

## Synoxyl® HSS:

A Breakthrough Photostabilizer with  
SPF Boosting & Unique Skin Protection Properties

Sytheon Ltd., USA

[info@sytheonltd.com](mailto:info@sytheonltd.com)

973-988-1075

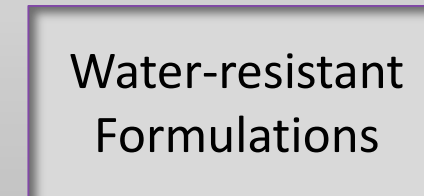
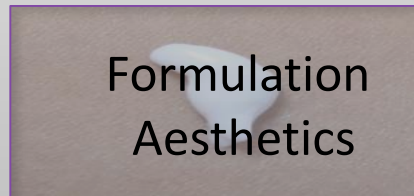
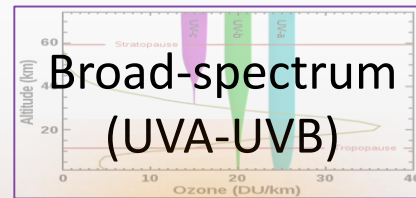
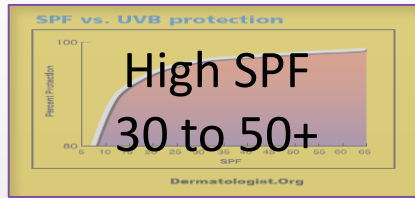
Sytheon SARL, France

[sytheon@sytheonltd.com](mailto:sytheon@sytheonltd.com)

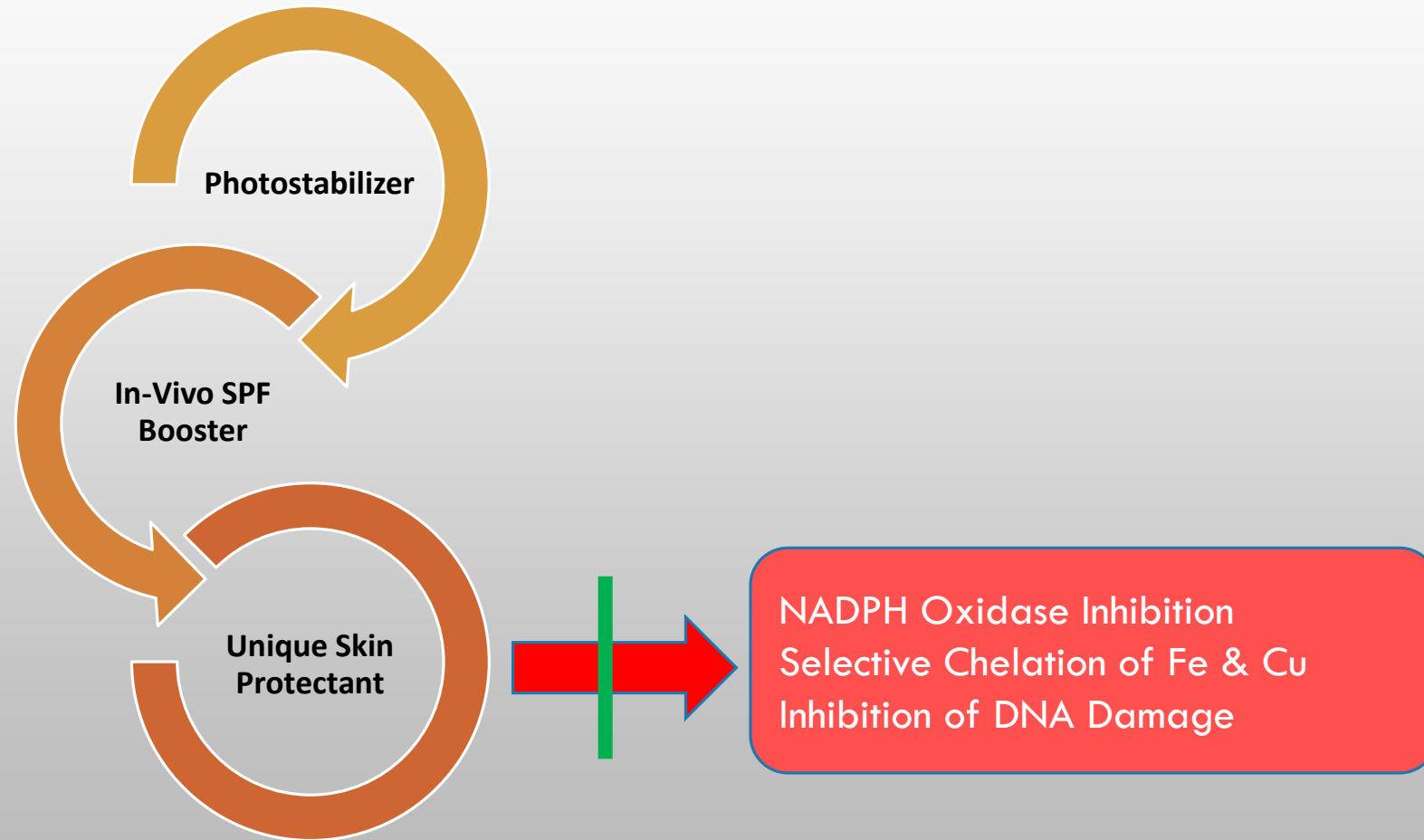
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[www.sytheonltd.com](http://www.sytheonltd.com)

