/Translation from Czech:/

SÚKL

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ADDRESSEE Frankl Pharma s.r.o. (Mrs. Jutka Kovács)		Počernická 96 Prague 10 108 00	
Ref. No. sukl293352/2016	File No. sukls159926/2016	Dealt with by / email MUDr. Markéta Holubová marketa.holubova@sukl.cz	Date Dec. 15, 2016

Opinion of the State Institute for Drug Control on the Dr. Michaels Skin Care Cream ands Dr. Michaels Skin Care Gel Products

On Jun. 02, 2016, the State Institute for Drug Control received a request for an opinion sent by Frankl Pharma s.r.o., Mrs. Jutka Kovács, Počernická 96, Prague10, Company Registration No. 27092127, regarding an appraisal of the nature and classification of Dr. Michaels Skin Care Cream ands Dr. Michaels Skin Care Gel products. The documentation for the request was supplemented on Nov. 04, 2016.

In evaluating the products, the Institute proceeded from the following source documents:

- The cover letter and the request for the expert opinion including the reasoning of the request and the specification of the intended use of the products, supplied by the requesting party;
- The information attached with the quality and quantity composition and function of individual components of the products, supplied by the requesting party;
- Act No. 268/2014 Coll., on Medical Devices and on Amendments to Act No. 634/2004 Coll., on Administrative Fees, as amended by subsequent regulations (hereinafter referred to only as the "Act on MD");
- Government Regulation No. 54/2015 Coll., on the Technical Requirements on Medical Devices (hereinafter referred to only as the "Government Regulation");
- The recommended document of the European Commission MEDDEV 2.4/1 REV. 9 CLASSIFICATIONS OF MEDICAL DEVICES, June 2010;
- Expert literature - see the text below.

In view of the fact that the manufacturer intendeds to market the Dr. Michaels Skin Care Cream ands Dr. Michaels Skin Care Gel products as IIa or possibly IIb medical devices, in its evaluation the Institute initially focused on the nature of the products, their intended use and the mechanism of action with the aim of evaluating whether they met the definition of a medical device in accordance with law.

Dr. Michaels Skin Care Cream Product:

The product contains 61.2 weight percent (henceforth %) of liquid paraffin, 30 % hard paraffin, 3 % potato starch, 3 % zinc oxide, 2 % salicylic acid, 0.2 % almond oil, 0.08% jojoba oil, 0.08% avocado oil 0.08% wild carrot seed oil, 0.08% Calendula Officinalis extract, 0.08% orange essential oil, 0.08%

purified wheat germ oil, 0.08 % apricot oil, 0.04%, lavender essential oil, 0.04% sandalwood essential oil, 0.04% patchouli essential oil, 0.04% essential oil of Pelargonium graveolens, 0.04% rosemary essential oil, 0.04% emu oil, 0.02% bergamot essential oil, 0.02% primrose oil, 0.01% eucalyptus essential oil, 0.0005% pine essential oil, 0.0005% camomile essential oil, 0.0005% common myrrh oil and 0.0005% essential oil from bitter orange tree blossoms.

The product is a cream intended to relieve the symptoms of psoriasis, specifically the chronic stationary type. The data about the frequency of use or detailed information about the method of application have not been provided.

Whereas for the purpose of the prevention and treatment of the disease it is also possible to use medical devices as arises from Act No. 268/2014 Coll., on Medical Devices and on Amendments to Act No. 634/2004 Coll., on Administrative Fees, as amended by subsequent regulations, and the product is to be marketed as a medical device, the Institute dealt with the key mechanism of action of the product, which is especially taken into consideration when deciding whether a product is a medicinal product or a medical device (Article 1, Paragraph 5c) of Council Directive 93/42/EEC concerning Medical Devices in its amended wording).

The Institute identified emollients, i.e. softening agents, and salicylic acid in the product, as substances that can be used for treatment of psoriasis, which is the indication of the product. As to the emollients, the Dr. Michaels Skin Care Cream product contains particularly liquid and hard paraffin, which forms an occlusive oil film on the stratum conrneum. This film prevents excessive evaporation of water from the skin surface and provides hydration and lubrication (Summary of the OILATUM GEL product characteristics). In addition, the product contains vegetable oils with emollient effects, whose significance for the total effect of the product, however, is not known due to their low concentration in the product. The said effect of the emollients is considered by the Institute to be physical. The salicylic acid has proven anti-inflammatory effects as it inhibits the synthesis of prostaglandins, nonetheless in the treatment of psoriasis it is used for its keratolytic effect (*Peters BP, Weissman FG, Gill MA. Pathophysiology and treatment of psoriasis. Am J Health Syst Pharm. 2000 Apr 1;57(7):645-59; Jacobi A, Mayer A, Augustin M. Keratolytics and emollients and their role in the therapy of psoriasis: a systematic review. Dermatol Ther (Heidelb). 2015 Mar;5(1):1-18).* The mechanism of its keratolytic effect lies in dissolving the intercorneocyte bonds and reducing the stratum conrneum pH, resulting in the increased hydration and softening (*Jacobi A, Mayer A, Augustin M. Keratolytics and emollients and their role in the therapy of psoriasis: a systematic review. Dermatol Ther (Heidelb)*. The keratolytic effect of the salicylic acid is considered by the Institute to be physico-chemical.
With respect to the product, the Institute did not prove that if used in humans as intended, it was capable of appreciably modifying physiological functions by exerting a pharmacological, immunological or metabolic action.
Proceeding from the above facts, the Institute therefore notes that the key effect of the Dr. Michaels Skin Care Cream product in the treatment of psoriasis is based on the physical effect of emollients and the physico-chemical effect of the salicylic acid. In view of the prevailing physico-chemical effect of the salicylic acid in the product, the Institute does not consider it to be an active substance, which is an integral part of the product.

