

## TEGO® Pep 4–Even

Balancing skin tone

- A peptide sequence derived from the skin's own structure
- Effective on skin tone for all skin types
- Appears to visibly diminish hyperchromatic spots
- Brightens skin
- Visually improves the evenness of skin tone
- Improves the appearance of blemish-prone skin
- Alleviates the appearance of melasma on ethnic skin
- Calms and soothes the skin
- Preservative-free peptide solution
- Patent-protected application by Evonik
- Shows good stability in formulation and is compatible with sunscreens
- Usage concentration: 0.5 – 5.0 %

Personal Care

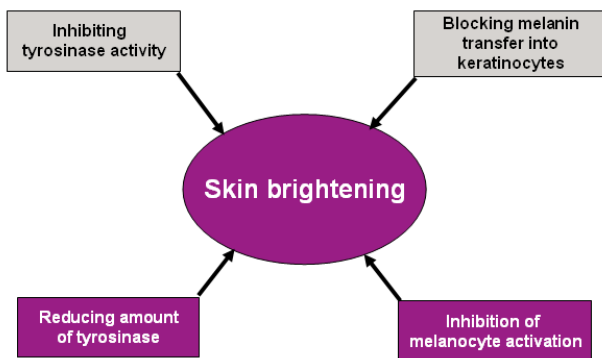
**INCI Name (PCPC name)**  
Tetrapeptide-30; Glycerin

<b>Chemical and physical properties (not part of specifications)</b>	
Form	colorless, clear liquid
Active matter	approx. 1600 ppm

TEGO® Pep 4–Even is a preservative–free solution of Tetrapeptide–30 (Amino acid sequence Proline – Lysine – Glutamic Acid – Lysine; PKEK) in glycerin and water.

**Properties**

Skin tone and its evenness are very important cosmetic concerns worldwide. While people in Asia want to achieve a lighter overall skin tone, people in Europe focus more on the reduction of hyper–chromatic spots (age spots). People with ethnic skin, on the other hand, often suffer from an irregular skin appearance (mottled hyperpigmentation), so their main intention is the improvement of the evenness of skin tone. All of these concerns have been linked in the scientific literature to natural pathways of skin pigmentation (Figure 1).



**Figure 1: Factors involved in skin tone modulation**

When considering these factors, it may be proposed that an even skin tone could be achieved via a reduction in the amount of tyrosinase, and an inhibition of melanocyte activation.

To obtain optimal results for skin brightening, most cosmetic formulations combine two or more functional ingredients that address additional factors involved in skin tone modulation, like a tyrosinase inhibitor or a substance reducing the melanin transfer. In contrast, TEGO® Pep 4–Even, formulated in a compatible vehicle, is able to deliver the appearance of an even skin tone in the absence of additional cosmetic ingredients.

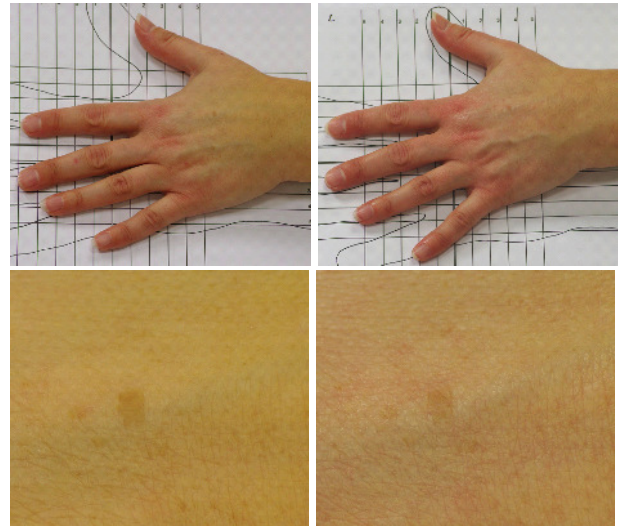
***In vivo* cosmetic consumer panel study overview:**

Test	Number of panelists	Measurement
Biopsy study	10	qRT-PCR of melanogenic and inflammation markers after UV-irradiation
Skin lightening study on Caucasian skin, hand	38	Skin color (Colorimeter) Digital images
Age spot study on Caucasian skin, face	40	Skin color (Chromameter) Digital images
Study on Asian skin, face	27	Skin color (Colorimeter) Digital photographs
Study on ethnic skin, face	50	Digital photographs Clinical assessment (expert grading)

**Concentration of pure Tetrapeptide–30 in all studies:  
40 ppm (or 2.5 % of TEGO® Pep 4–Even)**

- **Cosmetic consumer panel study on Caucasian skin: Lightening the the appearance of skin tone on the hand**

To evaluate the performance of Tetrapeptide–30, the study was performed against a vehicle containing a Vitamin C derivative (Sodium Ascorbyl Phosphate), a well–known tyrosinase inhibitor *in vitro*.