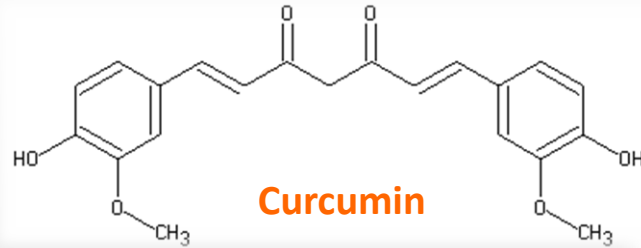
# Global Market Requirements for Effective Sun Protection



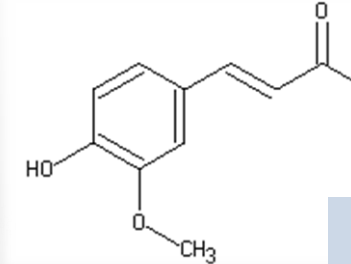
## Synoxyl<sup>®</sup> HSS Provides 3-in-1 Solutions to Skin Protection



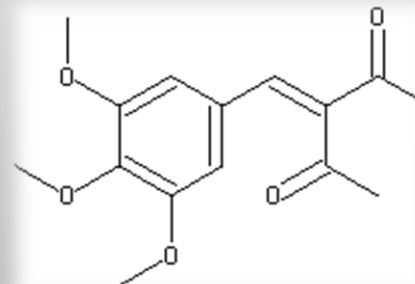
## Synoxyl® HSS Design Rationale: Inspired by Nature...



Photochemically unstable; Pro-oxidant  
Intense yellow



Photochemically unstable; Phototoxic;  
Intense yellow

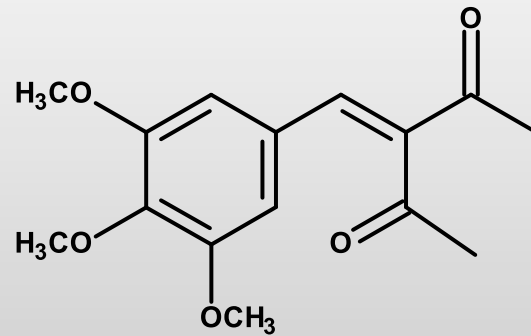


**Synoxyl® HSS**  
Trimethoxybenzylidene Pentanedione



Photochemically stable; Non-phototoxic;  
Off-white to pale yellow

## Product Overview



Synoxyl® HSS

Trade Name	Synoxyl® HSS
Chemical name	3-(3,4,5-Trimethoxybenzylidene)-2,4-pentanedione
CAS #	945558-97-4
INCI name	Trimethoxybenzylidene Pentanedione
REACH Status	Registration # 01-2120085337-50-0000
Appearance	Off-white to pale yellow powder
Purity	99% min
Storage stability	3 yrs. min
Melting point	79 to 84 °C
Solubility	>30% in DMI; ~15% in PEG-8 ~ 15% in PEG-6; ~ 20% in Ethanol; ~15% Phenylethyl benzoate; ~10% in HMS; ~10% in HydraSynol™ DOI; ~ 10% in Tween 20; ~ 7% in Polysorbate 80; ~5% in C <sub>12-15</sub> Alkyl benzoate
Formulation	pH < 6.5; Avoid using basic materials; Use antioxidant & β-cyclodextrin
Patent status	US 8,617,528; 8,414,870; EP 2649033; 2649034; other pending patents

### Publication

RK Chaudhuri, MA Ollengo, P Singh and BS Martincigh, 3-(3,4,5-Trimethoxybenzylidene)-2,4-pentanedione: Design of a Novel Photostabilizer with In-vivo SPF Boosting Properties and Its Use in Developing Broad-spectrum Sunscreen Formulations, International J Cosmetic Science, Version of Record online: *International J of Cosmetic Science*, 39(1):25-35, 2017; First published 29 JUN 2016 | DOI: 10.1111/ics.12344

## Importance of Photochemical Stability for Sunscreen

### ❑ Ref: L. Marrot et al., *British J dermatol*, 151(6):1234-1244, 2004

- Marrot et al tested the effect of
  - Photo-unstable (1.5% avobenzene + 2% octyl triazone + 5% octyl methoxy cinnamate) vs.
  - Photostable sunscreen (1.5% avobenzene + 2% octyl triazone + 5% methylbenzylidene camphor) using reconstructed skin