Having evaluated these source materials, **the Institute arrived at the conclusion that the Dr. Michaels Skin Care Cream product met the definition of a medical device in accordance with the provisions of Section 2 of the Act, Sub-section 1 of the Act on MD, and therefore the Institute considers it to be a medical device.**

On the basis of the request the Institute dealt with the issue of risk classification of the medical device based on the degree of risk corresponding to the use of the given medical device in accordance with the provisions of Section 6 of the Act. Rules for risk classification are laid down in the implementing legislation, namely the Government Regulation.

Following the above and considering the intended use of the medical device, including the impossibility to prove that the medical device incorporates, as an integral part, a substance, which, if used separately, can be considered to be a medicinal product and which is liable to act on the human body with action ancillary to that of the device, in accordance with Section 2, Sub-section (2) e) of the Act, it is possible to apply the **Classification Rule No. 4,** stipulated in Annex No. 9 (III - Classification, 3 - Classification of a non-invasive medical device, 3.4 – Rule 4) of the Government Regulation, where:

*"**A non-invasive medical device which comes into contact with injured skin falls** under Class I if it is intended to be used as a mechanical barrier, for compression or for absorption of exudates;*
under Class IIb if it is intended to be used with wounds which have breached the dermis and can only heal by secondary intent;
***under Class IIa in all other cases**, including medical devices intended to manage the micro-environment of a wound."*

Whereas it is noted that the medical device in question is not used either as a mechanical barrier, or for compression or absorption of exudates; neither is it intended to be used with wounds which have breached the dermis and can only heal by secondary intent; and considering the fact that with the psoriasis disease the integrity of the skin does not have to be ensured and that the use of this medical device results in the removal of keratinized structures of the epidermis, the hydration and lubrication of the skin because the key intended use of the Dr. Michaels Skin Care Cream product is to *relieve the symptoms of psoriasis, specifically the chronic stationary type*, **it is the opinion of the Institute that it concerns a medical device of Class IIa (that is to say use in other cases)**.

Dr. Michaels Skin Care Gel Product

The product contains 10 weight percent (henceforth %) of ethanol (alcohol), 8 % sodium-lauryl-sulfate 31.0, 6 % solution of cocamidopropyl betaine 30%, 3.5 – 5 % trolamine 99%, 4 % trolamine-lauryl-sulfate 39.2 %, 2 % coconut fatty acid diethanoamide, 1.75 % salicylic acid, 1.25 % alkyl acrylate cross-polymer, 1 % Plantaserv M (benzyl alcohol, salicylic acid, glycerin, sorbic acid), 0.71 70% glycolic acid, 0.5 % citric acid, 0.15 % tetra-sodium-edetate and purified water.

The product is a gel intended to relieve the symptoms of psoriasis, specifically the chronic stationary type. The data about the frequency of use or detailed information about the method of application have not been provided.

Whereas for the purpose of the prevention and treatment of the disease it is also possible to use medical devices as arises from Act No. 268/2014 Coll., on Medical Devices and on Amendments to Act No. 634/2004 Coll., on Administrative Fees, as amended by subsequent regulations, and the product is to be marketed as a medical device, the Institute dealt with the key mechanism of action of the product, which is especially taken into consideration when deciding whether a product is a medicinal product or a medical device (Article 1, Paragraph 5c) of Council Directive 93/42/EEC concerning Medical Devices in its amended wording).