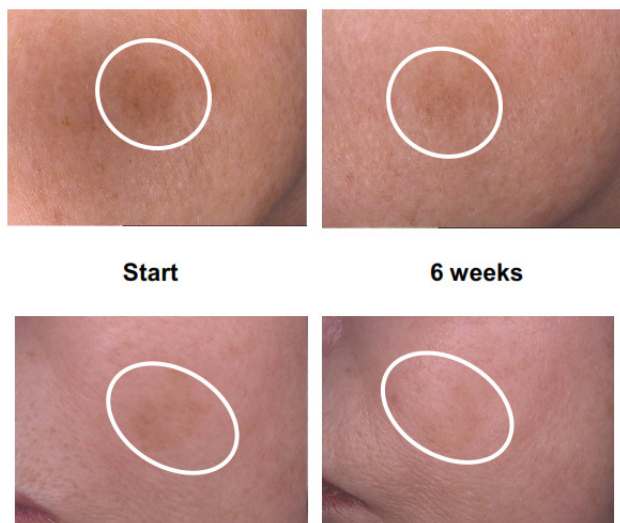
**Figure 2: Reduction in the visibility of yellowish skin color and age spots on the hand by Tetrapeptide–30 in combination with Sodium Ascorbyl Phosphate (left side: start, right side: after 8 weeks)**

The results underlined that Tetrapeptide–30 has a skin brightening activity that is also accompanied by a reduction in the appearance of skin redness. Additionally, a strong fading in the appearance of hyperchromatic age spots was observed.

- **Cosmetic consumer panel on Caucasian skin: anti– age spot study**

An *in vivo* study was conducted on facial skin of 40 panelists for six weeks. Digital images of application

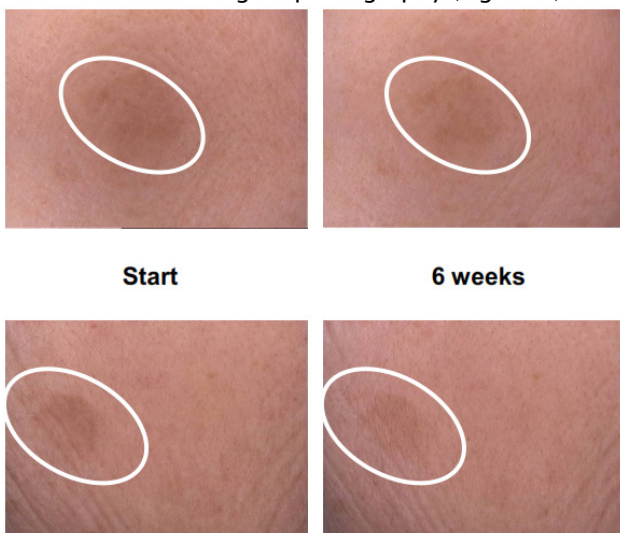
sites were taken at study start and after 6 weeks. Skin images of two panelists where 40 ppm Tetrapeptide-30 (2.5% TEGO® Pep 4-Even) was applied are shown (Figure 3).



**Figure 3: Reduction of facial age spots by Tetrapeptide-30 (left side: start, right side: after 6 weeks)**

There is a noticeable reduction in the appearance of the age spot highlighted on the facial skin of both panelists.

Tetrapeptide-30 was also tested in combination with Sodium ascorbyl phosphate and the results documented with digital photography (Figure 4)..



**Figure 4: Reduction of facial age spots by Tetrapeptide-30 in combination with Sodium Ascorbyl Phosphate (left side: start, right side: after 6 weeks)**

Tetrapeptide-30 led to a visible fading of the hyperchromatic spots which make it an interesting choice for skin care products. In combination with

Sodium Ascorbyl Phosphate, the efficacy of the cosmetic formulations was further optimized.