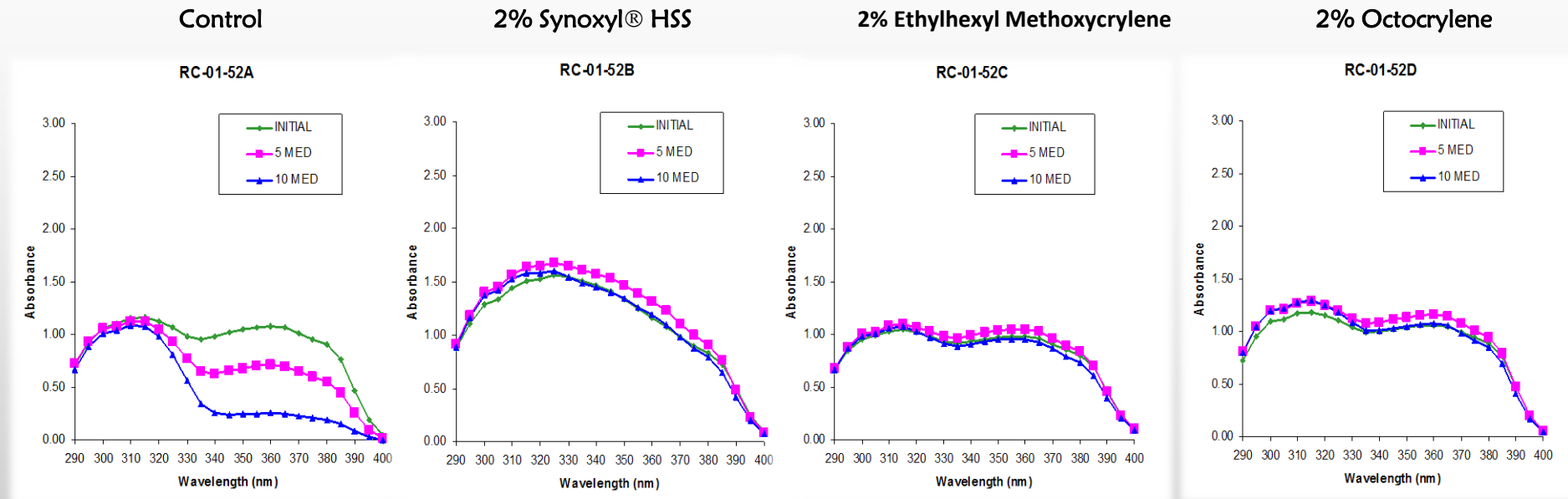
### ❑ Photo-unstable broad-spectrum sunscreen products cause

- Formation of sunburn cells
- DNA damage with increased formation of pyrimidine dimers
- Dermal alterations with superficial fibroblasts; higher dose causes destruction of dermal fibroblasts
- Formation of higher level of MMP-1

### ❑ Octocrylene is a not a good choice for avobenzene stabilization

- Recent studies have reported many instances of contact allergy and photocontact allergy due to octocrylene  
(*dermatitis*, 21(3):127-137, 2010; *contact dermatitis*, 54(5):295, 2006)