The Institute identified salicylic acid and glycolic acid in the product as substances that can be used for the treatment of psoriasis, which is the indication of the product. The salicylic acid has proven anti-inflammatory effects as it inhibits the synthesis of prostaglandins, nonetheless in the treatment of psoriasis it is used for its keratolytic effect (*Peters BP, Weissman FG, Gill MA. Pathophysiology and treatment of psoriasis. Am J Health Syst Pharm. 2000 Apr 1;57(7):645-59; Jacobi A, Mayer A, Augustin M. Keratolytics and emollients and their role in the therapy of psoriasis: a systematic review. Dermatol Ther (Heidelb). 2015 Mar;5(1):1-18).* The mechanism of its keratolytic effect lies in dissolving the intercorneocyte bonds and reducing the stratum conrneum pH, resulting in the increased hydration and softening (*Jacobi A, Mayer A, Augustin M. Keratolytics and emollients and their role in the therapy of psoriasis: a systematic review. Dermatol Ther (Heidelb)*. The keratolytic effect of the salicylic acid is considered by the Institute to be physico-chemical. The glycolic acid has complex

effects including a keratolytic effect. The keratolytic effects of the glycolic acid are determined partly by its physico-chemical properties and partly by the metabolic effect. Physico-chemical effects lie in the reduction of intercorneocyte bonds due to increased water content, by reducing the charges on the surface of cells, and by breaking desmosomes as a result of the decreased pH. Metabolic effects are based on influencing the activities of enzymes involved in the forming and dissolving of the intercorneocyte bonds due to a change in pH. Furthermore, an effect of glycolic acid on collagen production in the dermis was observed, which is also considered by the Institute to be a metabolic effect. *(Jacobi A, Mayer A, Augustin M. Keratolytics and emollients and their role in the therapy of psoriasis: a systematic review. Dermatol Ther (Heidelb). 2015 Mar;5(1):1-18; Horikoshi T, Matsumoto M, Usuki A, Igarashi S, Hikima R, Uchiwa H, Hayashi S, Brysk MM, Ichihashi M, Funasaka Y. Effects of glycolic acid on desquamation-regulating proteinases in human stratum corneum. Exp Dermatol. 2005 Jan;14(1):34-40; Okano Y, Abe Y, Masaki H, Santhanam U, Ichihashi M, Funasaka Y. Biological effects of glycolic acid on dermal matrix metabolism mediated by dermal fibroblasts and epidermal keratinocytes. Exp Dermatol. 2003;12 Suppl 2:57-63).* However, proceeding from the existing knowledge, the Institute is unable to prove what effects of the glycolic acid are useful mainly in the treatment of psoriasis and in addition the glycolic acid is contained in the Dr. Michaels Skin Care Gel product in such a concentration that the Institute could not have proven any significant effect on psoriasis.

Proceeding from the above facts, the Institute therefore notes that the key effect of the Dr. Michaels Skin Care Gel product in the treatment of psoriasis is based on the physico-chemical effect of the salicylic acid. In view of the prevailing physico-chemical effect of the salicylic acid in the product, the Institute does not consider it to be an active substance, which is an integral part of the product. Similarly, the Institute does not consider any of the other components of the Dr. Michaels Skin Care Gel product to be an active substance.

Having evaluated these source materials, **the Institute arrived at the conclusion that the Dr. Michaels Skin Care Gel product met the definition of a medical device in accordance with the provisions of Section 2 of the Act, Sub-section 1 of the Act on MD, and therefore the Institute considers it to be a medical device.**

On the basis of the request the Institute dealt with the issue of risk classification of the medical device based on the degree of risk corresponding to the use of the given medical device in accordance with the provisions of Section 6 of the Act. Rules for risk classification are laid down in the implementing legislation, namely the Government Regulation.

Following the above and considering the intended use of the medical device, including the impossibility to prove that the medical device incorporates, as an integral part, a substance, which, if used separately, can be considered to be a medicinal product and which is liable to act on the human body with action ancillary to that of the device, in accordance with Section 2, Sub-section (2) e) of the Act, it is possible to apply the **Classification Rule No. 4,** stipulated in Annex No. 9 (III - Classification, 3 - Classification of a non-invasive medical device, 3.4 – Rule 4) of the Government Regulation, where:

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under Class IIb if it is intended to be used with wounds which have breached the dermis and can only heal by secondary intent;
***under Class IIa in all other cases**, including medical devices intended to manage the micro-environment of a wound."*

Whereas it is noted that the medical device in question is not used either as a mechanical barrier, or for compression or absorption of exudates; neither is it intended to be used with wounds which have breached the dermis and can only heal by secondary intent; and considering the fact that with the psoriasis disease the integrity of the skin does not have to be ensured and that the use of this medical

device results in the removal of keratinized structures of the epidermis, the hydration and lubrication of the skin because the key intended use of the Dr. Michaels Skin Care Gel product is to *relieve the symptoms of psoriasis, specifically the chronic stationary type*, **it is the opinion of the Institute that it concerns a medical device of Class IIa (that is to say use in other cases)**.

With regards,

Ing. Vendula Doudová
Authorised to Manage
the Marketing and Notification Department
Medical Device Section

Interpreter's Statement

As an interpreter

of English language,

appointed by the decision of the Regional Court in Prague on December 7th 2000, Ref. No. Spr 4056/2000, I certify that this is a true and correct translation of the attached document.

I implemented the following corrections-----.

The interpreting act is recorded under the consecutive No. 1/2017 of the interpreter's record book.

I am charging in compliance with the enclosed bill.

Prague, on Jan. 8, 2017

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