- **Cosmetic consumer panel study on Asian skin: Improvement of evenness of skin tone**

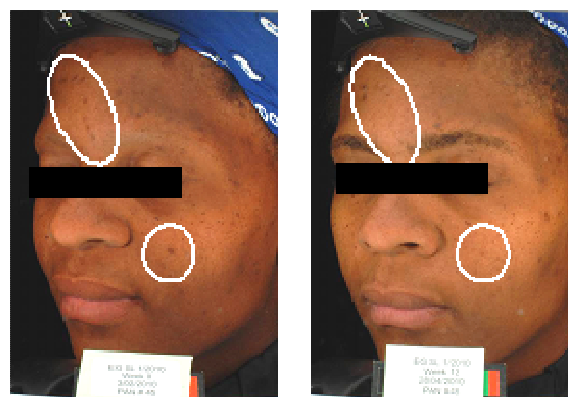


**Figure 5: Panelist with reduced hyperpigmentation by Tetrapeptide-30 in combination with Sodium Ascorbyl Phosphate (left side: start, right side: after 8 weeks)**

Over the period of the study, no change in the appearance of hyperpigmentation was observed for the vehicle group (only Sodium Ascorbyl Phosphate) whereas the combination of SAP with 40 ppm Tetrapeptide-30 (2.5% TEGO® Pep 4-Even) showed a reduction in the appearance of hyperpigmentation of about 15 %. This demonstrated that Tetrapeptide-30 is able to address the major concerns of Asian skin: the skin appears lighter and skin tone appears more even.

- **Cosmetic consumer panel study on ethnic skin: evenness of skin tone**

An *in vivo* study was conducted on facial skin of 50 panelists where 40 ppm Tetrapeptide-30 (2.5% TEGO® Pep 4-Even) was applied for twelve weeks. Digital images were taken and expert grading of application sites were done at study start and after 12 weeks. Skin images of a panelist is shown below (Figure 6).



**Figure 6: Panelist with reduced number of acne lesions (left side: start, right side: after 12 weeks)**

There is a noticeable reduction in the appearance of blemishes on the cheek and forehead after 12 weeks.



Figure 8. Panelist with a reduction in the appearance of melasma

There is also an evening in the appearance of skin tone on the cheek of a panelist with melasma (Figure 8).

The study results revealed that Tetrapeptide-30 is also able to reduce the appearance of the major concerns of ethnic skin: it improves the evenness and the overall appearance of skin. Additionally, it reduces the appearance of acne lesions.

A detailed test summary report (technical dossier) is available on request.

### Claim Summary

#### TEGO® Pep 4–Even

- is appropriate on all kinds of skin types
- has a smart skin tone brightening mechanism
- improves the evenness of skin tone
- brightens skin
- visibly diminishes hyperchromatic spots
- visible reduces acne lesions
- alleviates the appearance of melasma on ethnic skin

#### Patent position

The use of TEGO® Pep 4–Even (Sequence “PKEK”) in cosmetic formulations is subject of patent application WO 2009068351.

A second, yet undisclosed, application claiming the use of PKEK for certain cosmetic use has been filed by Evonik Goldschmidt GmbH in November 2009.

Helix Biomedix is the applicant and owner of PCT application WO2008085494 claiming short bioactive peptides for cellular and immunological modulation. Evonik Goldschmidt GmbH and Helix Biomedix have entered into a licensing agreement in August 2007

assuring Evonik Goldschmidt GmbH exclusive rights to market peptides under said IP worldwide.

To the best of our knowledge, no third party patent right exists that generally prevents customers from using TEGO® Pep 4–Even in cosmetic formulations.

### Formulation hints

TEGO® Pep 4–Even is a water soluble, easy to formulate peptide solution.

For the preparation of any kind of cosmetic formulation, TEGO® Pep 4–Even is simply added to the water phase and the emulsion (O/W or W/O) is prepared as usual. For O/W emulsions, it is also possible to add TEGO® Pep 4–Even during the cooling process.

Store at 4 – 8 °C.

### Recommended usage concentration

Recommended use level 0.5 % – 5.0 %; clinically tested at 2.5 %.

