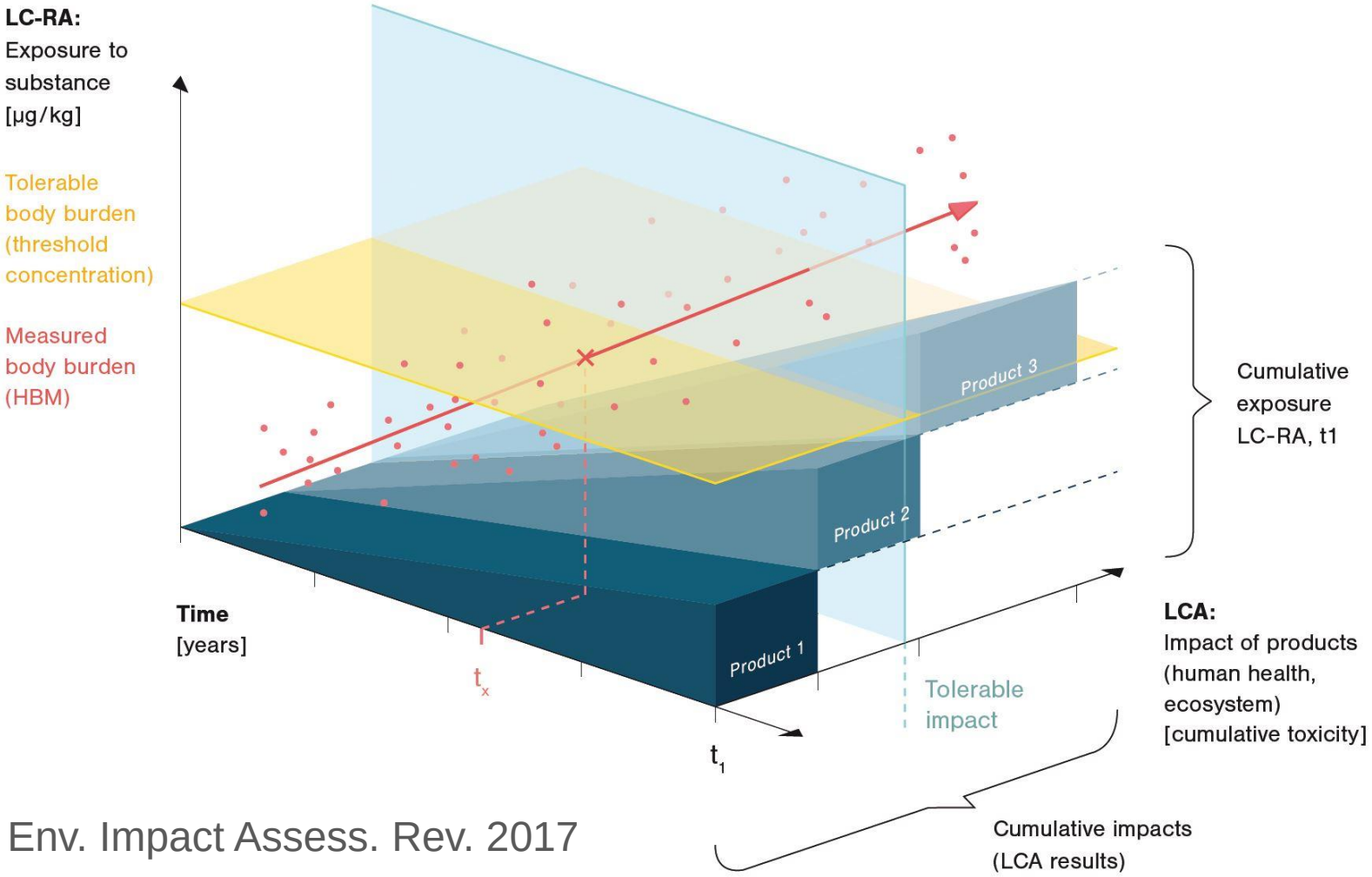
Tony wants to generate and use the safety data more holistically



