Titanium dioxide in sunscreens

Cosmetic Solutions

BASF
The Chemical Company

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- Introduction
- Nano-particulate TiO_2 as a UV filter for sunscreens
  - Surface Treatments
  - Formulation examples
  - References for skin studies

Introduction

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- ✓ **In the USA, all sunscreens are OTC drugs and are subject to FDA regulation**
  - **SPF is a drug claim – prevention of sunburn**
- ✓ **The FDA currently approves of 16 active ingredients (UV Filters) for prevention of sunburn in the pending Sunscreen Monograph**
  - **14 are organic**
  - **2 are inorganic – Titanium Dioxide and Zinc Oxide and are approved up to 25%**
  - **4 more are pending approval**
  - **An additional one (Mexoryl) is allowed through NDA**
- ✓ **All active ingredients must conform to the USP**

Range of solar UV exposure

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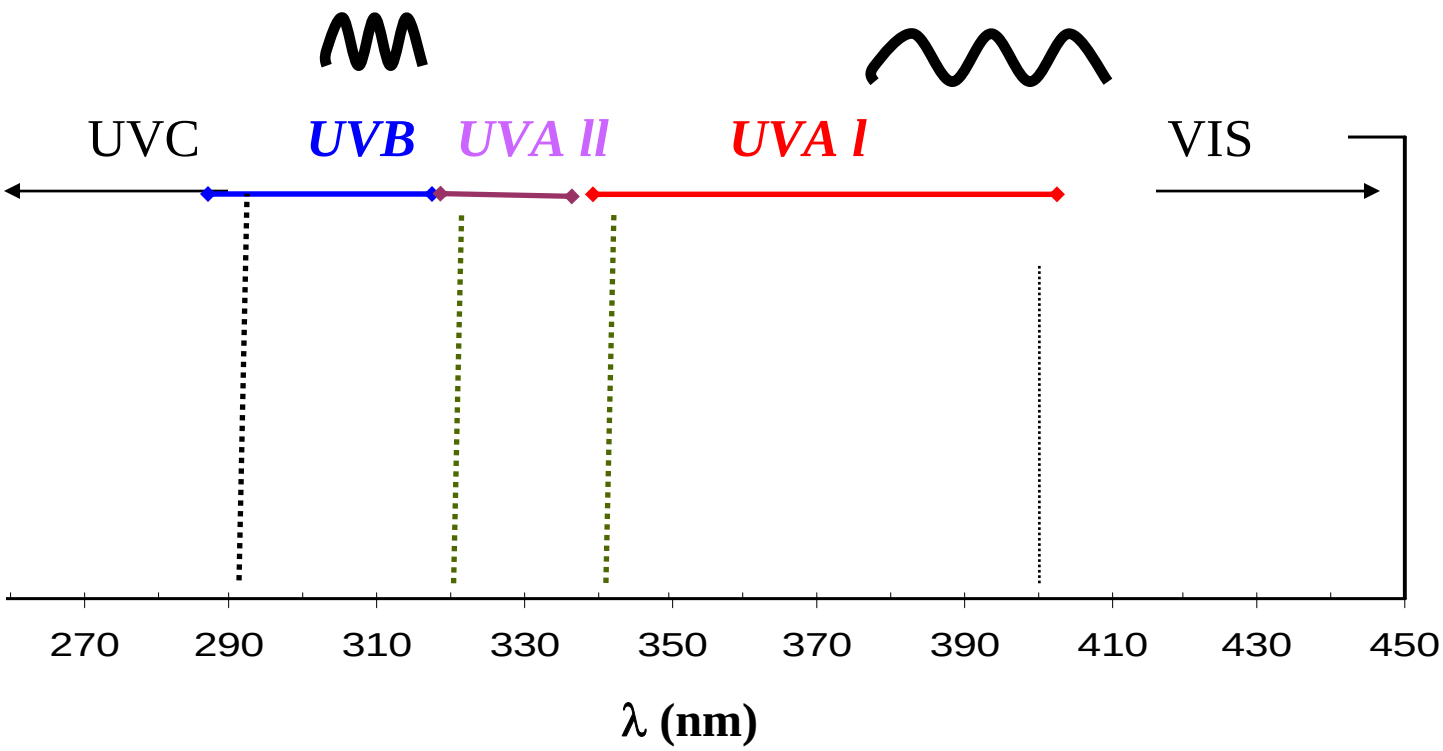

