GRACIOUS
Hypotheses and IATAs

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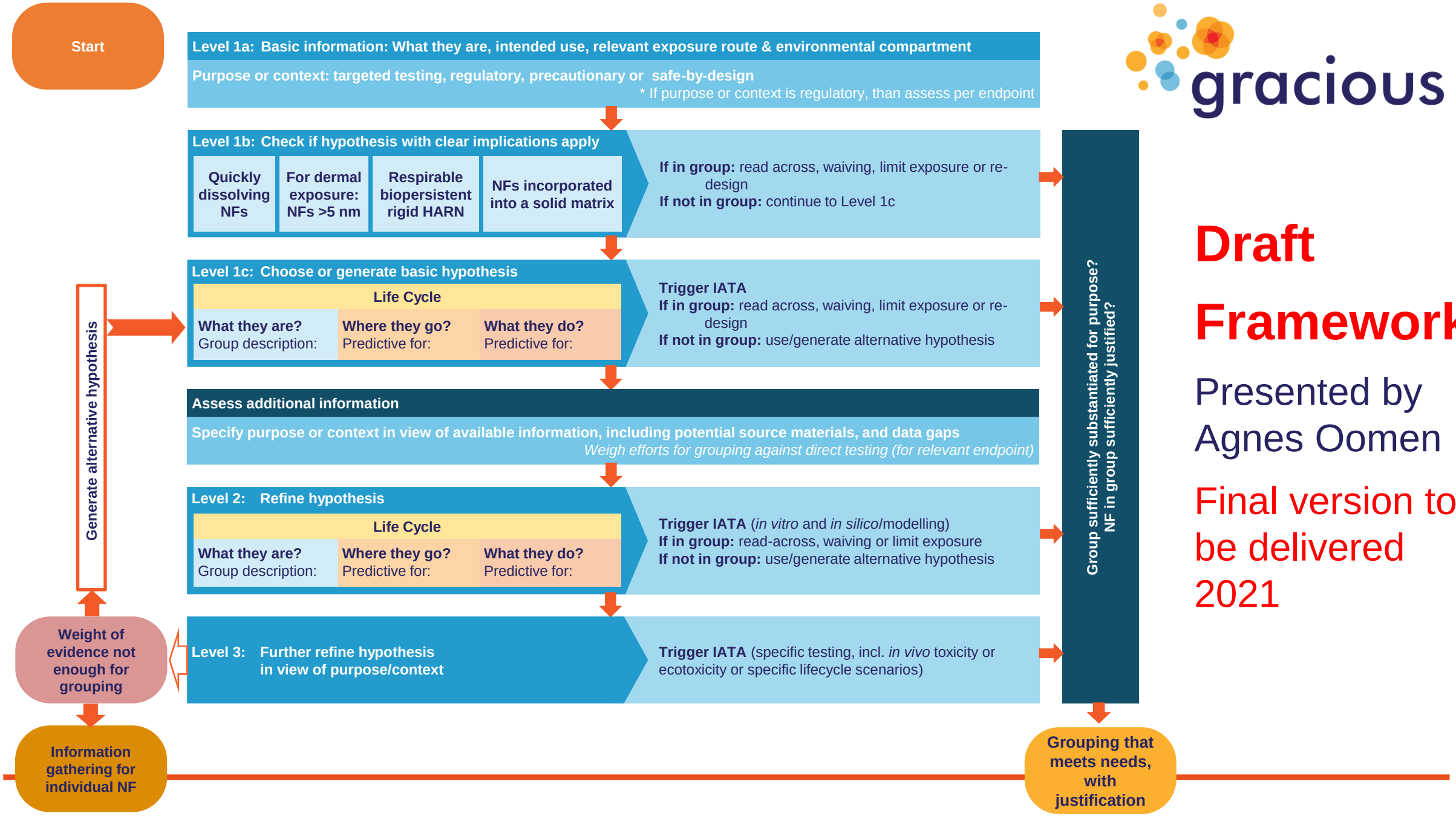

