

Re: Position Paper on Titanium Dioxide – E171 – use in gelatin / hypromellose hard two-piece capsules - UPDATE

Alcobendas, 04th June 2021

To Whom It May Concern,

Opaque hard two-piece gelatin and hypromellose capsules, branded as Quali-G™ / Nutra'G and Quali-V® / Quali-V®-I / Nutra'V respectively, are manufactured by Qualicaps® Europe S.A.U. using Titanium Dioxide (E171) compliant with Pharmacopeias as a colorant and opacifying agent.

The present document provides background information as per the available scientific data regarding the use of E171 as a food additive and the conclusions of the ongoing discussion pertaining to its potential impact in medicinal and consumer healthcare products. This document does not pretend to be an exhaustive scientific review, but rather has the objective of stating Qualicaps® Europe SAU's current position regarding the use of E171 in gelatin and hypromellose products.

In recent years, there have been several communications in the media and from different authorities regarding the potential toxicity of Titanium Dioxide as a food additive, due to the possibility of the existence of particles that are of a size categorized as nanomaterial.

In 2015, the European Commission (EC) requested that the European Food Safety Authority (EFSA) review the safety of E171 as a food additive (*Question EFSA-Q-2011-00348*), to which a EFSA Panel concluded in June of 2016 that no real concerns existed about the continued safe use of E171 to this end but recommended that more testing be performed to complete toxicological studies (*doi: 10.2903/j.efsa.2016.4545*). The Titanium Dioxide Manufacturers Association (TDMA) and other parties registered their interest with EFSA to provide additional data by agreed timelines (summer of 2019, depending on laboratory availability but still not completed as of today).

Following newly published papers on E171 safety, the EC asked EFSA in March 2019 to provide an opinion on these four additional studies and to indicate whether a reassessment of the original 2016 findings should be performed (*Question EFSA-Q-2018-00271*). EFSA published its response in early July (*doi: 10.2903/j.efsa.2018.5366*), concluding “*the outcome of the four studies did not merit re-opening the existing opinion of EFSA related to the safety of TiO₂ (E171) as a food additive*”.

During the time between the two EFSA scientific reviews, specifically in April of 2018, a draft Bill to the French National Assembly (FNA) was amended to include a suspension of the use of E171 as a food additive from June 1st, 2018. No other EC members supported this position, deciding rather to wait for all ongoing studies to be completed before taking further action. The draft Bill to the FNA has since been modified to change the proposed suspension date to June 1st, 2020, i.e. after the studies in course are completed, and thus essentially updating the French Government’s position to delay action until the results from the studies are available, and the EFSA/EC comes out with its conclusions and recommendations. Nevertheless, in April 2019 *official communication*¹ the French authorities announced the prohibition of use of TiO₂ as a food supplement in this country from January the 1st 2020 onwards. This one-year suspension has been extended one additional year on December 21st until 1st January 2021.

Titanium Dioxide (E171) used by Qualicaps® Europe SAU in gelatin and hypromellose hard two-piece capsules’ production is compliant with EP/USP-NF/EC Directive 2009/35-2012/231 and CFR 73.575, although no particle size specifications nor test is required by either of these compendia monographs.

Qualicaps® Europe SAU obtains E171 on a regular basis from our qualified suppliers, which certify the absence of nanomaterials.

However, in relation with this information received from our suppliers, in July 2019 EFSA published a new scientific opinion where it was recommended to amend the E171 specifications⁶ with regards to its particle size distribution and following this publication, a Commission Working Group (CWG) has worked on this amendment to Regulation (EU) N° 231/2012⁷ regarding food additives. In February this year, this CWG communicated that

the specifications of TiO₂ E171 will be amended as recommended by EFSA but without a transition period, because according to the Titanium Dioxide Manufacturers Association (TDMA), all E171 used in the EU meet this requirement.

Recently, EFSA published in May 2020 an updated scientific opinion regarding E171 toxicity⁸. They assessed the new toxicological information available since their previous scientific opinion in May 2018 with the following conclusion:

“Overall, on the basis of all currently available evidence along with all the uncertainties, In particular the fact that genotoxicity concern could not be ruled out, the Panel concluded that E 171 can no longer be considered as safe when used as a food additive. This conclusion applies to E 171 as described in Commission Regulation (EU) No 231/2012 as well as to E 171 specified in the EFSA FAF Panel opinion in 2019.

¹ Press release N° 1177 from the French Ministry of Economy and Finances dated 17th April 2019.

² ISO/TC 229 Nomenclature system for nanoparticles.

³ European Commission Recommendation of October 18th, 2011 on the definition of a nanomaterial (2011/696/EU).

⁴ European Commission 1169/211 Art.2.

⁵ French Decree N° 2012-232 of 17 February 2012.