UVB is the main contributor to sunburn

Absorbance of UV radiation with TiO_2

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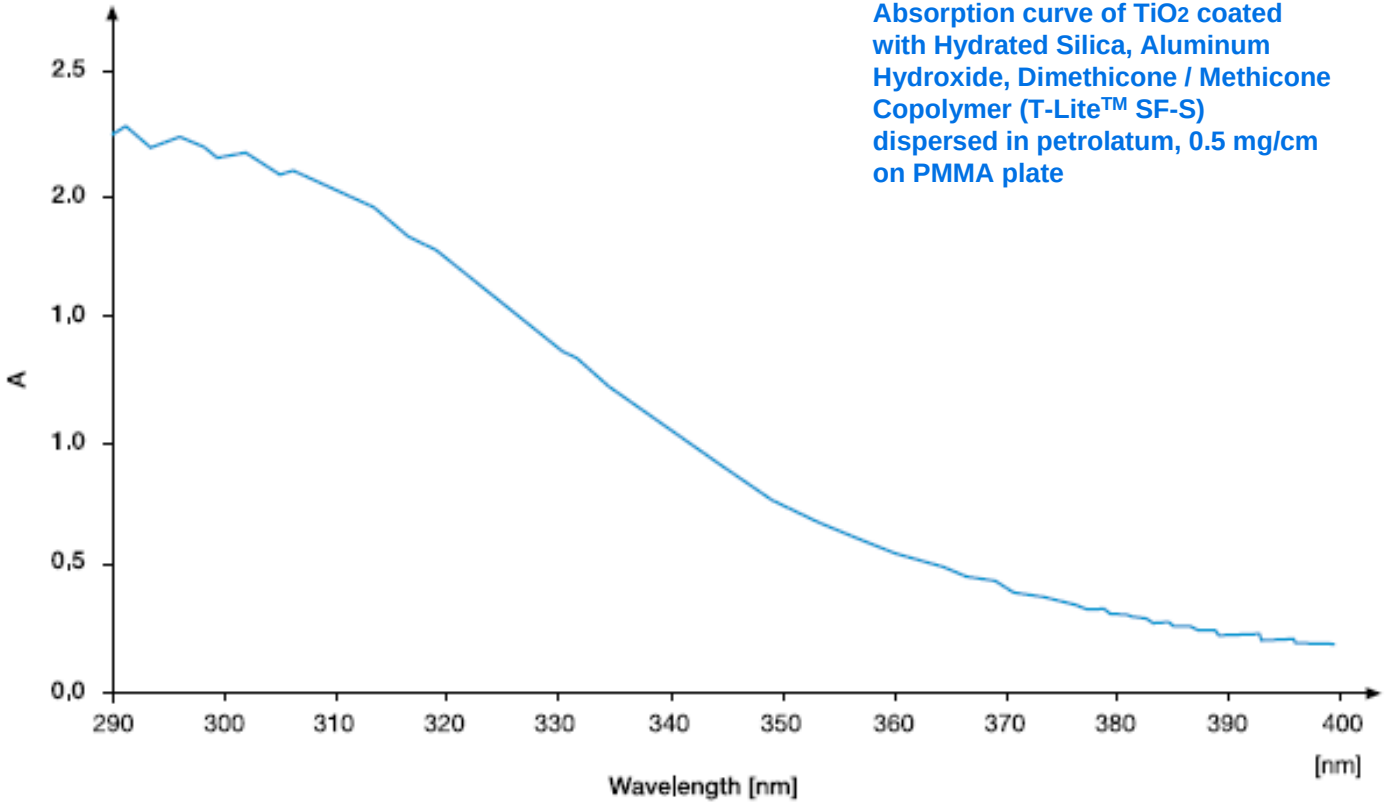

Absorption curve of TiO_2 coated with Hydrated Silica, Aluminum Hydroxide, Dimethicone / Methicone Copolymer (T-Lite™ SF-S) dispersed in petrolatum, 0.5 mg/cm on PMMA plate

