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FOOD AND FEED INGREDIENT SUBMISSIONS: THE IMPORTANCE OF PARTICLE SIZE

UNDERSTANDING AND INTERPRETING EFSA'S GUIDANCE ON NANOTECHNOLOGIES

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NANO GUIDANCE DOES NOT JUST APPLY TO NANOMATERIALS

- Regardless of whether your new ingredient is a deliberately “Engineered Nanomaterial”, EFSA guidance needs to be applied on a case by case basis of the assessment of all:
  - Food Additives
  - Food Enzymes
  - Food Flavourings
  - Food Contact Materials
  - Novel Foods
  - Feed Additives
- The guidance applies retrospectively to evaluations already in progress, re-evaluations and proactively to new submissions with all Panels now focusing more than ever before on this aspect
- The results of particle size analysis can challenge, change and even remove well-established ADIs
- In some cases it seems we are asked to prove a negative

EFSA GUIDANCE IS COMPREHENSIVE – APPLICATION OF IT IS COMPLEX

- One size does not fit all
- Toxicologists and non-specialist scientists do not have sufficient understanding of the test methods
- Analytical laboratories understand the test methods but not when and why to apply
- The result is time delays and misunderstandings between EFSA and applicants, especially for retrospective re-evaluations
- Increases EFSA's workload and increases applicants frustration
- Toxicologists and dossier writers need to understand what to do at a much earlier stage in order to satisfy EFSA

PHYSICOCHEMICAL CHARACTERISTICS

"As an essential requirement, all dossiers related to nanomaterials … have to be accompanied by thorough information on the particle size distribution and other parameters … of the material obtained through validated methods based on suitable analytical techniques as detailed in the present Guidance…"

Even if the primary particle size is <100 nm:

"The following parameters **may** indicate a loss of nano properties or a low exposure to nanoparticles:

1. high dissolution rate (e.g. in water, food/feed matrix or body fluids)
2. high rate of degradability (e.g. biological or photocatalytic) to non-nanosized degradation products,
3. the presence of/as aggregates rather than agglomerates (e.g. determined by conditions of production),
4. fixed, permanent bonding in matrices (e.g. stability of matrix, type of bond, end-of-life behaviour) or effective entrapment in food contact materials (e.g. polymer nanocomposites)."