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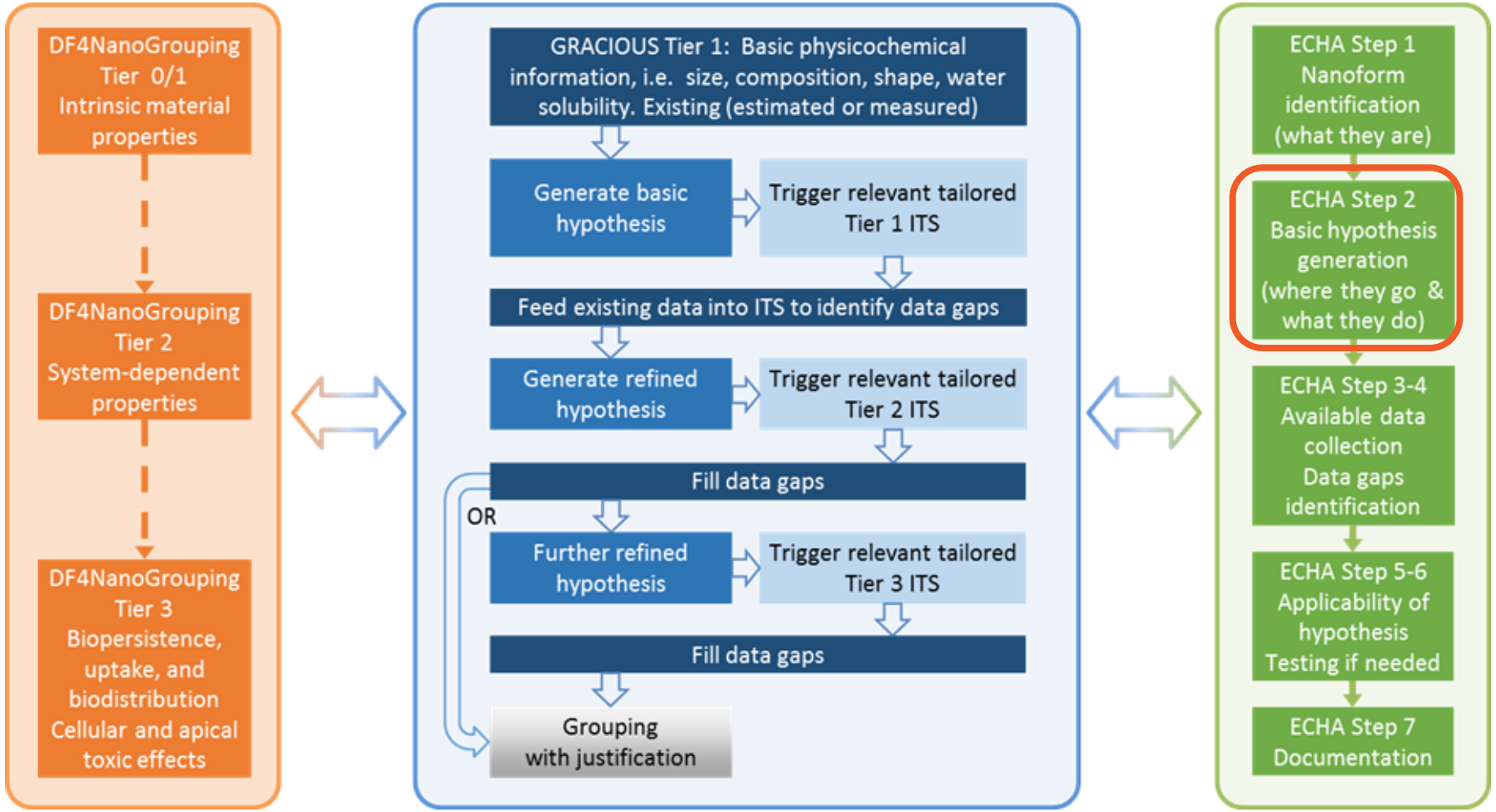
Draft Framework