Particle Size vs UV-Attenuation

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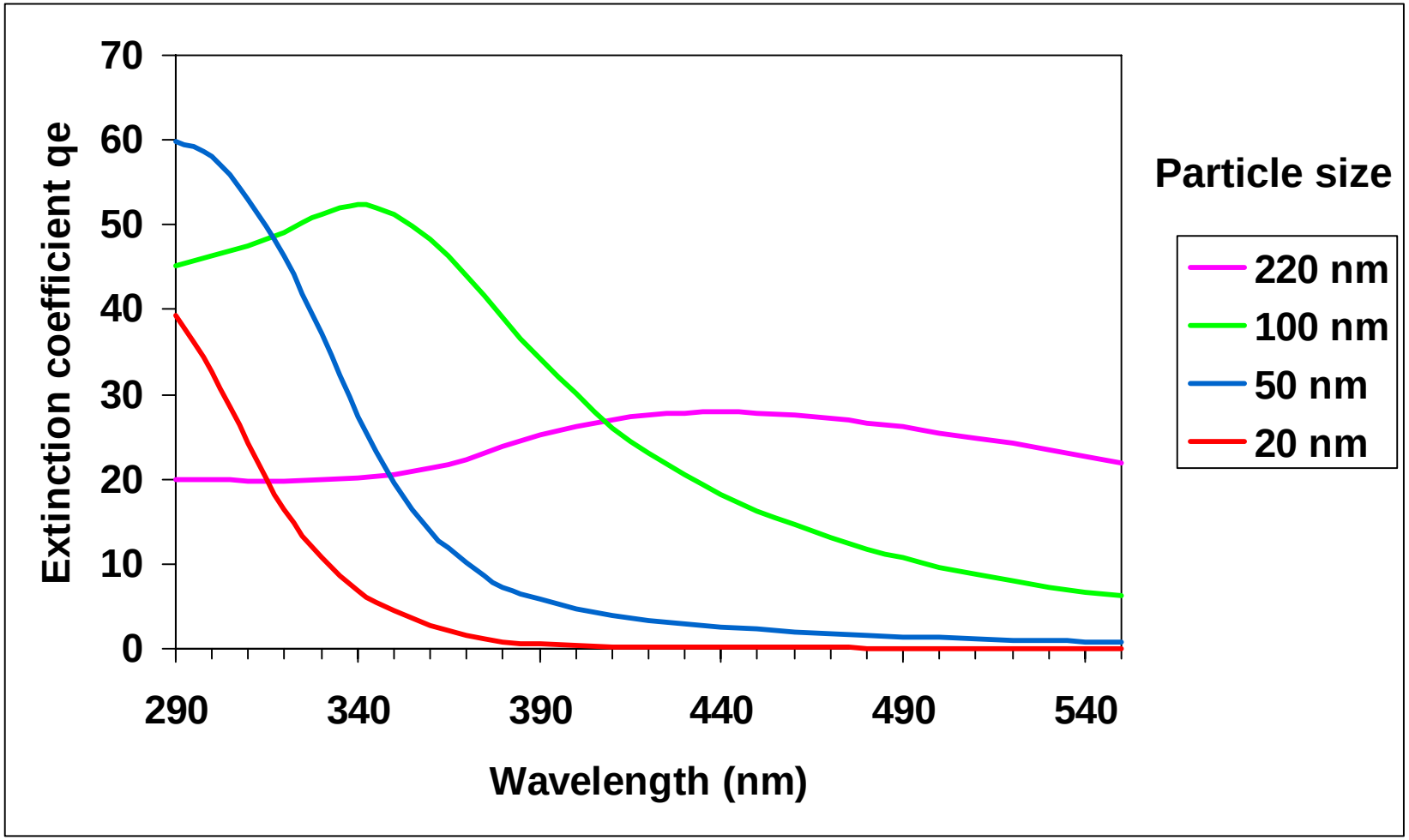

