Implications of In-Use Photostability: Proposed Guidance for Photostability Testing and Labeling to Support the Administration of Photosensitive Pharmaceutical Products, Part 2: Topical Drug Product

STEVEN W. BAERTSCHI,[1] DAVID CLAPHAM,[2] CHRIS FOTI,[3,4] MARK H. KLEINMAN,[5] SOLVEIG KRISTENSEN,[6] ROBERT A. REED,[7] ALLEN C. TEMPLETON,[8] HANNE HJORTH TØNNESEN[6]

[1]Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, Indiana 46285
[2]GlaxoSmithKline Pharmaceuticals, Ware SG12 0DP, UK
[3]Pfizer Inc., Analytical Research and Development, Eastern Point Road, Groton, Connecticut 06340
[4]Gilead Sciences, Foster City California 94404
[5]GlaxoSmithKline Pharmaceuticals, King of Prussia, Pennsylvania 19406-0940
[6]School of Pharmacy, University of Oslo, Oslo 0316, Norway
[7]Celsion Corporation, Lawrenceville, New Jersey 08648
[8]Merck Research Laboratories, Merck and Company, Inc., West Point, Pennsylvania 19486

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ABSTRACT: Although essential guidance to cover the photostability testing of pharmaceuticals for manufacturing and storage is well-established, there continues to be a significant gap in guidance regarding testing to support the effective administration of photosensitive drug products. Continuing from Part 1, (Baertschi SW, Clapham D, Foti C, Jansen PJ, Kristensen S, Reed RA, Templeton AC, Tønnesen HH. 2013. J Pharm Sci 102:3888–3899) where the focus was drug products administered by injection, this commentary proposes guidance for testing topical drug products in order to support administration. As with the previous commentary, the approach taken is to examine "worst case" photoexposure scenarios in comparison with ICH testing conditions to provide practical guidance for the safe and effective administration of photosensitive topical drug products. © 2015 Wiley Periodicals, Inc. and the American Pharmacists Association J Pharm Sci 104:2688–2701, 2015

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INTRODUCTION

Part 1 of this series of commentary papers[1] outlined the importance of photostability testing to support in-use handling and administration of pharmaceutical products intended for injection. In particular, a systematic approach to evaluating realistic light exposure scenarios, information to develop a photostability testing plan, and the generation of a dataset to provide valuable insight into the safe and effective administration to a patient was proposed. This initial paper in the series laid much of the foundation for how to think about in-use photostability testing, including an in-depth discussion on relevant light sources, supply chain considerations, and a recommended photostability testing strategy. The interested reader is referred to Part 1 for additional background information on these topics as these will only be treated in a cursory fashion in the present work. The current paper applies the concepts and principles outlined in Part 1 to the testing of pharmaceutical products that are administered topically. Expanding the principles of photostability testing to support use of this class of drug products is important for a number of reasons:

- A deficit continues to exist in the literature and in general understanding of the photostability testing needed to support the administration of pharmaceutical products;
- Product light exposure during handling and use can adversely impact the efficacy and safety of a pharmaceutical product;
- Topical drug products are administered by application to external body surfaces and, as a result, have the potential to be exposed to a significant amount of light during use by the patient;
- Formulations are often applied as thin films maximizing the surface to volume ratio and hence increasing the potential to react with incident light;
- For some indications (e.g., psoriasis), exposure of the skin to sunlight, high-intensity UV, or simulated solar light after application of a topical drug is part of the treatment;
- Increasing the dialogue in the scientific community on the topic will lead to improved testing approaches, more effective labeling, better patient and practitioner education, and hence ultimately improved health outcomes.