Presented by Agnes Oomen

Final version to be delivered 2021

Generating the First Draft

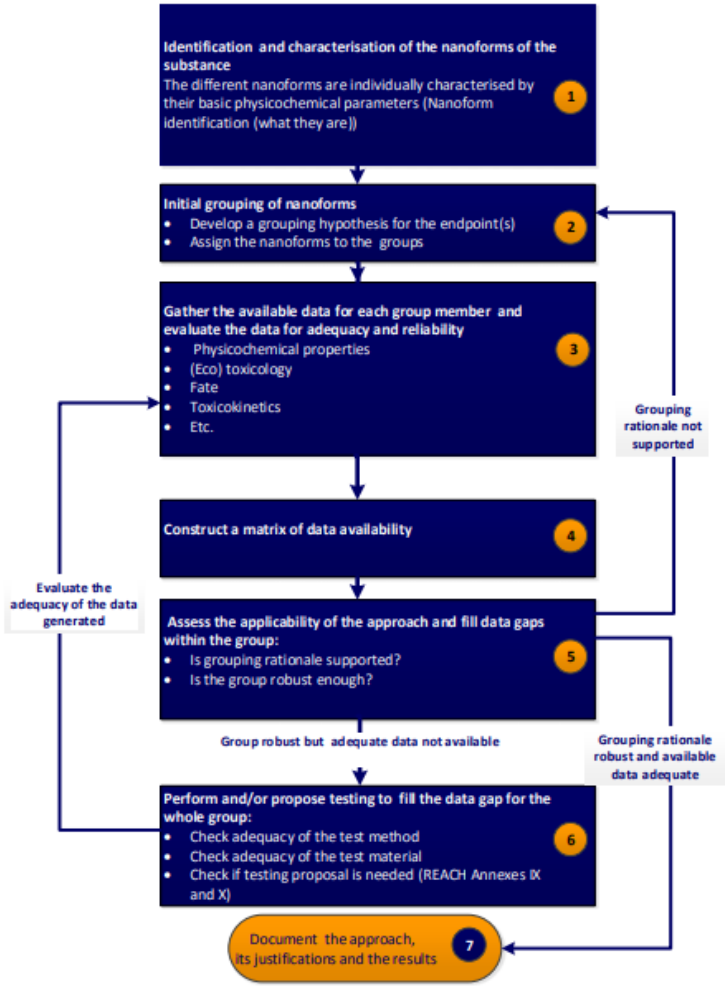


ECHA require a hypothesis driven approach

ECHA Guidance on Grouping

- Follows updated OECD 2014 Guidance on Grouping of Chemicals
- States that general concepts on grouping of chemicals are applicable to nanomaterials
- Describes a stepwise approach in which nanoforms are grouped
- Outlines the general principles to gather and combine information on:
  - physicochemical properties,
  - toxicokinetic
  - (eco)toxicological behaviour
  - expert judgement