Slide kindly provided by CRODA

Particle Sizes in Inorganic Sunscreens

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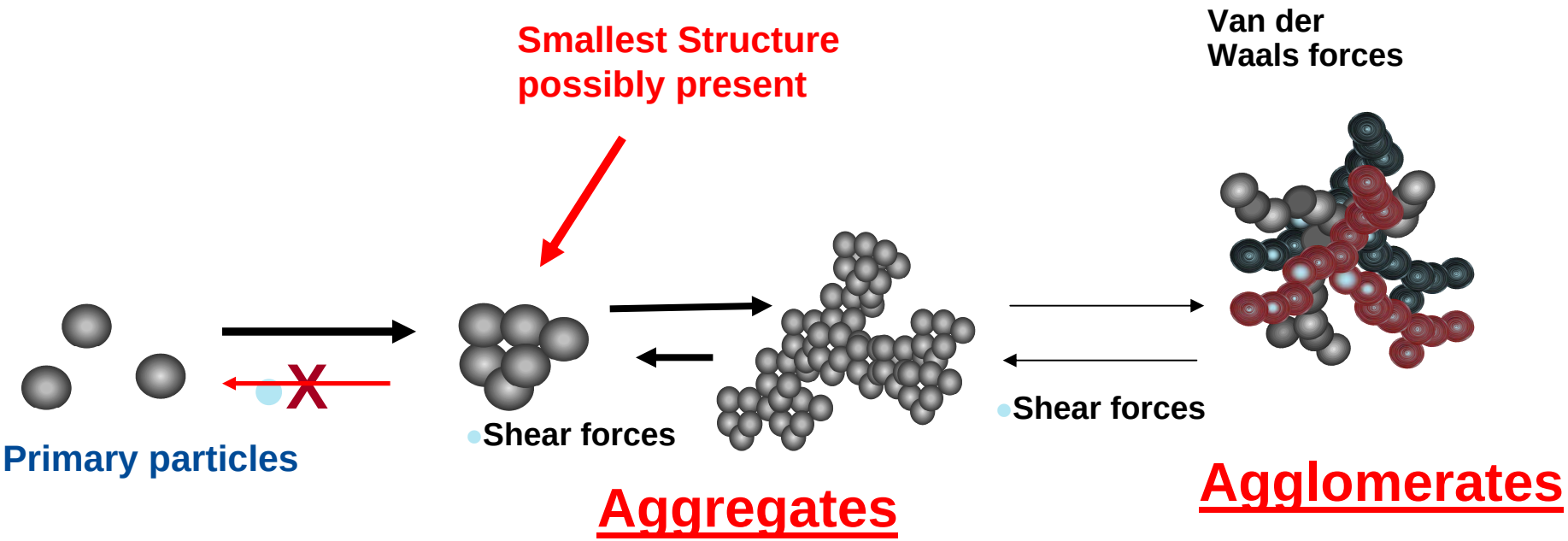
- Individual TiO_2 primary nanoparticles (crystals) of spherical or acicular shape, size typically 10 – 50 nm
- Individual nanoparticles are extremely difficult to isolate and do not occur as such in practical systems



Some surface treatments / coatings for attenuation – grade TiO2 used in the sunscreen industry

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- **BASF – T-Lite™**
  Hydrophobic powders of TiO_2 coated with:
  - Aluminum Hydroxide, Dimethicone / Methicone Copolymer
  - Hydrated Silica, Aluminum Hydroxide, Dimethicone / Methicone Copolymer
  - Hydrated Silica, Aluminum Hydroxide, dimethoxydiphenyl silane / triethoxycaprylyl silane crosspolymer

- **EMD – Eusolex® T** brands – TiO_2 coated with
  - Alumina
  - Silica
  - Alumina / Stearic Acid
  - Simethicone
  - Alumina / Simethicone

  (Some dispersed in water or organic oils with surfactant)

- **SunJin – Softitan, Sunsil-T, SunClear**
  - TiO_2 encapsulated within Silica beads
  - TiO_2 Agglomerates with Silica and Alkyl Silanes
  - Dispersions of TiO_2 coated with Aluminium Hydroxide / Stearic Acid

Some surface treatments / coatings for attenuation – grade TiO2 used in the sunscreen industry

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- **Tayca – MT**; several brands
  - Aluminium Hydroxide / Silica
  - Aluminium Hydroxide / Hydrated Silica
  - Aluminium Hydroxide / Stearic Acid
  - Aluminium Hydroxide / Silica / Triethoxycaprylyl silane
  - Aluminium Hydroxide / Stearic Acid / Triethoxycaprylyl silane
  - Aluminium Hydroxide / Hydrated Silica / Triethoxycaprylyl silane

- **Kemira – UV Titan®** brands
  - Alumina/ Stearic Acid
  - Alumina
  - Aluminum Hydroxide/ Stearic Acid
  - Dimethicone / Alumina
  - Silica / Methicone

- **DSM – Parsol TX -** TiO_2 coated with silica and dimethicone

- **Ishihara Sangyo Kaisha – TTO** brands TiO_2 coated with:
  - Aluminium Hydroxide
  - Silica
  - Aluminium Hydroxide / Silica
  - Aluminium Hydroxide / Stearic Acid
  - Aluminium Hydroxide / Iron Oxide
  - Aluminium Hydroxide / Iron Oxide / Zirconium Oxide
  - Aluminium Hydroxide / Zirconium Oxide
  - Aluminium Hydroxide / Stearic Acid / Zirconium Oxide

- **Rhodia – MiraSun** TiO2 coated with silica, aluminia in water

Some surface treatments / coatings for attenuation – grade TiO2 used in the sunscreen industry

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- **Kobo**; several brands including dispersions in organic oils of TiO_2 coated with:
  - Silica
  - Triethoxycaprylylsilane
  - Aluminium Hydroxide / Isopropyl Titanium Triisostearate
  - Aluminium Hydroxide / Hydrated Silica
  - Aluminium Hydroxide / Stearic Acid
  - Alumina / Triethoxycaprylylsilane
  - Alumina / Methicone
  - Alumina / Triethoxysilylethyl Polydimethylsiloxyethyl Methicone Crosspolymer
  - C9-15 Fluoroalcohol Phosphate
  - Aluminium Hydroxide / Stearic Acid / Triethoxycaprylyl silane
  - Silica / Triethoxycaprylyl silane