https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5327

HOW TO DECIDE

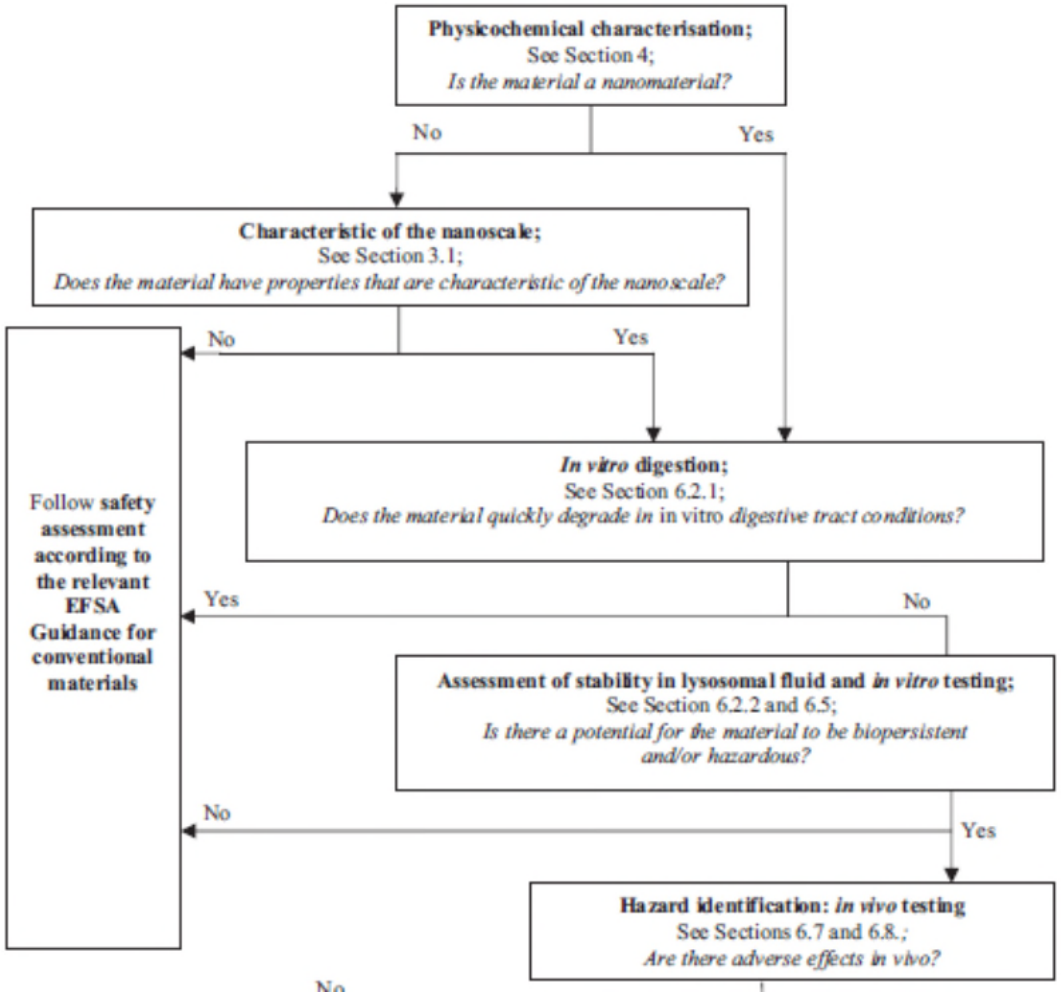

Figure 1: Schematic outline for risk assessment of ingested nanomaterials for human and animal health, focussing on hazard characterisation

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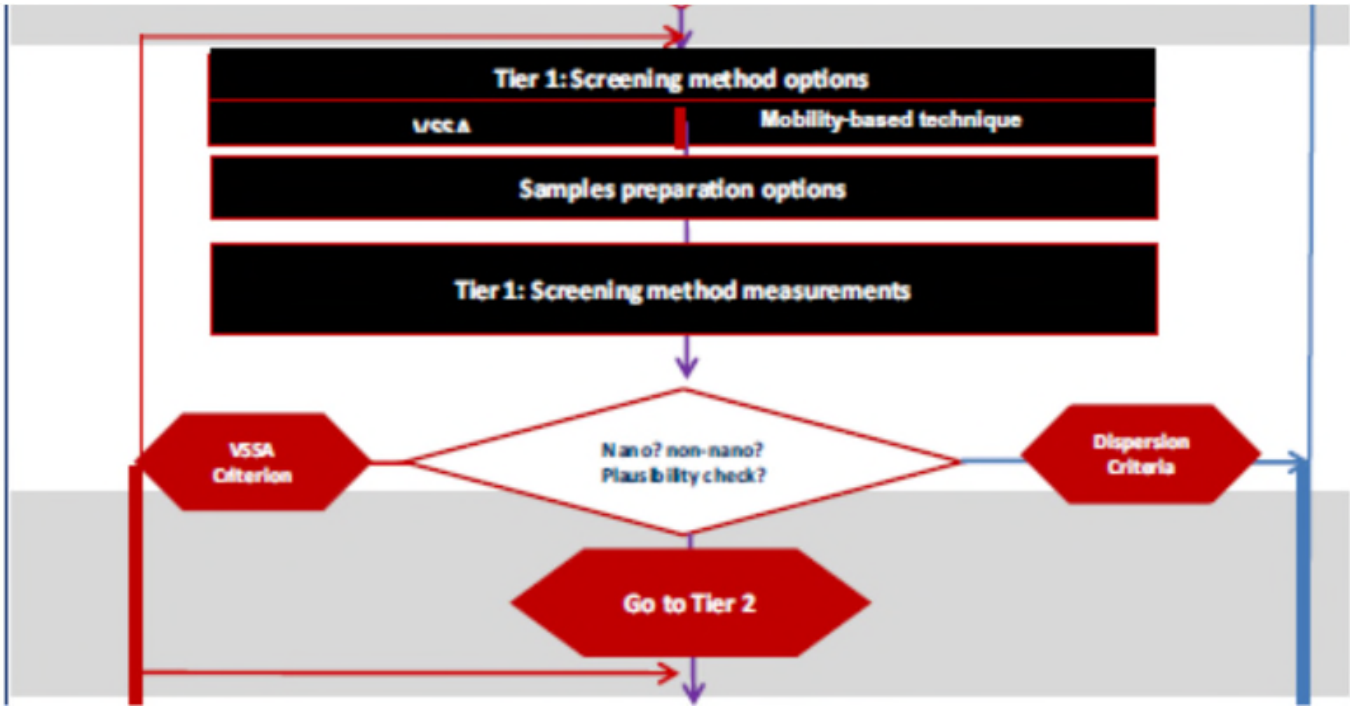
DECISION TREE – TIER 1



“VSSA” (Powders)
Surface area (volume, mass specific) Adsorption isotherms methods, e.g.
Brunauer Emmett Teller method (BET) (ISO 9277, ISO 15901-2/-3, ISO 18757)
“Dispersion Criteria” (Dispersions)
Dynamic light scattering (DLS) ISO22412
Method Optimisation may be required.