ECHA Guidance on Grouping



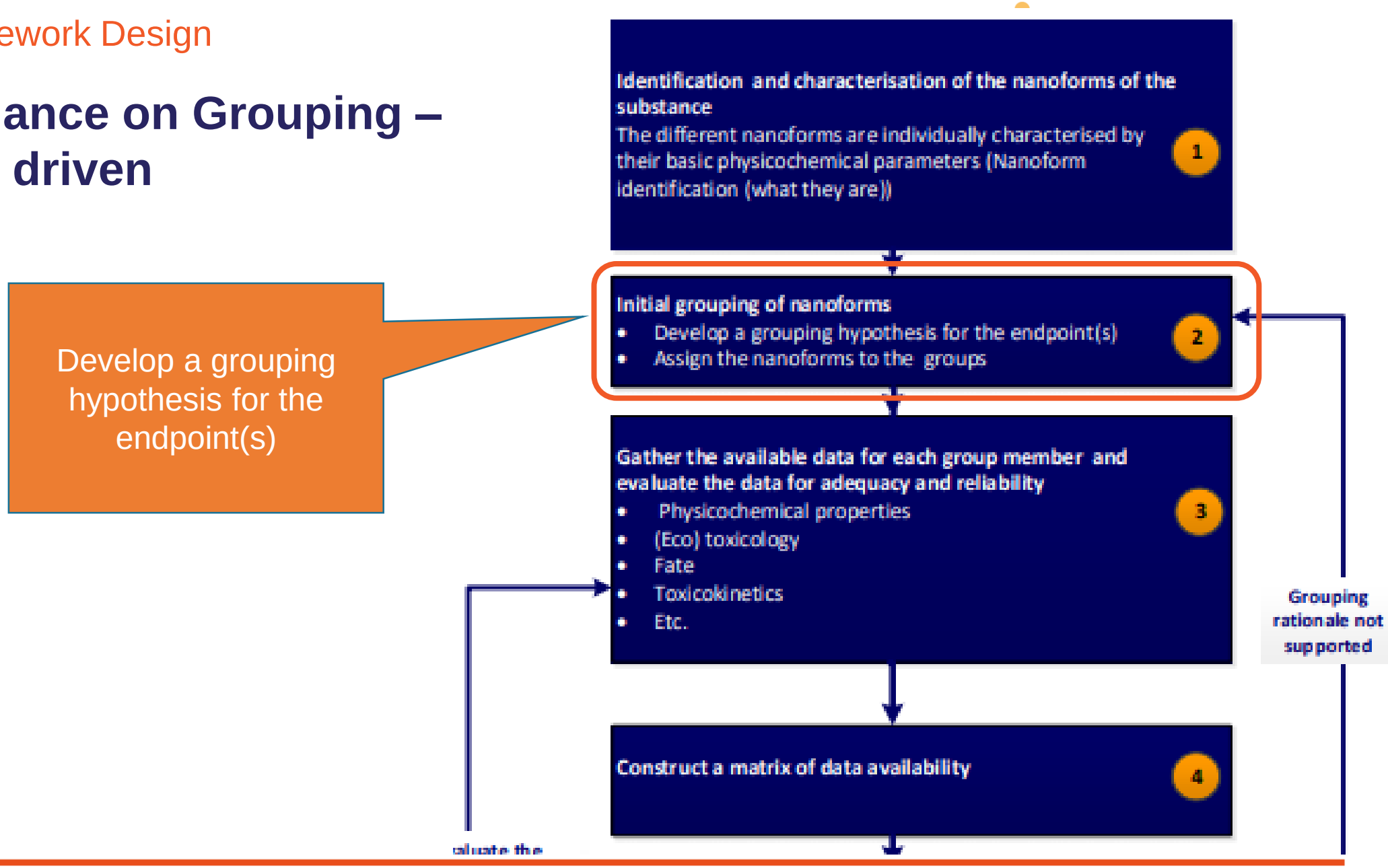
"By seeking similarities in physicochemical properties, toxicokinetic behaviour and fate, and (eco)toxicological behaviour between different nanoforms,

mainly using physicochemical parameters and/or in vitro screening methods,

it may be possible to develop a robust scientific explanation, which supports the assumption of similar hazard properties within a defined group of nanoforms"

https://echa.europa.eu/documents/10162/23036412/appendix_r6_nanomaterials_en.pdf

ECHA Guidance on Grouping – hypothesis driven



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GRACIOUS framework - Hypothesis Driven

Purpose: Precautionary, Targeted testing, Regulatory, Safety by Design

Context: Occupational, Consumer, Environmental

Input from life cycle (WP2)	**What they are? (WP3)**
• Physical form when being handled (powder, suspension/liquid/ embedded in solid matrix, …) • Stability (agglomeration, solubility…) • Exposure form (quasi-spherical, elongated, plate, pure, attached to a particle, embedded in a matrix, ionic form)	Physicochemical identity
• Intended use, specific process (occupational) • Environmental compartment where they are released (workplace atmosphere, outdoors atmosphere, water, soil as waste) • Population exposed • Exposure route	**Where they go? (WP4)** Environmental fate, uptake and toxicokinetics
• Exposure dose. This can be unfolded in several tiers: - Qualitative; unlikely, negligible, likely - Quantitative; short/peak exposure, long-term exposure	**What they do? (WP5)** Human and environmental toxicity

Potential implications:

if in group:

if not in group:

- There are many ways to word and formulate a hypothesis
- To provide guidance to the user GRACIOUS has developed a Hypothesis Template

- Purpose
  - Precautionary
  - Targeted testing
  - Regulatory
  - Safety by design
- Context
  - Occupational
  - Consumer
  - Environmental

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What they are? (WP3)

Physicochemical identity

Where they go? (WP4)

Environmental fate, uptake and toxicokinetics

What they do? (WP5)

Human and environmental toxicity

Potential implications:

if in group:

if not in group:

- Input from life cycle
  - Physical form where handled (e.g. powder)
  - Stability (e.g. agglomeration, solubility)
  - Exposure form (e.g. spherical, elongated, plate)
  - Intended use
  - Environmental compartment to which released
  - Population exposed
  - Exposure route
  - Exposure dose

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What they are? (WP3)

Physicochemical identity

Where they go? (WP4)