- **Sakai – STR-100W**
  TiO2 coated with Trimethylolpropane / Hydrated Silica

- **Evonik – TegoSun T;**
  TiO2 coated with trimethoxycaprylylsilane

- **Croda – Tioveil™** TiO_2 dispersed in organic oils or water containing surfactants; TiO2coated with either;
  - Alumina / aluminum stearate
  - Alumina / silica

****This list is not all-inclusive; there are other suppliers and surface coatings for TiO2**

Typical formulation using microfine TiO_2

SPF 30 Sunscreen Lotion
Featuring T-Lite SF-S (KG 6131/1)

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Ingredients	W/W%
Phase A	
Deionized Water 5	9.50
EDETA® BD (Disodium EDTA)1	0.20
D-Panthenol 75 W (Panthenol)1	0.40
Phase B	
Propylene Glycol	3.00
Xanthan Gum	0.30
Magnesium Aluminum Silicate	0.50
Phase C	
Uvinul® M 40 (Oxybenzone)1	2.00
Uvinul N 539 T (Octocrylene)1	3.00
Isopropyl Myristate	8.00
DEA-Oleth-3 Phosphate	0.20
Cetearyl Alcohol (and) Cetearyl Glucoside	2.00
Cremophor® A 25 (Ceteareth-25)1	1.50
Cremophor A 6 (Ceteareth-6 (and) Stearyl Alcohol)1	1.00
Behenyl Alcohol	0.50
Cetearyl Alcohol	1.50
T-Lite™ SF-S (Titanium Dioxide (and) Silica Hydrate (and) Dimethicone/Methicone Copolymer (and) Aluminum Hydroxide)	4.00
Vitamin E Acetate (Tocopheryl Acetate)1	0.10
Bisabolol, rac (Bisabolol)1	0.20
Phase D	
Z-COTE HP1® (Zinc Oxide (and) Triethoxycaprylylsilane)1	4.00
Uvinul MC 80 (Octinoxate)	7.50
Phase E	
DMDM Hydantoin (and) Iodopropynyl Butylcarbamate	0.50
Fragrance	0.10
	100.00

Procedure

•Combine phase A.

•Combine phase B

•Under propeller mixing add phase A/B to phase A and heat to 75-80°C.

•Combine phase C and heat to 75-80° C and homogenize for 2-3 minutes.

•Use prepared grind of phase D and add to phase C. (To make a grind, combine the phase and homogenize it for 10 minutes until uniform). Homogenize phase C/D for 3 minutes until uniform.

• Using homogenizer, add phase C/D to phase A/B and homogenize for 4-5 minutes until uniform. Transfer to sweep mixing.

•At 40° C, add phase E one at a time and mix well. Cool to room temperature.

Typical formulation using microfine TiO_2

W/O emulsion SPF25, PA++ from SUNJIN

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- See SunJin website for formulation details

Reference: **www.sunjinchem.com**

Typical formulation using microfine TiO_2

High SPF Transparent Sunscreen from Kobo using dispersions of TiO2

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- See KOBO website for formulation details