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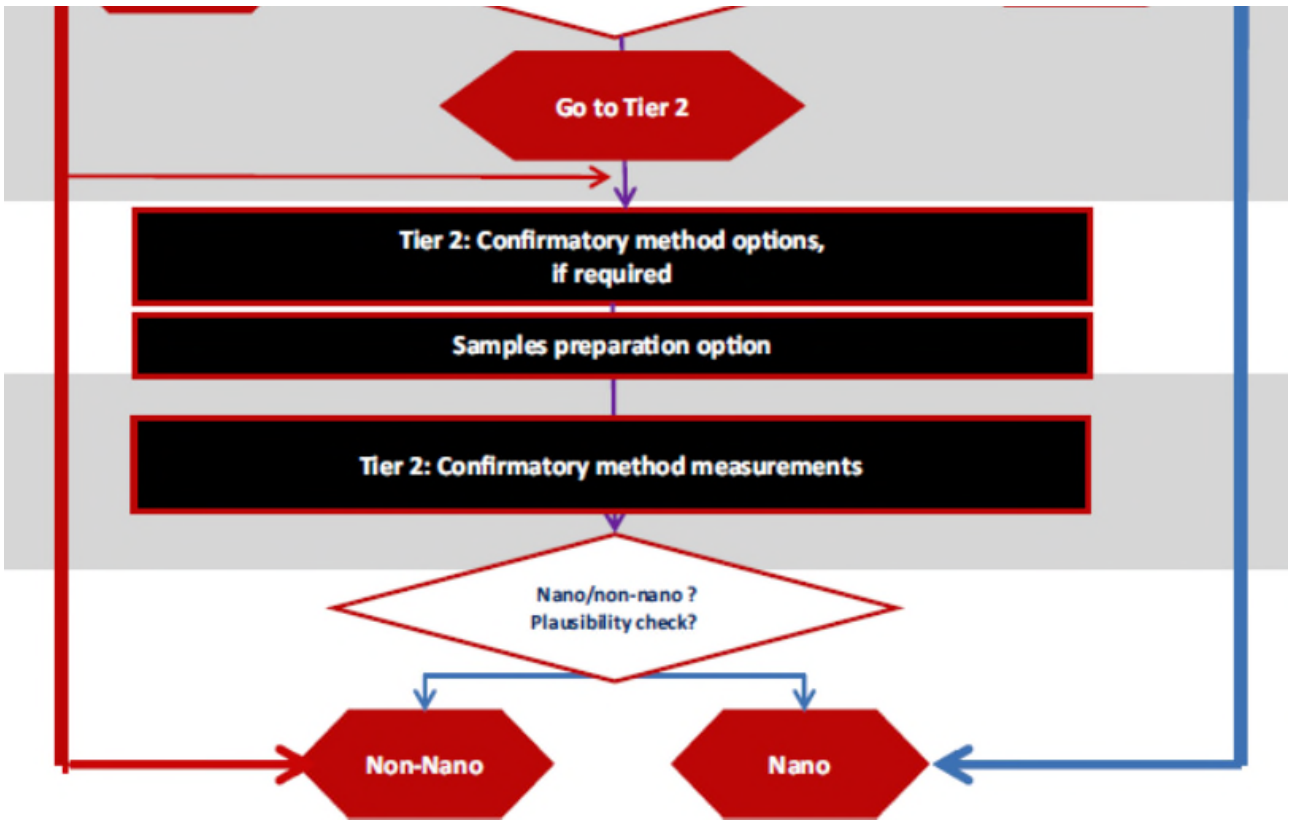
DECISION TREE – TIER 2



PRACTICAL APPLICATION – FERRIC SODIUM EDTA

- EFSA Scientific opinion (3 August 2018)(extension of existing approval)
- "…both Ferrazone® and Ferrazone XF® have a **solubility in water of 90 g/L at 20°C**"
- "The information **provided indicated that the particle size corresponding to 10% of the cumulative undersize distribution by volume was around 3 µm**. However, the Panel noted that the data provided did not follow the recommendation from the EFSA Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed (EFSA Scientific Committee, 2011, 2018) where information on particle size, number based size distribution and mass based size distribution of the material is requested to be measured by **more than one independent technique, one being electron microscopy (EM)** and if EM cannot be applied, the use of a different imaging technique is suggested. Therefore, based on the information provided, **the Panel cannot exclude the presence of particles of ferric sodium EDTA in the nano range in Ferrazone XF® in the solid form**."

https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2018.5369

WHAT WE NEED AS APPLICANTS

- An overview and understanding of particle size testing for non-specialists
- Clearer understanding of how the decision trees works for laboratory specialists that are not toxicologists or dossier writers
- Where and when to apply each test
- Where to start and stop
- Broader implications to the safety assessment even if “non-nano”
  - Retrospective
  - Prospective
- Practical examples
- The guidance needs further amendments/clarifications

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