HOW TO ENSURE A RELIABLE METHOD DEPLOYMENT? AN EXAMPLE WITH THE IN VITRO SPF DOUBLE PLATE METHOD

#413

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1 INTRODUCTION

While the in vivo measurement method of SPF (Sun Protection Factor) remains the gold standard and has recently been revised (ISO 24444:2019(Amd1), FDA 2022 ongoing), industry and the photoprotection experts' community continue their efforts to offer a reliable, robust and ethical alternative method.

Developed and supported by Cosmetics Europe, the in-vitro SPF Double Plate method is currently being worked on at the Committee Draft stage by the ISO experts of TC 217/WG7. This method is based on UVR transmittance spectroscopy, whereby spectroradiometric measurement of UVR transmission through appropriate UVR-transparent substrates, allows prediction of in vivo SPF values **[1;2]**. Recently, Cosmetics Europe called on the entire industry to start familiarizing themselves with this method **[3]**, the ongoing statistical characterization of which within the ALT-SPF Consortium **[4]** could lead to publication as an ISO method in 2025. Previously, some methods published by ISO may have experienced interpretation problems during their implementation in test laboratories, so how can you be sure that this new method will be reliably deployed in the industry?

Here we highlight the key steps in the process of appropriation of a new method, based on our collaborative experience on the In Vitro SPF Double Plate method.

2 MATERIALS & METHODS

10 laboratories (3 internal and 7 external ones) localized in France, Poland, Germany, Ireland, USA and Japan involved in this approach.

3 laboratories which were in the core group of this method development for years, were identified for reference and support. Each of these "reference laboratories" followed nevertheless the global process in 3 stages:

Suitability of equipment
- List of the equipments and specifications.
- Adequacy checked through a declarative form

Mastery of practical implementation
- Video monitoring with referent auditor(s) who observed the practice of an operator in real conditions

Validation of the results
- Inter-laboratory testing
- 10 sunscreen training formulae (W/O emulsion, variable UV filters systems, large range of SPF)

Each of the steps of the method **[5;6]** were monitored through this approach:
1. Preparation of reagents and materials
2. Product application on substrates and robot automatic spreading
3. Measurement of initial absorbance using ≥3 pairs of molded and sandblasted plates (290 nm to 400 nm).
4. Calculation of initial in vitro SPF.
5. Calculation of irradiation dose (based on initial in vitro SPF).
6. Irradiation with calculated dose by pair of plates.
7. Measurement of final post irradiation absorbance on the ≥ 3 pairs of molded and sandblasted plate (290 nm to 400 nm).
8. Calculation of final in vitro SPF.

$$Final\ in\ vitro\ SPF_i = \frac{\int_{290}^{400} E(\lambda)\, I(\lambda)\, d\lambda}{\int_{290}^{400} E(\lambda)\, I(\lambda)\, 10^{-Final\ A(\lambda)}\, d\lambda}$$

Where:
$E(\lambda)$ = CIE erythema action spectrum;
$I(\lambda)$ = Midday mid-summer global irradiance at 40°N;
$d\lambda$ = Wavelength step (1 nm);
Final A $(\lambda) = C_{Moulded} * A_{Moulded\text{-}post\text{-}irradiation}(\lambda) + C_{Sandblasted} * A_{Sandblasted\text{-}post\text{-}irradiation}(\lambda)$;
$A_{Moulded\text{-}post\text{-}irradiation}$ = absorbance of the moulded plate after UV exposure;
$A_{Sandblasted\text{-}post\text{-}irradiation}$ = absorbance of the sandblasted plate after UV exposure;
$C_{Moulded}$ and $C_{Sandblasted}$ = Correction factors defined according to product type [6]

When necessary, the 2nd and 3rd stages of this process were repeated to understand and improve inconsistent results.

3 RESULTS & DISCUSSION

Each step of this process proved to be crucial for the success of the implementation and the appropriation of the method.

A/ Suitability of equipment

This step revealed as being the most limiting, resulting in withdrawal of 5 laboratories out of the initial 10.