Reference: www.koboproductsinc.com/UVPigments.html

Nanostructured TiO_2 in a Sunscreen Formulation by Cryo TEM

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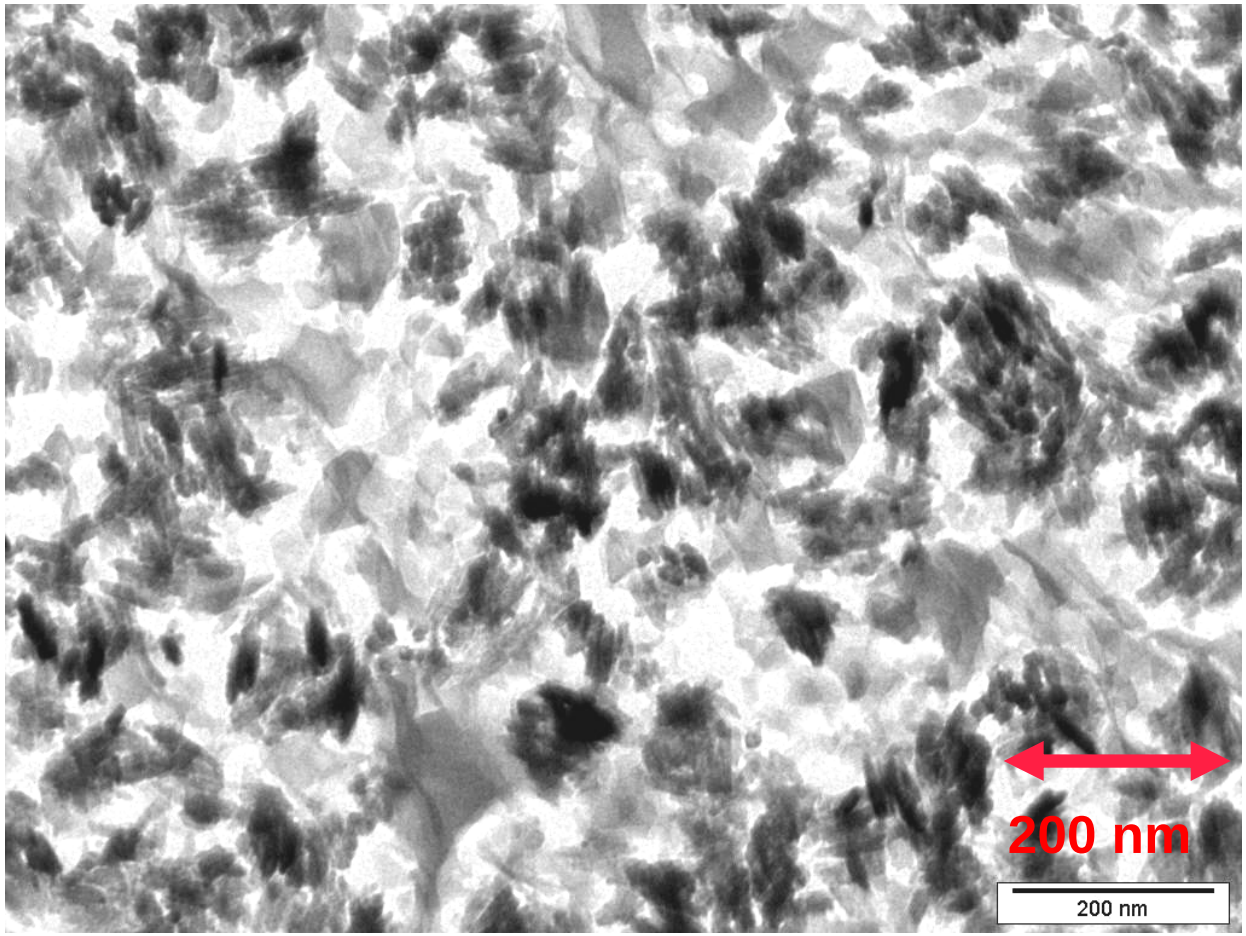