⁶ doi: 10.2903/j.efsa.2019.5760 “Scientific opinion on the proposed amendment of the EU specifications for titanium dioxide (E171) with respect to the inclusion of additional parameters related to its particle size distribution”.

⁷ Commission Regulation (EU) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council Text with EEA relevance.

⁸ doi: 10.2903/j.efsa.2021.6585 “Safety assessment of titanium dioxide (E171) as a food additive”.

Then now, EFSA’s scientific advice will be used by risk managers (the European Commission, Member States) to inform any decisions they take on possible regulatory actions deciding to maintain or to modify the authorization of E171 for food use in Europe but as in France, a ban of this food additive in Europe may happen in the next months.

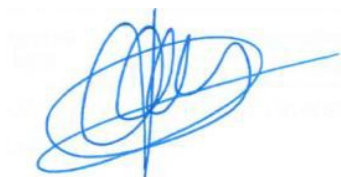
Taking into account the above-mentioned information, Qualicaps® Europe SAU’s position regarding Titanium Dioxide (E171) as of today is to continue its use for Pharmaceutical application products as per our customers requirement, updating the implementation of the new specifications’ regulation closely together with our qualified suppliers but

cancelling its use for Consumer Health Care applications and implementing any new regulatory action from the European Commission that could happen on this matter.

In any case, should you be concerned with this new situation of potential suspension of use of E171 as a food additive in Europe, Qualicaps® is pleased to offer you support in any reformulation initiative that you undertake in order to replace this colorant/opacifier in our gelatin and hypromellose products through our Scientific Business Development team of experts.

Please find as an annex to this position statement, a list of opaque colors offered by Qualicaps® Europe S.A.U that do not contain Titanium Dioxide for your reference.

Attentively,

A handwritten signature in blue ink, appearing to read 'Federico García Sagrado', with a stylized flourish extending to the right.

Federico García Sagrado, PhD
Vice President of QC/QA, EMEA & South Asia
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Annex: Qualicaps Europe offer of colours without TiO₂ (last update: June 4th, 2021)

1. Hard two-piece capsules for Consumer Healthcare applications



(Hard two-piece hypromellose capsules)

	Red iron O	Yellow iron O	Black iron O	S. C. Chlorophyllin
Hp. Yellow 10 (ZSZ)		●		
Hp. Brown 11 (ZTA)	●			
Hp. Brown 13 (ZTC)	●	●		
Hp. Green 13 (ZTJ)		●	●	
Hp. Green 14 (ZTL)				●



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(Hard two-piece gelatin capsules)

	Red iron O	Yellow iron O	Black iron O	FC&C Blue 1
Brown 13 (WV)	●	●	●	
Brown 14 (WW)	●	●	●	
Brown 15 (XF)	●	●	●	
Red 209 (FFX)	●			
Red 264 (XD)	●			
Green 31 (XP)		●		●
Orange 16 (WY)	●	●		
Orange 24 (XE)	●	●		
Gold 176 (UG)		●		
Yellow 268 (XB)		●		
Yellow 269 (XC)		●		
Black 18 (CDN)			●	

2. Hard two-piece capsules for Pharmaceutical applications



(Hard two-piece gelatin capsules)

	Red iron O	Yellow iron O	Black iron O	Patent Blue V	FC&C Blue 2	FC&C Blue 1	Ponceau 4R	Quinoline
Brown 13 (WV)	●	●	●					
Brown 14 (WW)	●	●	●					
Brown 15 (XF)	●	●	●					
Red 209 (FFX)	●							
Red 264 (XD)	●							
Green 23 (WR)		●			●			
Green 147 (WX)		●				●		
Green 28 (XA)		●				●		
Green 31 (XP)		●				●		
Orange 16 (WY)	●	●						
Orange 24 (XE)	●	●						
Gold 176 (IUG)		●						
Yellow 268 (XB)		●						
Yellow 269 (XC)		●						
Blue 5 (IPC)					●			
Black 18 (CDN)			●					
Black 3 (WZ)				●			●	●



(Hard two-piece hypromellose capsules)

	Red iron O	Yellow iron O	Black Iron O	S. C. Chlorophyllin
Hp. Yellow 10 (XSZ)		●		
Hp. Brown 11 (XTA)	●			
Hp. Brown 13 (XTC)	●	●		
Hp. Green 13 (XTJ)		●	●	
Hp. Green 14 (XTL)				●



(Hard two-piece hypromellose capsules -inhalation-grade)

	Red iron O	Yellow iron O	Black Iron O	S. C. Chlorophyllin
Hp. Yellow 10 (TSZ)		●		
Hp. Brown 11 (TTA)	●			
Hp. Brown 13 (TTC)	●	●		
Hp. Green 13 (TTJ)		●	●	
Hp. Green 14 (TTL)				●