Proposal of Scope of Clinical Assays of Safety and Effectiveness of Cosmetic Products

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Abstract. The demand for accreditation for clinical assays involving cosmetic products has led the Division of Laboratory Accreditation (Dicla) to study the possibility of implementing the General Coordination for Accreditation (Cgcre) which is a specific accreditation program for Good Clinical Practice (GCP). This work represents the very beginning of such a study thus conveying a proposed model of scope for clinical assays on safety and effectiveness.

1. Introduction

1.1. The Mission and Function of Inmetro Cgcre/Dicla

The Inmetro is a federal agency whose mission is to “provide confidence to the Brazilian Society regarding measurements and products through metrology and conformity assessment, thus promoting harmonization of consumption relationships innovation and competitiveness of the country” [1]. Among the powers and duties of Inmetro the accreditation activities stand out, structured under Cgcre (General Coordination for Accreditation), which is in charge of accreditation of conformity assessment bodies recognized by the Brazilian government [2].

In this context, it is noteworthy that the laboratory accreditation by Cgcre is performed by the Division of Laboratory Accreditation (Dicla), which operates in the following modes of accreditation/recognition: i) accreditation of testing and calibration laboratories, following the requirements of ABNT NBR ISO/IEC 17025:2005; ii) accreditation of clinical laboratories in accordance with ABNT NBR NM ISO 15189:2008; iii) accreditation of producers of reference materials in accordance with ABNT ISO Guide 34:2012; iv) accreditation of proficiency testing providers, through ABNT NBR ISO IEC 17043:2010 and v) recognition of conformity to the principles of Good Laboratory Practice (GLP) according to the definitions explained in NIT-Dicla-035: Principles of Good Practice Laboratory.

1.2. Conformity Assessment Bodies (CABs)

In order to promote the CABs as well as the testing facilities, which are recognized under GLP, Cgcre provides, at the site of Inmetro the scope of each accredited CAB and test facility that has recognition of conformity with the GLP.

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The scope of each CAB is a formal document, which sets Cgcre tests, calibrations, certified reference materials and proficiency testing of accredited providers, as well as the tests that were recognized by Cgcre.

1.3. The Current Demand for Accreditation of Testing on Cosmetics

Currently, Dicla has faced a demand of requests for accreditation for tests involving cosmetic products.

Perhaps this situation can be best explained by the fact that the companies have increasingly looked for recognition for the services they provide, coupled with the high rate of use of cosmetic products in Brazil. In 2011, Brazil was ranked as the third largest consumer of cosmetics [3].

Just as occurs with other products that promote health and the well-being of consumers, cosmetic products may occasionally experience adverse reactions in users due to individual factors or improper use of the product [4-5].

Therefore, the National Health Surveillance Agency (Anvisa) establishes several regulations so as to standardize the registration of cosmetics in the country.

This work is aimed at studying the main Standards and Guidelines established by Anvisa, regarding the regulation of cosmetic products in order to begin a study to verify the feasibility of establishing a program at Cgcre/Dicla accreditation/recognition of a clinical assay for those products.

2. Materials and Methods

The development of the work consisted of 4 distinct and subsequent phases.

The first phase consisted in the study and bibliographic surveys of the Standards and Guidelines established by Anvisa.

In the second phase the tests required by Anvisa that Dicla does not yet have were verified.

The third phase consisted of a query to the sites of organizations from different body country accreditors.

In the fourth and final stage, a model of scope for clinical trials of safety and effectiveness of cosmetic products was suggested.

3. Results and Discussions

3.1. 1st phase: Study and Surveys of Anvisa Standards

A study of the Standards requested by Anvisa was carried out in order to establish criteria concerning the registration of products in Brazil.

3.1.1. RDC Resolution 211, July, 14th, 2005

The classification of cosmetics is established in this resolution, which was defined in terms of the likelihood of unwanted effects due to inappropriate use of the product, its formulation, purpose of use, areas of the body as intended and precautions to be observed when using it [6]. The products were classified as "Product Grade 1 and Product Grade 2" [6].

According to this resolution, required physic-chemical and microbiological tests are required on raw materials and finished products for Risk Level 1 products. For Risk Level 2 products are required in addition to those listed for the Risk Level 1, the pre-clinical safety assays and the clinical assays of safety and effectiveness in the finished products are also required.

3.1.2. RDC Resolution 38, March, 21th, 2001

This resolution describes the criteria and procedures for the registration of new categories of cosmetic products intended for children use [7].

In conformity with resolution, the cosmetic products for children are classified as Product Grade 2.
The relevant information of this resolution is the specification of clinical assays that are required by ANVISA for registration of children cosmetic product.

3.1.3. RDC Resolution 237, August, 22nd, 2002
This resolution approves the technical regulations for sunscreens in cosmetics.

According to this resolution, ANVISA states specifically what are the tests to be used for sunscreens for determining the Sun Protection Factor (SPF) as well as the use of the terms “water resistant” or “very water resistant” on product labeling [8]. All assays are classified as effectiveness assays.