Agglomerates
>> 100 nm

Cluster and Particles
> 50 - 150 nm

BASF SE, unpublished data

Nanostructured TiO_2 in a Sunscreen Formulation - Cryo Replica TEM

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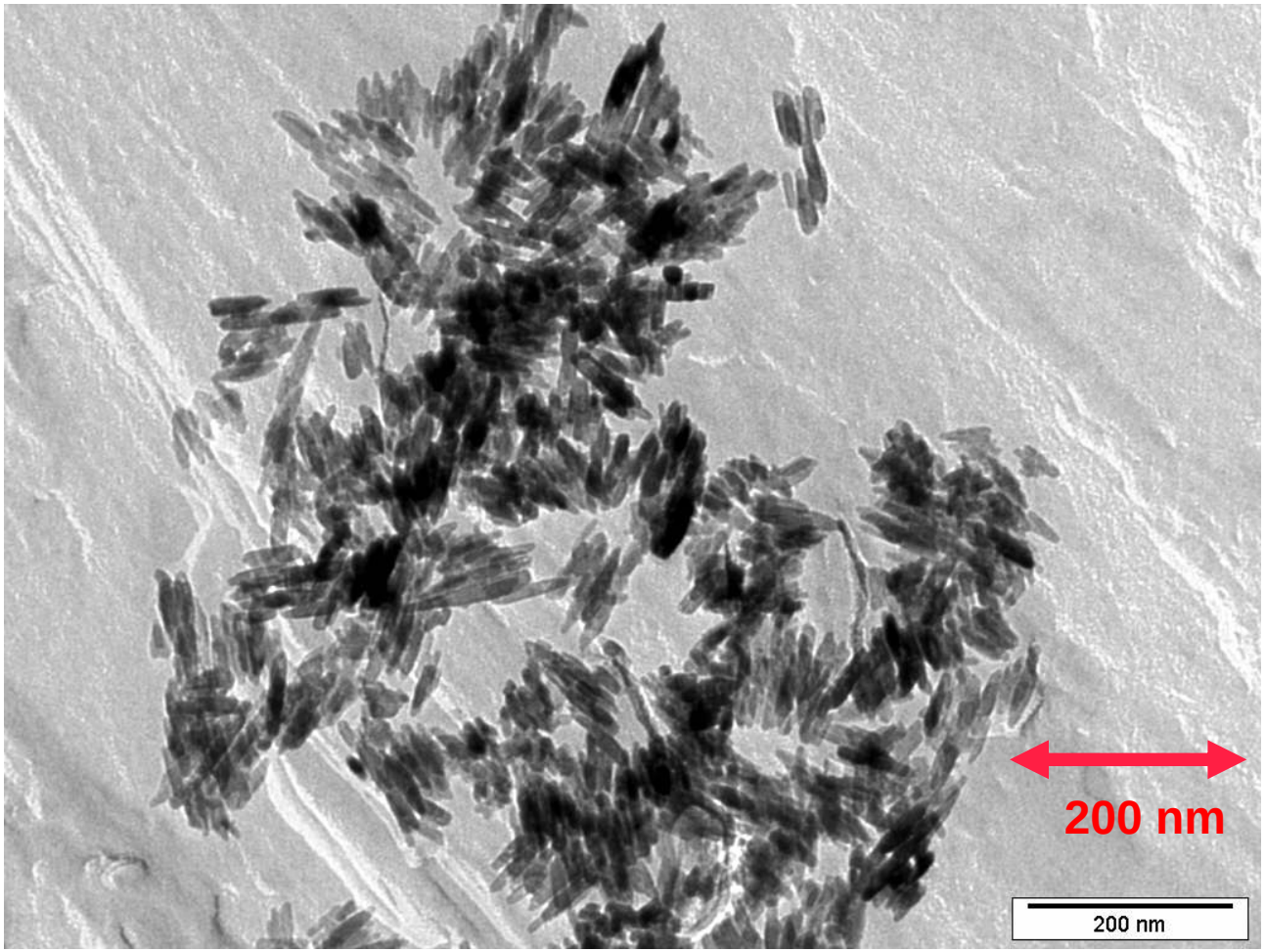

Agglomerates
>> 100 nm

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BASF SE, unpublished data

Nanostructured TiO_2 in a Sunscreen - TEM images

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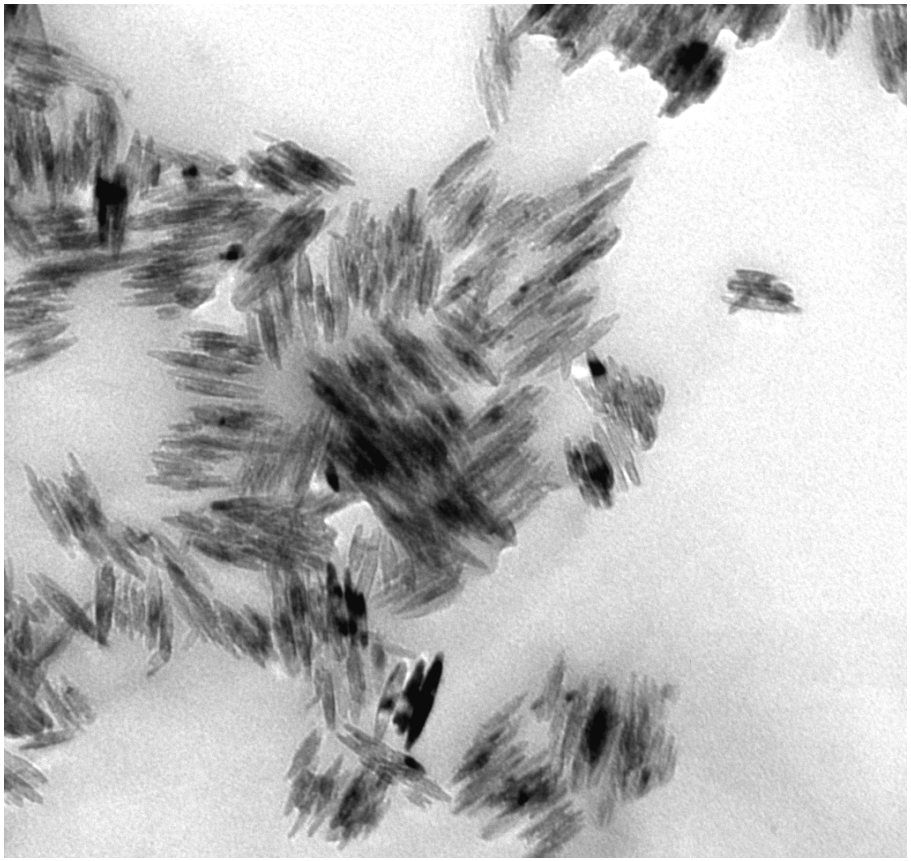