Environmental fate, uptake and toxicokinetics

What they do? (WP5)

Human and environmental toxicity

Potential implications:

if in group:

if not in group:

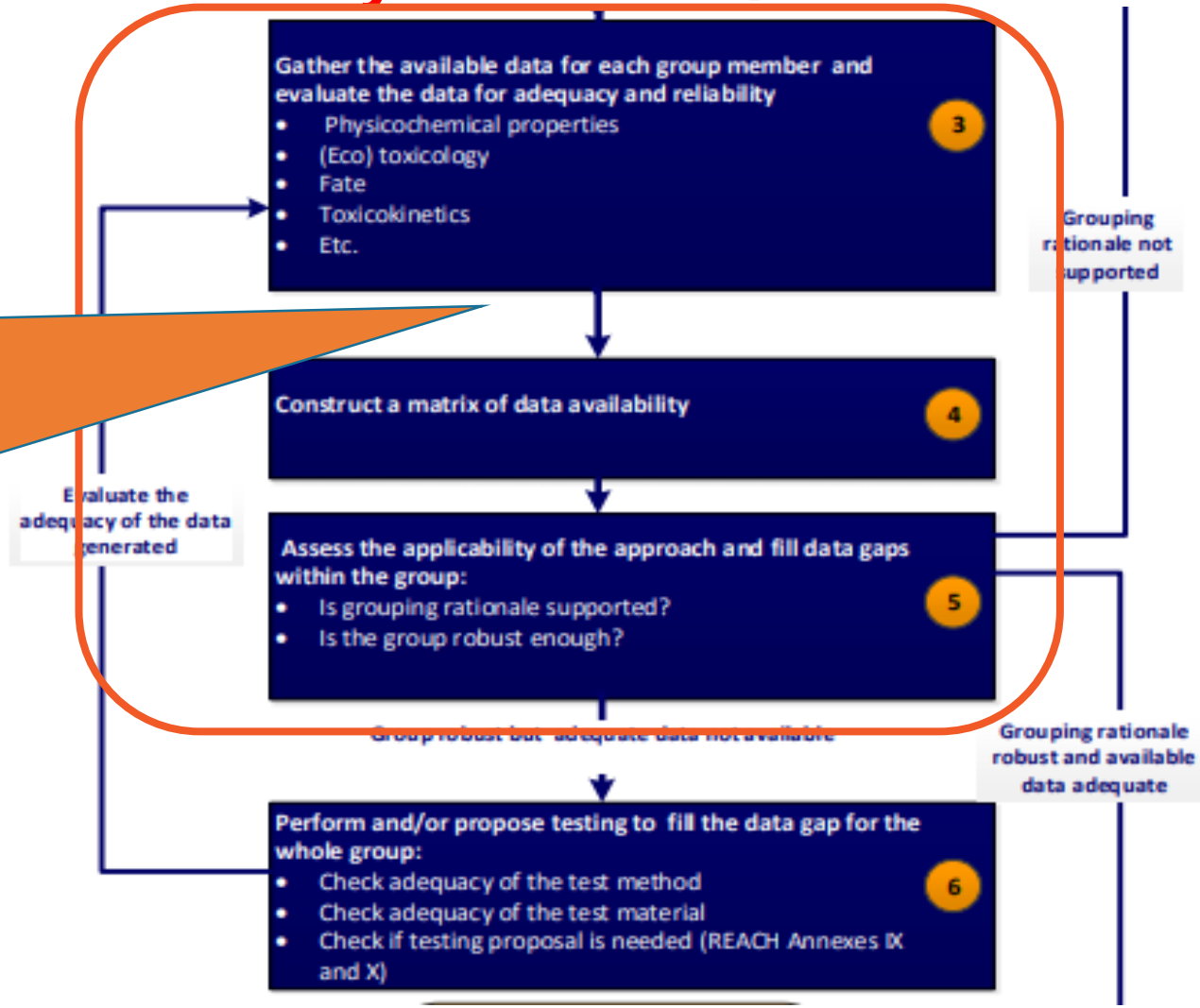
- What they are?
  - Physicochemical identity
- Where they go?
  - Environmental fate, uptake and toxicokinetics
- What they do?
  - Human and environmental toxicity