Our analysis of topical products in the USP[2] showed that 95 of the 342 products (28%) listed have monograph language that indicates storage in a light-protective container. The situation is similar in Europe[3] with many topical products labeled as requiring protection from light (Table 1); however, the label

Correspondence to: David Clapham (Telephone: +44 1920 883943; E-mail: david.clapham@gsk.com); Allen C. Templeton (Telephone: +215 652-0041; E-mail: allen_templeton@merck.com)

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Table 1. Topical Products with a Protect from Light Designation or Light Protective Immediate Pack

Active Pharmaceutical Ingredient	Dosage Form	Immediate Container	Source	Administration Route
Topical light mineral oil	Oil	Preserve in tight, light-resistant containers	USP	Skin
5-Aminolevulinic acid hydrochloride	Gel	Aluminum tube	UK[a]	Skin
Acetylcysteine	Solution	Type I amber glass	UK[a]	Eye
Aminobenzoic acid gel	Gel	Preserve in tight, light-resistant containers	USP	All exposed skin (i.e., nose)
Aminobenzoic acid topical solution	Solution	Preserve in tight, light-resistant containers	USP	All exposed skin (i.e., nose)
Anthralin cream	Cream	Preserve in tight containers, in a cool place; Protect from light	USP	Skin
Anthralin ointment	Ointment	Preserve in tight containers, in a cool place; protect from light	USP	Scalp
Atropine sulfate	Solution	NS	UK[a]	Eye
Azithromycin dihydrate	Solution	LDPE	UK[a]	Eye
Beclometasone dipropionate	Suspension	HDPE	UK[a]	Nose
Benzethonium chloride tincture	Tincture	Package in tight, light-resistant containers	USP	Skin (hands)
Benzethonium chloride topical solution	Solution	Preserve in tight, light-resistant containers	USP	Skin
Benzocaine cream	Cream	Preserve in tight containers, protected from light, and avoid prolonged exposure to temperatures exceeding 30°C	USP	Skin, mouth
Benzocaine ointment	Ointment	Preserve in tight containers, protected from light, and avoid prolonged exposure to temperatures exceeding 30°C	USP	Skin
Benzocaine topical solution	Solution	Preserve in tight containers, protected from light, and avoid prolonged exposure to temperatures exceeding 30°C	USP	Ear
Betamethasone dipropionate	Gel	HDPE	UK[a]	Scalp
Betamethasone valerate	Solution	Plastic bottle	UK[a]	Scalp
Betamethasone valerate lotion	Lotion	Preserve in tight, light-resistant containers, and store at controlled room temperature	USP	Skin
Betaxolol hydrochloride	Solution	LDPE	UK[a]	Eye
Brimonidine tartrate	Solution	LDPE	UK[a]	Eye
Calcipotriol monohydrate	Gel	HDPE	UK[a]	Scalp
Carbamide peroxide topical solution	Solution	Preserve in tight, light-resistant containers, and avoid exposure to excessive heat	USP	Ear
Carbol–Fuchsin topical solution	Solution	Preserve in tight, light-resistant containers	USP	Skin
Chloramphenicol	Solution	LDPE, HDPE, white bottle	UK[a]	Eye
Chlorhexidine acetate topical solution	Solution	Preserve in well-closed containers, protected from light	USP	Mouth
Chlorhexidine gluconate solution	Solution	Preserve in tight containers, protected from light, at controlled room temperature	USP	Skin
Chlorhexidine gluconate topical solution	Solution	Preserve in well-closed containers, protected from light; store at controlled room temperature	USP	Skin
Chlortetracycline hydrochloride ointment	Ointment	Preserve in collapsible tubes or in well-closed, light-resistant containers	USP	Eye
Ciclopirox topical solution	Solution	Preserve in well-closed containers, protected from light; store at controlled room temperature	USP	Skin (nails)
Clioquinol and hydrocortisone cream	Cream	Preserve in collapsible tubes or in tight, light-resistant containers	USP	Skin
Clioquinol and hydrocortisone ointment	Ointment	Preserve in collapsible tubes or in tight, light-resistant containers	USP	Skin
Clioquinol cream	Cream	Preserve in collapsible tubes or tight, light-resistant containers	USP	Skin
Clioquinol ointment	Ointment	Preserve in collapsible tubes or tight, light-resistant containers	USP	Skin
Clocortolone pivalate cream	Cream	Preserve in collapsible tubes or in tight, light-resistant containers	USP	Skin

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