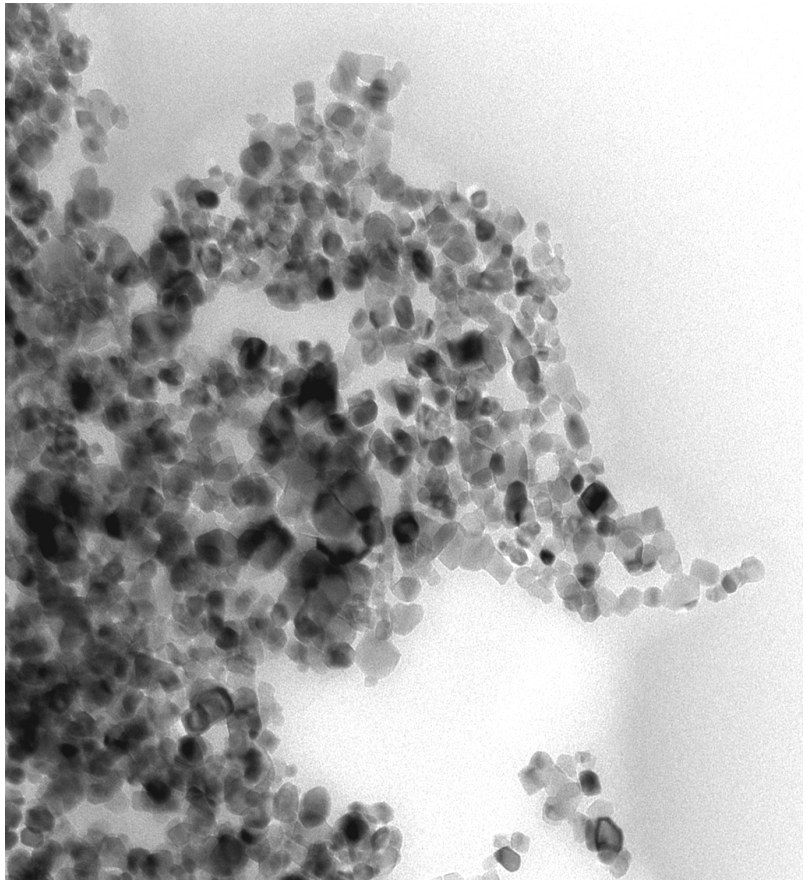

Images prepared at BASF on behalf of COLIPA / Cefic / EFfCI consortium, 2009

Some safety studies on nano-particulate TiO_2 published in scientific literature

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- Gamer, et al *; Toxicology in Vitro* (2006): 20/ 301–307: Examined the potential for penetration of nanoparticulate TiO2 through ski; This study showed that nanoparticle TiO2 did not penetrate beyond the stratum corneum on an animal model (*ex-vivo* with pigskin), supporting other studies
- Fabian, et al *; Arch. of. Toxicology* (2008) 82:3/:151 – 157, examines the fate of nanoparticulate TiO2 after intravenous injection (*in-vivo* with rats). No evidence of harmful effects seen to vital organs was seen.
- Schulz, et al; *Advanced Drug Delivery Reviews* (2002) 54 Suppl. 1 / S157–S163; Micronised titanium dioxide is solely deposited on the outermost surface of the stratum corneum and cannot be detected in deeper stratum corneum layers, the human epidermis and dermis.
- Lademann et al; *Skin Pharmacology and Applied Skin Physiology (*1999);12 / 247-256; TiO2 microparticles in a sunscreen formulation remained in the the horny layer and the follicular orifices of the skin with no penetration into viable epidermis
- Mavon, et al *Skin Pharmacol Physiol* (2007) ;20/10–20; More than 90% of micronized TiO2 in sunscreen applied to skin was recovered in 15 tape strippings, the remainder was in furrows of the skin, none detected in receptor fluid of Franz Cell.
- Pfluecker F, et al; *Int. J. Cosmet. Sci*. (1999); 21(6):399-411.The outermost stratum corneum layer is an effective barrier against dermal uptake of topically applied micronized titanium dioxide
- Sugibayashi et al. *J. Toxicol. Sci*, (2008), 33, 293-298, Toxicological effects and clearance rates of microfine TIO2 on rodent organs .
- Australian TGA (2005) A review of the scientific literature on the safety of nanoparticulate titanium dioxide or zinc oxide in sunscreens