# Photostability Profile in Formulated Products Synoxyl® HSS vs Commercial Stabilizers



**Vehicle:** O/W emulsion

**Sunscreens:** Avobenzone (2%); HMS (10%); OS (5%)  
with or without a stabilizer (2%)

**Irradiation levels:** 5 & 10 MED

**Instrument:** Labsphere 1000 UV Analyzer

**Substrate:** Vitro-Skin® (IMS Testing Goup)

**Application rate:** 2 µl/cm<sup>2</sup>

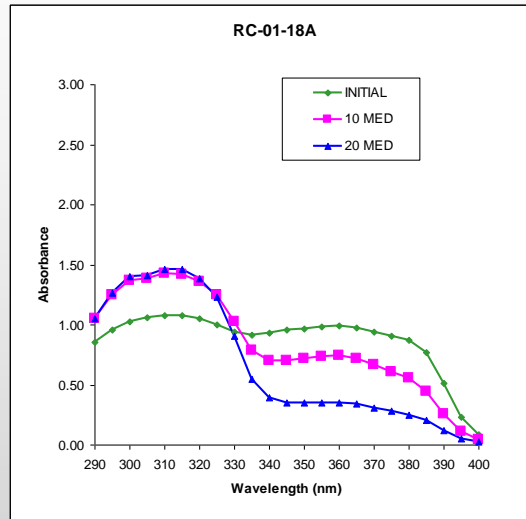
**Work done by IMS, Inc.**

## CONCLUSION

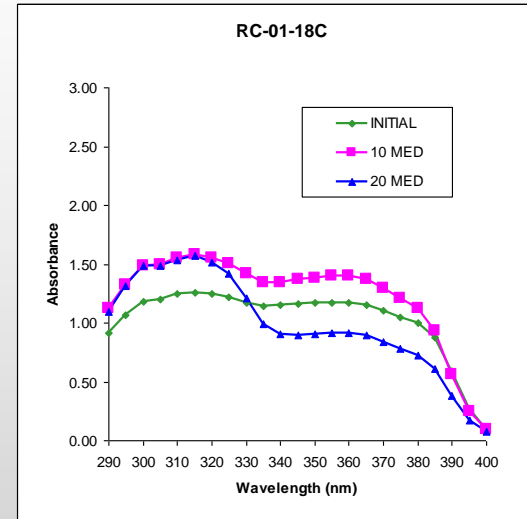
- Comparable photostabilization vs. commercial stabilizers
- Excellent coverage between 310-340 nm with Synoxyl® HSS
- Expected higher SPF performance

# Photostability Profile in Formulated Products: Synoxyl® HSS vs. Commercial Stabilizers

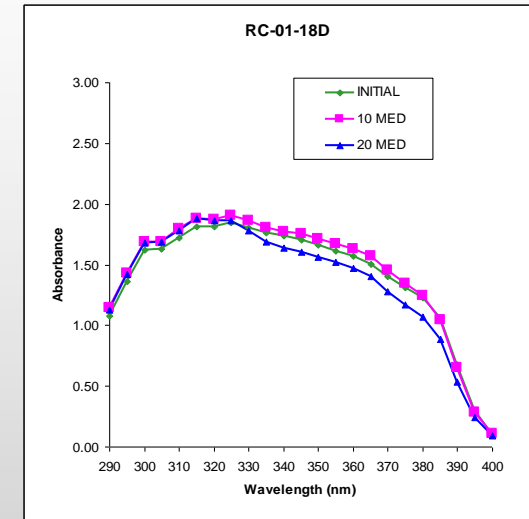
No stabilizer



2%Diethylhexyl Syringylidene Malonate



2% Synoxyl® HSS



**Vehicle:** O/W emulsion  
**Sunscreens:** Avobenzone (2%); HMS (10%); OS (5%)  
 with or without a stabilizer (2%)  
**Irradiation levels:** 10 & 20 MED  
**Instrument:** Labsphere 1000 UV Analyzer  
**Substrate:** Vitro-Skin® (IMS Testing Goup)  
**Application rate:** 2  $\mu\text{l}/\text{cm}^2$   
**Work done by IMS, Inc.**

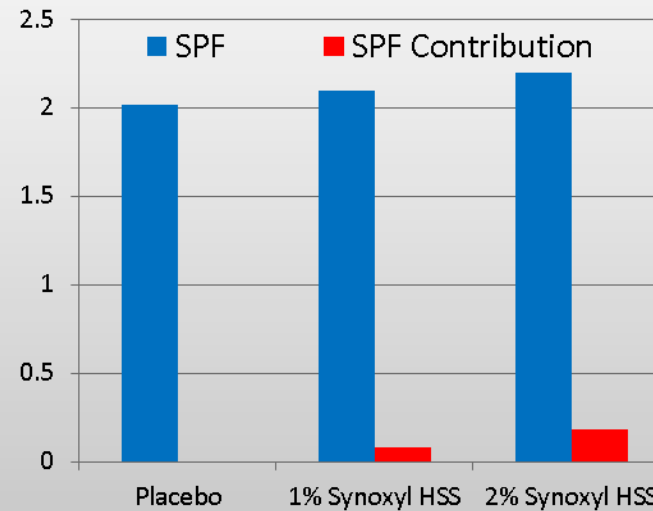
## Loss of Avobenzone at 20 MED

- No Stabilizer: 66%
- With DEHSM: 41%
- With Synoxyl® HSS: 6%
- Far superior to DEHSM