3.1.4. Guide for Safety Evaluation of Cosmetic Products
This Guide ranks the trials into two groups: studies of compatibility and acceptability studies [9]. It also lists the clinical safety trials according to the classification of the study.

Besides the description of these tests, this guide provides ANVISA clinical trials to be conducted in cosmetics when the manufacturer indicates to consumers that the product has the following security attributes: Tested in terms of Dermatology and Ophthalmology, Hypoallergenic. It also describes the tests to be performed when the product meets certain safety standards, according to the target audience, such as children or pregnant women or sensitive skin people [9].

3.1.5. Technical Chamber of Cosmetics (CATEC)
In addition to the standards cited, there are some opinions of CATEC of Anvisa establishing the need for proof of efficacy and safety for certain products. For example: Products containing Vitamin C, Dimethylaminoethanol (DMAE) and Fostatidilocolin; products indicated for dark circles; products for cellulite and stretch marks and fat, among others [10].

3.2. 2nd phase: Testing verification required by Anvisa
In this phase it was realized that Dicla does not only have a program for BPC accreditation / recognition for clinical assays, among the tests required by Anvisa for registration of cosmetic products in Brazil.

3.3. 3rd phase: Consultation on websites of accreditation bodies
A consultation was held on the websites of the following accreditation organizations to check if any of them has the accreditation program / recognition in BPC: IPAQ (Portugal), UKAS (United Kingdom), NATA (Australia), TVR (Netherlands), A2LA (USA) A Class (USA), EMA (Mexico) and CNCA (China).

Of all the bodies consulted, none has the accreditation program / recognition for BPC.

3.4. 4th phase: Proposal of Scope of Clinical Assays of Effectiveness and Safety of Cosmetic Products
Taking into consideration the consulted documents as well as the standard formatting of the Dicla Scope, two tables were devised, 1 and 2 below, one model of scope for clinical assays and another model for safety and effectiveness of cosmetic products.
Table 1. Model of Scope for Clinical Assays of Safety for Cosmetic Products

| Classification of Clinical Assay/Cosmetic Product | Classification of study/Assay description | Norm and/or procedure |
|---------------------------------------------------|-----------------------------------------|-----------------------|
| Safety Assays                                     | Compatibility Study                     | POP 540 Rev.01, 2013  |
| Chemical “peeling”                                | Evaluation of Dermal Sensitization      |                       |
| Safety Assays                                     | Acceptability Study                     | IT 98 Rev.00, 2012    |
| Products for acne prone skin                      | Evaluation of acnegenicity              |                       |

Table 2. Model of Scope for Clinical Assays of Effectiveness for Cosmetic Products

| Classification of Clinical Assay/Cosmetic Product | Assay description | Norm and/or procedure |
|---------------------------------------------------|-------------------|-----------------------|
| Effectiveness Assays                              | Evaluation of the dry solar sunscreen factor | International Sun Protection Factor (SPF) Test Method, Colipa 2006 |
| Sunblock / anti-solar sunscreen                    |                   |                       |
| Effectiveness Assays                              | Evaluation of the determination of “extremely resistant to the water” | Norm FDA 2012 – Sunscreen drug products for over-the-counter human use, Code of Federal Regulations, Title 21, Vol.5, Sec.352.76 |
| Kids sunscreen                                    |                   |                       |

4. Conclusions
After all the studies we came to the conclusion that this work can be viewed as a initial study regarding the possibility of the implementation of an accreditation program/recognition BPC under Cgcre/Dicla, and If it materializes it surely will be of great value to the Brazilian society.

References
[1] Inmetro. O que é Inmetro [on line]. Rio de Janeiro, Brazil; 2013. [captured 11 may 2013] Available in: http://www.inmetro.gov.br/inmetro/ouque.asp
[2] Brazil. Presidency of the Republic of Brazil. Law 1245, of 14 december of 2011.
[3] Chiari B G et al 2012 Int J Res CosmetSci 2 (2) 14
[4] Rogiers V 1999 Atla 27 4
[5] Santos H 2008 Cosm Toil 20 2.
[6] Brazil. Resolution 211, July, 14th, 2005, Establish the Definition and the Classification of Personal Care Products, Cosmetics and Perfumes, in conformity with Annex I and II this Resolution and give others recommendations. Union Official Journal. Brasilia, 18 jul. 2005.

[7] Brazil. Resolution 38, March, 21th, 2001, Approve the Technical Regulation of Cosmetic Products for Kids.

[8] Brazil. Resolution 237, August, 22th, 2002, Approve the Technical Regulation about Sunblocks in Cosmetic Products. Union Official Journal. Brasilia, 23 agos. 2002.

[9] Brazil. Guide for Evaluation of Safety of Cosmetic Products. Brasilia: Anvisa, 2012.

[10] Anvisa. Technical Chamber [on line]. Brasilia, Brazil; 2013. [captured 22 may 2013] Available in: http://portal.anvisa.gov.br/wps/content/Anvisa+Portal/Anvisa/Inicio/Cosmeticos/Assuntos+de+Interesse/Camara+Tecnica