	GENERAL ADEQUACY TO SPECIFICATIONS	SPECIFICATIONS ENCOUNTERED AS BEING LIMITING DURING THE METHOD DEPLOYMENT
SUBSTRACT	★★★	- Molded PMMA plates - Sandblasted PMMA plates
PLATES SURFACE TEMPERATURE CONTROLLER	★★☆	To store plates and product at 27 (± 2)°C in the dark
ANALYTICAL BALANCE	★★★	with at least 10^{-4} g precision
AUTOMATIC POSITIVE-DISPLACEMENT PIPETTE	★★☆	capable of delivering accurate and repeatable aliquots of approximately 1.6 mg to 1.8 mg of a sunscreen product
AUTOMATIC SPREADING ROBOT	★★☆	The robot spreading is defined in gesture and time to reproduce the in-vivo gesture. Vertical force (z axis), measured in the center of the plate (with the finger tool and finger cot, without x and y axis movement), shall be of 6,0 ± 0,5 N
UV TRANSMITTANCE SPECTROPHOTOMETER	★☆☆	As described in ISO24443. Precise positioning of the plate, which should remain positioned in a horizontal plan.
SOLAR SIMULATOR	★☆☆	A xenon arc solar simulator with appropriate filters. It shall be able to maintain a stable, sample-level temperature of 27 ± 2°C and to irradiate at least 2 plates at the same time with: - The SPF vivo spectrum (ISO24444) - No flux of air on the plates - Good temperature stability - Good homogeneity of UV irradiation - Possibility to place the plates without interrupting the UV flux
RADIOMETER / SPECTRORADIOMETER	★☆☆	Use a radiometer able to provide flux measurement in MED/Hr Or use a spectroradiometer and perform the right calculation (e.g. 1 MED = 210 J/cm²).

Table 1: General observed adequacy of the equipment regarding specifications and the most critical points encountered for the Double Plate method to be deployed in the participating laboratories.

B/ Mastery of practical implementation

In this 2nd stage, the 5 laboratories that have passed successfully the 1st stage were included. Also, 4 laboratories which were withdrawn during the first step requested to be involved in similar parallel process to get feedback on their partial practice (up to step n°4). This stage appeared to be an important phase in the transmission of expertise. No laboratory was withdrawn at this stage since it allowed the observation but also the correction of wrong practices.

C/ Validation of the results on a set of 10 training formulas

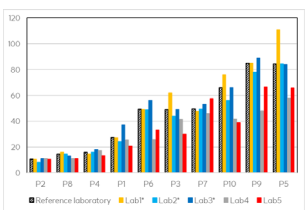

Figure 1 : Bar graph comparing the individual final in vitro SPF results for the 5 laboratories which pass the steps 1 and 2. The reference laboratory is created artificially by considering the median value from the 3 reference laboratories (Lab1*, Lab2* and Lab3*) which are mastering the method for long time, while Lab4 and Lab5 are new adopters. Such comparison allowed us to confirm consistency of results within the 3 reference laboratories and to detect underestimation for Lab4 and Lab5, to identify the cause and to suggest corrective actions.

The sources of underestimation identified were an equipment problem in the UV transmittance spectrophotometer or in the batch of the fingercot which was used. Once fixed, the values tends to get closer from the expected ones.

The observations "before exposure" are a good indicator of what would be the trend for the laboratories which cannot realize the full method. For one lab, a strong overestimation is observed for almost all the products, suggesting an issue in the product application (e.g. linked to the robotic arm pressure settings).

4 CONCLUSIONS

To obtain reliable measurement of the level of protection offered by a sunscreen is essential, as part of an efficient public health policy to help consumers to be adequately protected against the damaging impact of solar exposure. Efforts were deployed here to help voluntary laboratories to familiarize themselves with and appropriate the in vitro SPF Double Plate method, as it could be published as an ISO method in 2025. The key elements of the approach were: identification of referent laboratories, detailed resources checking, monitoring of the practice, validation of the results on a set of training samples. Such approach is based on generic steps which can be implemented for the deployment of any new instrumental method. It had the dual advantage of identifying possible ambiguities, thus indicating where it is relevant to strengthen the formalization of the procedure and ensuring easy and reliable implementation in laboratories new to the SPF in vitro Double Plate method.

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