# Synoxyl<sup>®</sup> HSS has no Contribution to In-Vivo SPF at Recommended Use Level

Synoxyl<sup>®</sup> HSS has No contribution to in-vivo SPF at 2% level

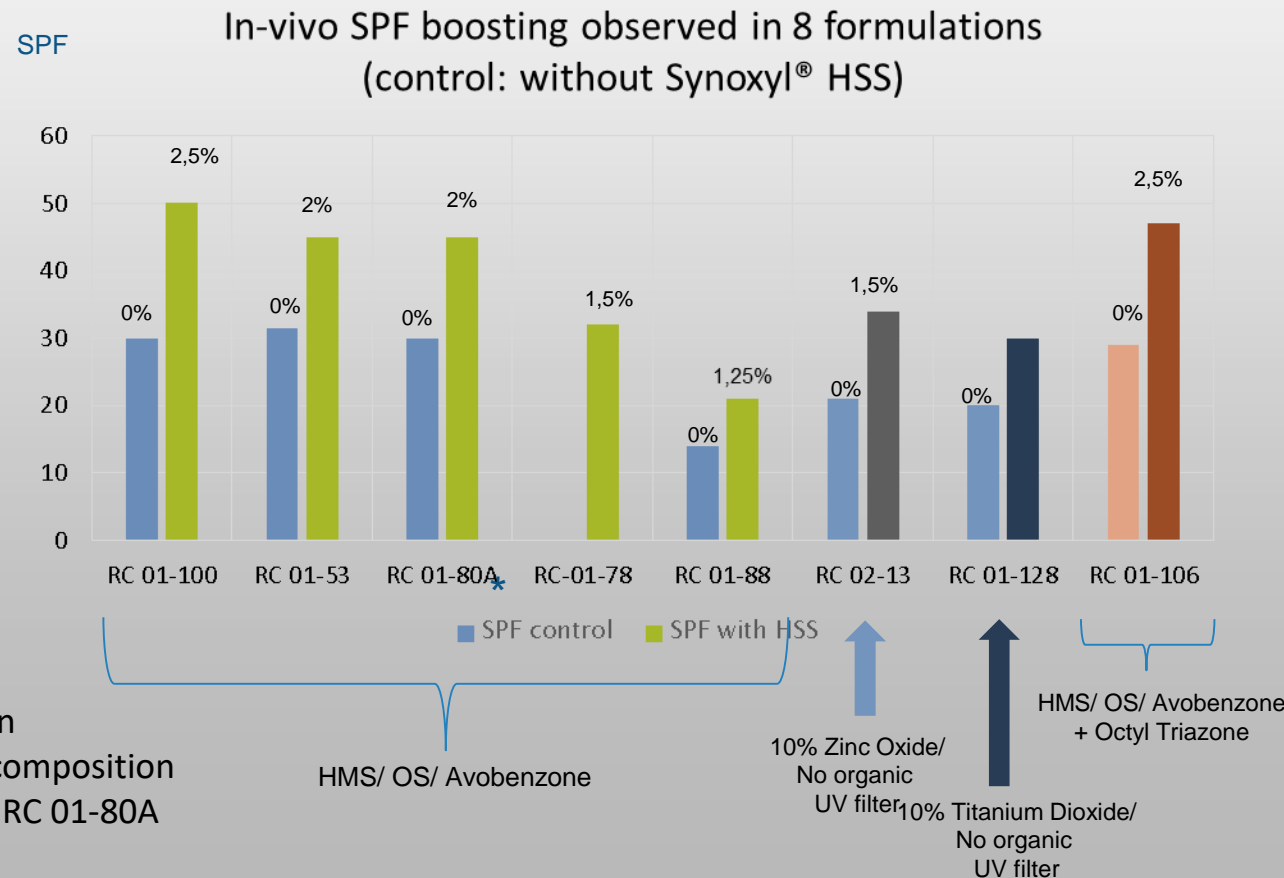


US FDA protocol; 5 subjects; In-vivo static SPF

# Synoxyl® HSS is an Excellent In-Vivo SPF Booster when used with Broad-Spectrum Sunscreens

(In-Vivo SPF testing/ FDA protocol)

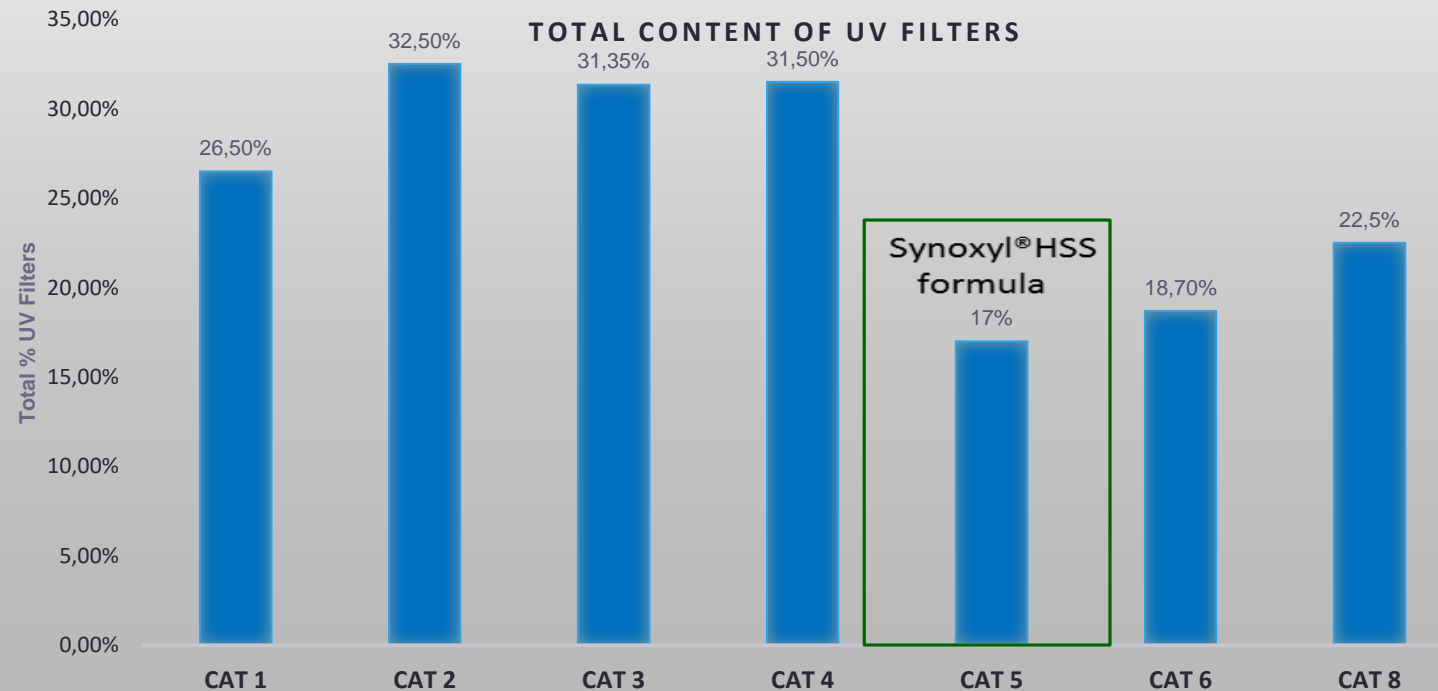
- ❑ Synoxyl® HSS boosts SPF by +50% or more; Results based on 8 different formulations tested in vivo
- ❑ Use 1:1 ratio of Synoxyl® HSS and Avobenzone for optimum stability & SPF boosting



