10. Anexos

10.1. Anexo I. Esquema para la implementación de SC Guidance on Nano-RA

Esquema de toma de decisiones. Identificación de materiales que requieren evaluación de riesgos y caracterización físico química (European Food Safety Authority, 2021)

AND THEIR PHYSICOCHEMICAL CHARACTERISATION (Sections 4 and 5) Guidance on Particle-Is the material legally defined as TR applies engineered nanomaterial/nanoform? (Section Does the material contain a 4.1) or does the material have Guidance for YES fraction of nanoparticles? properties characteristic of the (Section 4.2) ventional material nanoscale? (Section 4.3) is sufficient Physicochemical characterisation (Section 5), including SC Guidance on Nano-RA applies solubility and dissolution/degradation rate Guidance for conventional Are the nanospecific properties maintained? material is sufficient YES STEP 2: IN VITRO DIGESTION (Section 7) Does the material quickly and fully dissolve/degrade under digestive tract conditions? ↓ NO STEP 2A - REVIEW EXISTING INFORMATION **ORAL EXPOSURE** Review all information on physicochemical and toxicological ASSESSMENT OF aspects and/or relevant to grouping/read-across **PARTICLES** (Section 6) YES STEP 2B - GENERATE NEW IN VITRO DATA Direct Is there Including dissolution under lysosomal conditions, exposure: transfer from genotoxicity, cell toxicity FCM or does the material fully presence of dissolve/ residues of Is the material persistent Argument for waiving NO degrade in feed OR is there indication of the submission of nanothe food additives or toxicity? adapted in vivo studies matrix? pesticides in YES food as particles? STEP 3: IN VIVO TESTING (Section 7) NO STEP 3A - PILOT IN VIVO STUDY YES A pilot study for dose finding and assessment of ADME Does the material quickly and (≈ 14 days) is recommended fully dissolve/degrade under digestive tract conditions? STEP 3B - IN VIVO STUDIES In vivo genotoxicity if required + modified 90-day oral toxicity study + satellite group for assessment of ADME Exposure estimation based on (≈ 14 days, 90 days, elimination phase); histopathological quantification of nanoparticles and investigations of gastro intestinal sites and organs with nanosized degradation products emphasis on liver, brain, testis and spleen Do results warrant further testing? (e.g. slow elimination or accumulation and distribution to specific tissues) Integrate nano risk characterisation (Section STEP 4: TARGETED IN-DEPTH TESTS (Section 7.8) 8) and uncertainty For example, additional toxicokinetic studies (e.g. human analysis (Section 9) in studies), reproductive and developmental toxicity, sectoral framework for risk immunotoxicity, neurotoxicity, mutagenicity, carcinogenicity, assessment endocrine effects, effects on gut microbiome

STEP 1: IDENTIFICATION OF MATERIALS REQUIRING NANOSPECIFIC ASSESSMENT