ECHA Guidance on Grouping – Data delivery

Gather available data
- Physicochemical
- (Eco) toxicological
- Fate
- Toxicokinetics etc

Construct a matrix of data availability

Assess the applicability of the approach
Fill data gaps within the group



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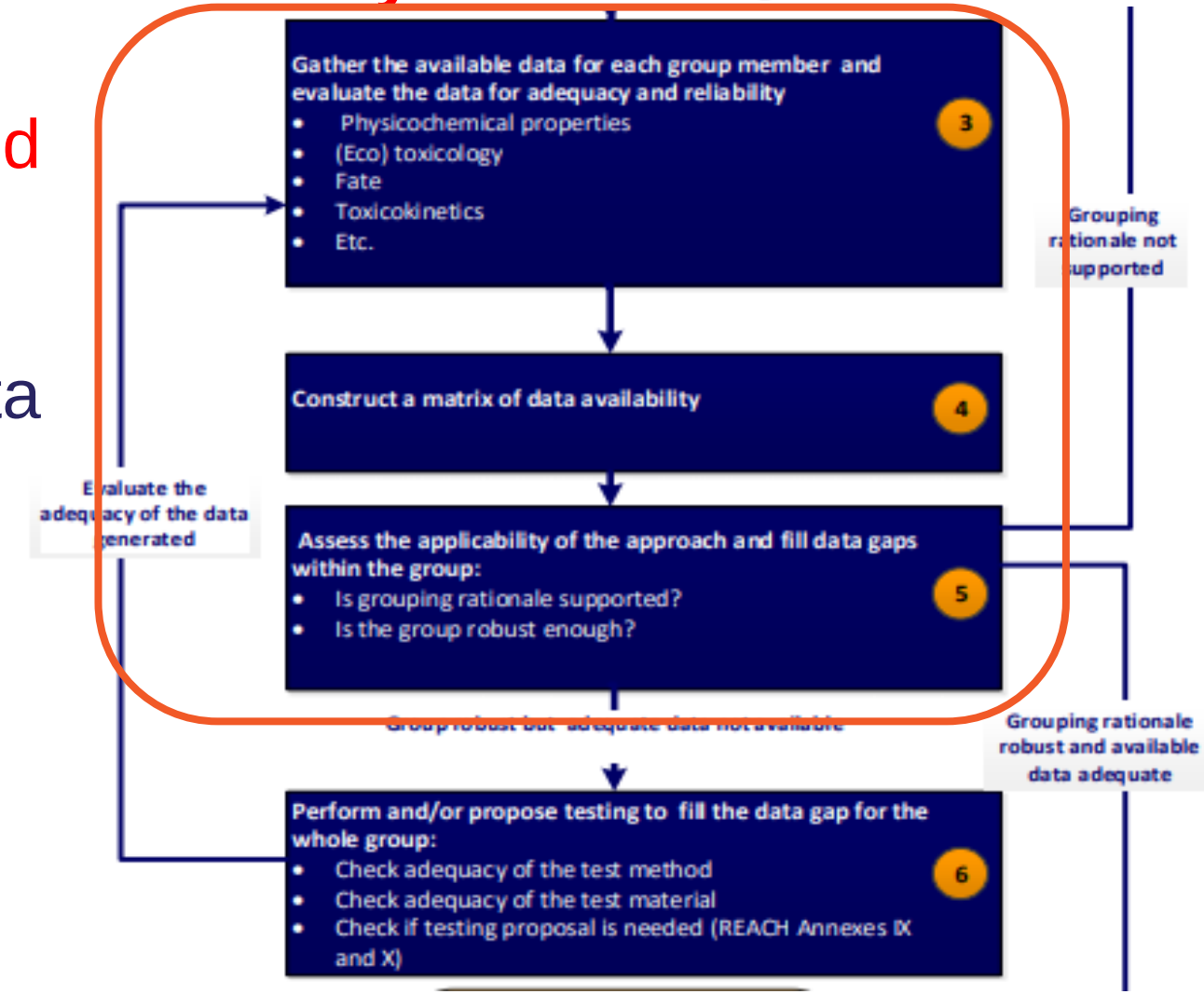
ECHA Guidance on Grouping – Data delivery

- GRACIOUS will develop Integrated Approaches to Testing and Assessment in order to
- Identify and utilise the existing data
- Identify essential data gaps
- Strategically fill data gaps
  - Using alternatives to animals where possible