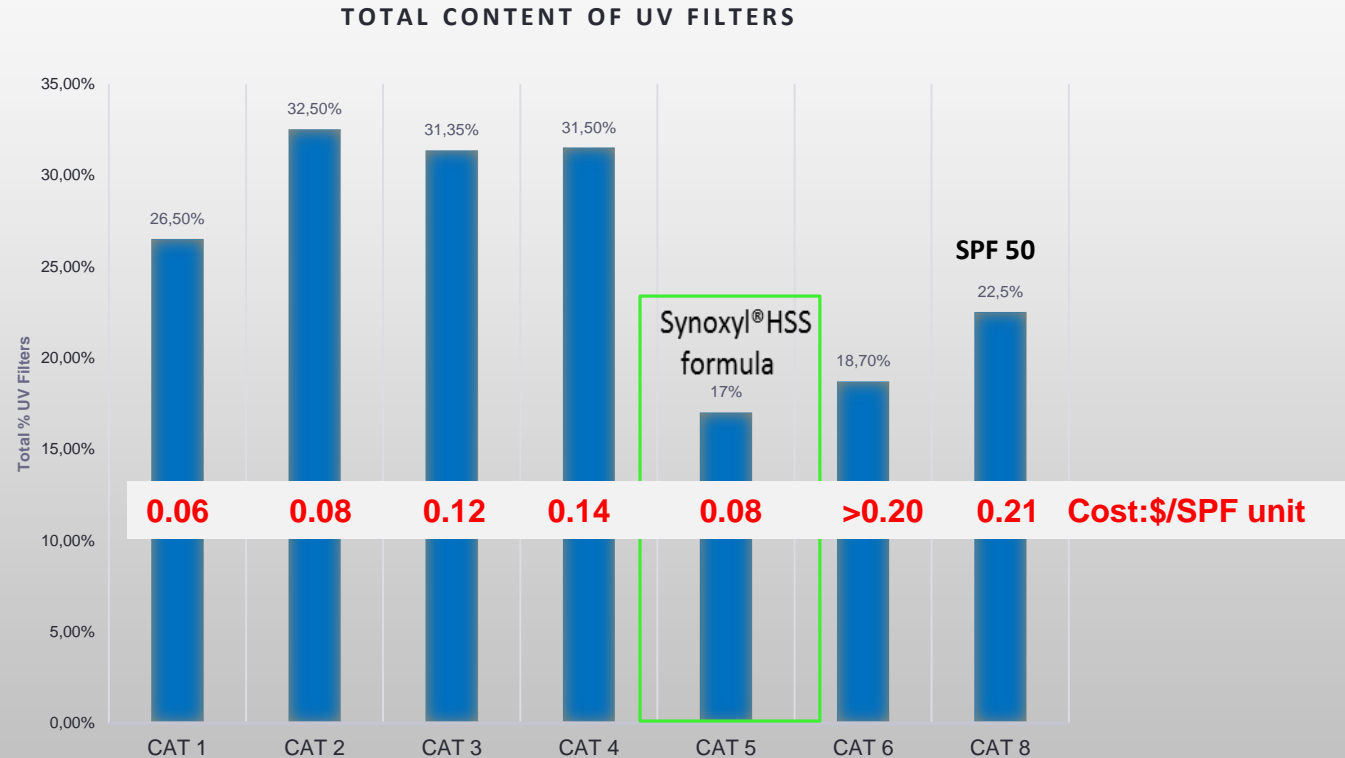
+Review formulation guidelines for full composition  
\*Sunscreen spray – RC 01-80A