Walser et al. Env. Impact Assess. Rev. 2017

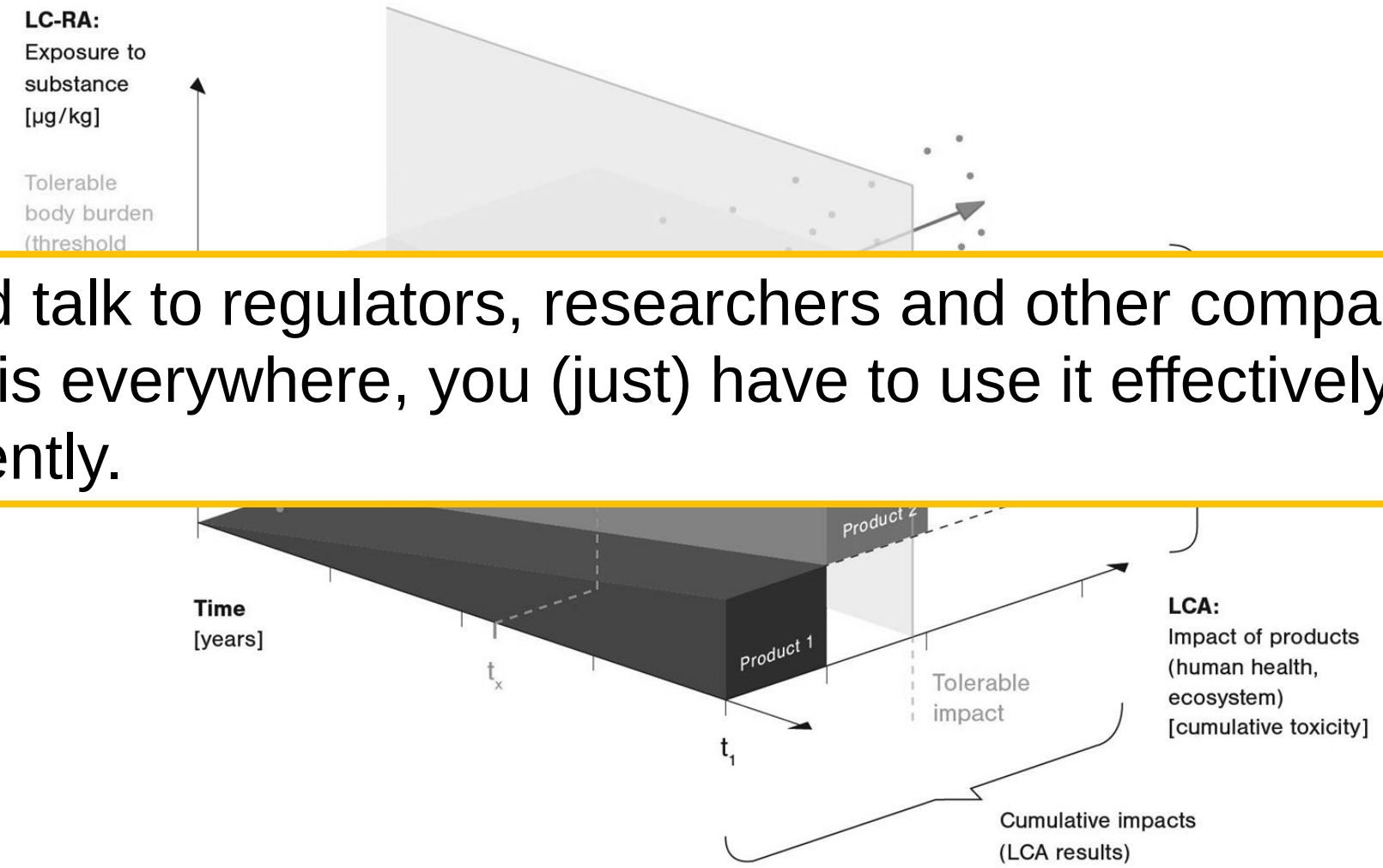
Life Cycle Assessment and Risk Assessment, two complementary methods

Take a precautionary and holistic approach!



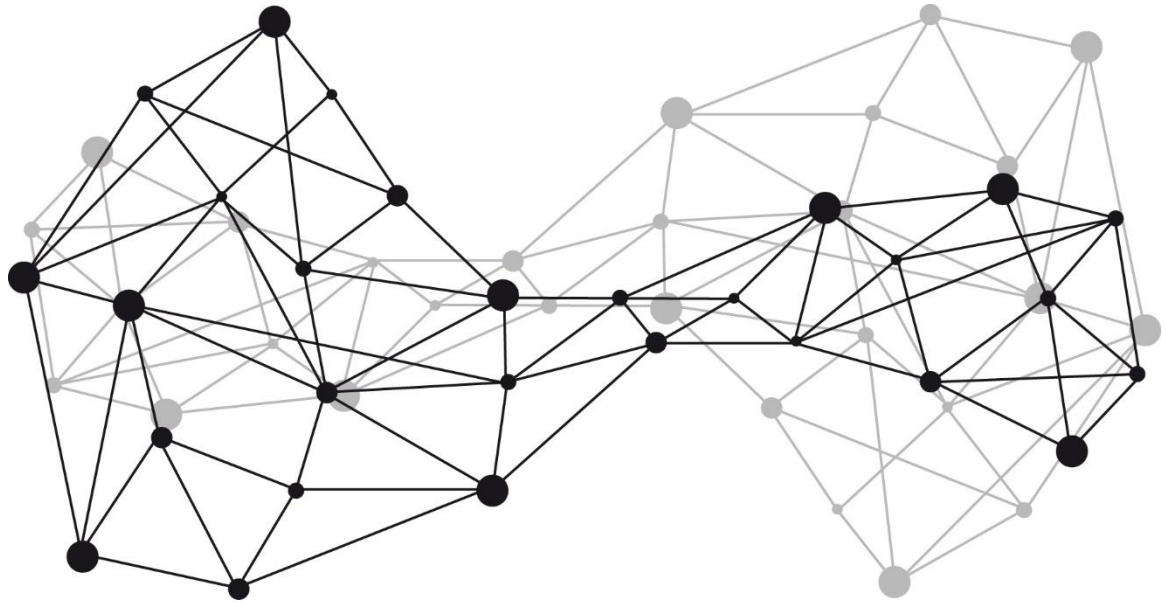
Walser et al. Env. Impact Assess. Rev. 2017

Take a precautionary and holistic approach!



…and talk to regulators, researchers and other companies! Data is everywhere, you (just) have to use it effectively and efficiently.

Thank you for your attention.



VEREALA

tobias.walser@vereala.com