### Applications

- Skin lightening preparations
- Anti–aging preparations with correction of age spots & pigmentation disorders
- Anti–aging products for even skin tone
- Ethnic skin care
- Hand creams
- Décolleté preparations

### Packaging

1.0 kg package

### Hazardous goods classification

Information concerning

- classification and labelling according to regulations for transport and for dangerous substances
- protective measures for storage and handling
- measures in accidents and fires
- toxicity and ecological effects

is given in our material safety data sheet.

## Guide Line Formulations

<b>Balancing Skin Tone Hand Cream, SPF 15 1/3 UVA CL 15/10-2</b>	
<b>Phase A</b>	
TEGO® Care PSC 3 (Polyglyceryl-3 Dicitrate/Stearate)	3.00 %
TEGO® Alkanol 1618 (Cetearyl Alcohol)	1.25 %
TEGIN® M Pellets (Glyceryl Stearate)	1.25 %
TEGOSOFT® DEC (Diethylhexyl Carbonate)	2.50 %
TEGOSOFT® OER (Oleyl Erucate)	2.00 %
TEGOSOFT® MM (Myristyl Myristate)	1.20 %
TEGOSOFT® CT (Caprylic/Capric Triglyceride)	3.00 %
Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (TINOSORB S, BASF SE)	3.00 %
Octocrylene	3.50 %
TEGO® Sun TDEC 45 (Titanium Dioxide; Diethylhexyl Carbonate; Polyglyceryl-6 Polyhydroxystearate)	4.40 %
<b>Phase B</b>	
Glycerin	3.00 %
Water	66.65 %
<b>Phase C</b>	
TEGO® Pep 4-Even	2.50 %
<b>Phase D</b>	
TEGO® Carbomer 134 (Carbomer)	0.15 %
TEGOSOFT® DC (Decyl Cocoate)	1.00 %
Xanthan Gum	0.20 %
<b>Phase Z</b>	
Sodium Hydroxide (10 % in water)	0.40 %
Phenoxyethanol; Ethylhexylglycerin (EUXYL PE 9010, Schülke & Mayr GmbH)	1.00 %
Perfume	q.s.

### Preparation:

1. Heat phase A and B separately to approx. 80 °C.
2. Add phase A to phase B with stirring<sup>1)</sup>.
3. Homogenise.
4. Cool with gentle stirring to approx. 50 °C and add phase C and D.
5. Homogenise for a short time.
6. Cool with gentle stirring and add phase Z below 40 °C. Adjust pH to 6-7.

<sup>1)</sup> Important: If phase A has to be charged into the vessel first, phase B must be added without stirring.

## Correcting Moisturizer for Even Skin

CD 935/1

<b>Phase A</b>	
AXOL® C 62 Pellets (Glyceryl Stearate Citrate)	1.5 %
TEGO® Alkanol 1618 (Cetearyl Alcohol)	3.0 %
TEGIN® M Pellets (Glyceryl Stearate)	1.0 %
TEGOSOFT® liquid (Cetearyl Ethylhexanoate)	11.0 %
TEGOSOFT® OP (Ethylhexyl Palmitate)	11.0 %
TEGOSOFT® MM (Myristyl Myristate)	2.0 %
<b>Phase B</b>	
Glycerin	5.0 %
Water	47.9 %
<b>Phase C</b>	
TEGO® Carbomer 134 (Carbomer)	0.2 %
TEGOSOFT® OP (Ethylhexyl Palmitate)	0.8 %
<b>Phase D</b>	
TEGO® Pep 4-Even	2.5 %
Sodium Ascorbyl Phosphate	1.5 %
Urea	2.5 %
Sodium Bisulfite	0.1 %
Water	10.0 %
<b>Phase E</b>	
Sodium Hydroxide (10 % in water)	q.s.
<b>Phase Z</b>	
Preservative, Perfume	q.s.

### Preparation:

1. Heat phase A and B separately to approx. 80 °C.
2. Add phase A to phase B with stirring<sup>1)</sup>.
3. Homogenise.
4. Cool with gentle stirring to approx. 50 °C and add phase C.
5. Homogenise for a short time.
6. Cool with gentle stirring and add phase D and E below 40 °C. Adjust pH to 7.

<sup>1)</sup> Important: If phase A has to be charged into the vessel first, phase B must be added without stirring.



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