# Comparison of Total Active Chemical Content in SPF 45/50 Sunscreen

	CAT 1	CAT 2	CAT 3	CAT 4	CAT 5	CAT 6	CAT 8
Description	Standard US OTC sunscreen, no UVA	Standard US OTC sunscreen Broad spectrum	US OTC sunscreen broad-spectrum, Photostabilized	Standard US OTC sunscreen Mixed organic & inorganic sunscreens	<b>With Synoxyl® HSS SPF Booster 100% organic</b>	US OTC sunscreen broadspectrum, Photostabilized. Proprietary L'Oreal	Non US approved Formula with EU sunscreen
UV Filer composition photostabilizers	Homosalate 8%; Octinoxate 7.5%; Octisalate 5%; Oxybenzone 6%	Avobenzone 2%; Homosalate 12%; Octinoxate 7.5%; Octisalate 5%; Oxybenzone 6%	Avobenzone 3%, Homosalate 15%, Octisalate 5%, Octocrylene 2.35%, Oxybenzone 6% + Diethylhexyl 2,6-Napthalate 3%.	Octinoxate 7.5%, Octocrylene 6%, Oxybenzone 3%, Zinc Oxide 15%	<b>Avobenzone 2%, Homosalate 10%, Octisalate 5%, Synoxyl HSS 2%</b>	Avobenzone 2%; Octocrylene 10%; Terephthalydene Dicamphor Sulfonic Acid 3%; Titanium Dioxide 3.7%	Tinosorb M: 15%, Uvinul A plus B: 15%
Commercial references	Coppertone SPF 45 Waterbabies, Schering Plough	Kids-Infants Sunblock Lotion SPF 45 , Tanning Research	Fresh Cooling SPF 45 / Helioplex/ Neutrogena & Aveeno Active Naturals Sunscreen Lotion SPF 45	Baby Blanket Kids 'faces' Zinc Oxide Sunscreen Stick, SPF 45+	<b>SPF 46 Formula RC01-53</b>	L'Oreal Roche Posay: Anthelios lotion SPF 45	Easy Handling UV Absorbers SPF50 (GEUV11098-1-4) BASF

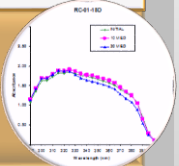
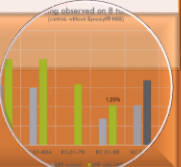


# Cost in US \$/SPF Unit for Making SPF 45-50 Sunscreen



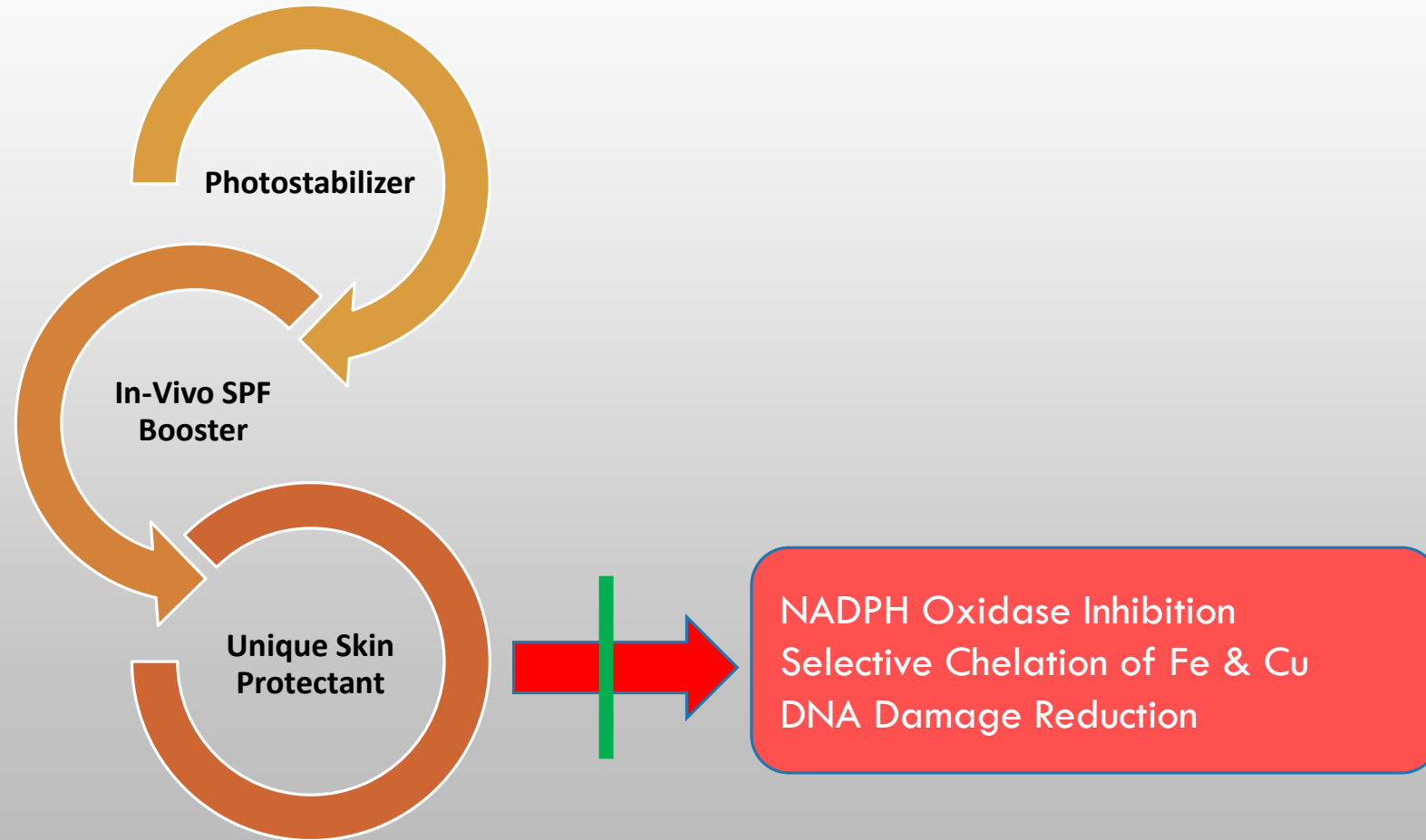
Photostability	-	--	+++	-	+++	+++	+++
Broad spectrum	no	yes	yes	yes	yes	yes	yes
Biological protection	no	no	no	no	yes	no	No
Environmental fate	Yellow	Yellow	Red	Yellow	Green	Yellow	Red
EU+ USA	yes	no	no	no	yes	yes	no