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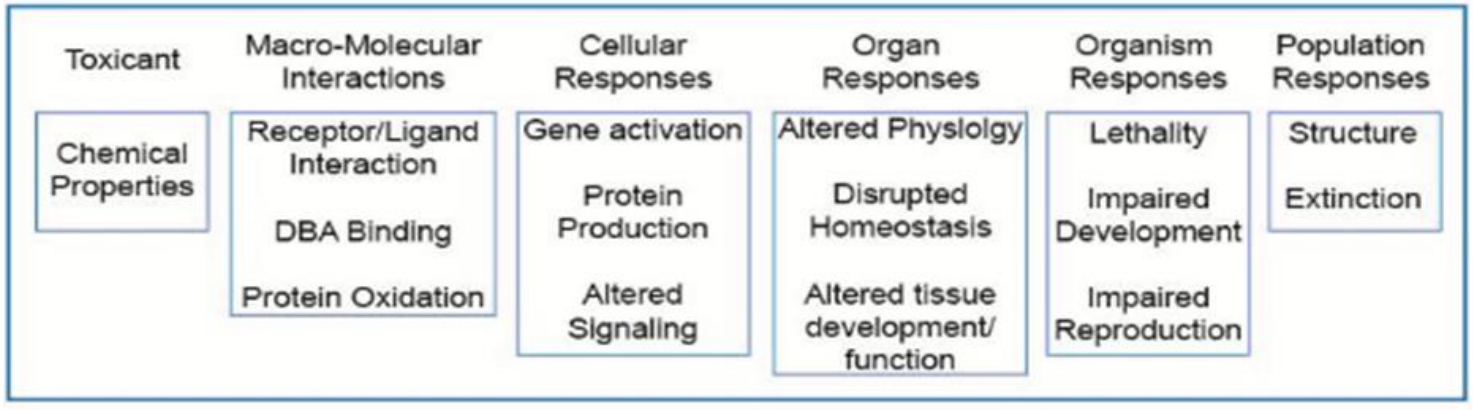
OECD Integrated Approaches to Testing and Assessment IATAs

- Pragmatic, science based approaches for chemical hazard characterisation
- Rely on integrated analysis of existing information coupled with the generation of new information using testing strategies
- Can include a combination of methods
- Design can be informed by Adverse Outcome Pathways



GRACIOUS framework - Hypothesis Driven IATAs

- Existing AOPs will inform IATA design where possible
- Testing will be guided via IATAs tailored to the hypothesis
- Data from the IATAs will allow the hypothesis to be refined
- Successive rounds of hypothesis refinement will generate a Grouping Decision with Justification

Lifecycle: Human exposure and environmental release		
What they are? Physicochemical identity	Where they go? Environmental fate, uptake and toxicokinetics	What they do? Human and environmental toxicity

The IATAs will cover each aspect of the hypothesis

Grouping Framework Design

Integrated Approaches to Testing and Assessment

- The IATA format uses the format suggested by OECD
- Each IATA design is ‘science based’ and tailored to the specific hypothesis
- Tailoring IATAs for the obvious hypotheses will be more straightforward than for bespoke hypotheses
- More detail on the IATA is available on a poster by Fiona Murphy

Grouping Framework Design

Integrated Approaches to Testing and Assessment

- GRACIOUS partners are now
  - working on the development of the IATA's
  - Identifying relevant, reliable, robust SOPs with a clear evidence base
    - OECD, ISO, others…
  - Formulating an appropriate structure
    - Sequential testing strategy (STS)
    - Integrated testing strategy (ITS)
- Stakeholder engagement is essential in the design of the IATAs
- Breakout sessions 2 and 3

Summary

- The GRACIOUS framework provides a structure to guide the Grouping of nanoforms to support read-across
- ECHA guidance suggests grouping should be hypothesis driven
- GRACIOUS has developed a template for grouping hypothesis generation that incorporates
  - Purpose
  - Live cycle
  - What they are, where they go and what they do
- The hypothesis can then be tested by an IATA, using OECD guidelines
- The IATA use Sequential testing strategy (STS) or Integrated testing strategy (ITS) formats, feeding in the tests developed and recommended by other projects such as NanoReg2.

We look forward to hearing your ideas

Thank you!

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