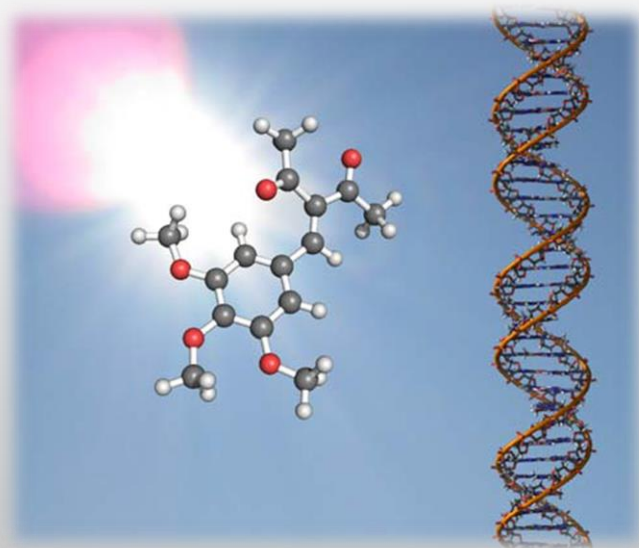
## Synoxyl<sup>®</sup> HSS: Summary of Key Benefits

<ul style="list-style-type: none"> <li>• Very effective in stabilizing avobenzone and many other photounstable compounds</li> </ul> <p>Excellent Photostabilization</p>  <p>SAFETY STABILITY PERFORMANCE</p>	<ul style="list-style-type: none"> <li>• In-vivo SPF boosting: <math>\geq 50\%</math> for both organic &amp; inorganic sunscreens</li> <li>• Enable high SPF/UVA formulations using fewer sunscreens/skin care actives</li> </ul> <p>50% in-vivo SPF boosting</p>  <p>SAFETY COST EFFECTIVENESS ENVIRONMENTALLY FRIENDLY</p>	<ul style="list-style-type: none"> <li>• Unique skin protectant: Inhibits upstream ROS cascade:             <ol style="list-style-type: none"> <li>(1) NADPH oxidase inhibitor</li> <li>(2) Selective chelator of iron &amp; copper in the presence of skin beneficial zinc and</li> <li>(3) inhibits DNA damage</li> </ol> </li> </ul> <p>Inhibition of DNA damage</p>  <p>SAFETY BROAD CLAIM INNOVATION</p>
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## Synoxyl<sup>®</sup> HSS Provides 3-in-1 Solutions to Skin Protection





## **Synoxyl® HSS:** A Breakthrough Photostabilizer with SPF Boosting & Unique Skin Protection Properties

Sytheon Ltd., USA  
[info@sytheonltd.com](mailto:info@sytheonltd.com)  
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Sytheon SARL, France  
[sytheon@sytheonltd.com](mailto:sytheon@sytheonltd.com)  
+33 1 41 10 81 82

[www.sytheonltd.com](http://www.sytheonltd.com)

Thank You