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CASE STUDY

Transfer of drug dissolution testing by statistical approaches: Case study

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Abstract The analytical transfer is a complete process that consists in transferring an analytical procedure from a sending laboratory to a receiving laboratory. After having experimentally demonstrated that also masters the procedure in order to avoid problems in the future. Method of transfers is now commonplace during the life cycle of analytical method in the pharmaceutical industry. No official guideline exists for a transfer methodology in pharmaceutical analysis and the regulatory word of transfer is more ambiguous than for validation. Therefore, in this study, Gauge repeatability and reproducibility (R&R) studies associated with other multivariate statistics appropriates were successfully applied for the transfer of the dissolution test of diclofenac sodium as a case study from a sending

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laboratory A (accredited laboratory) to a receiving laboratory B. The HPLC method for the determination of the percent release of diclofenac sodium in solid pharmaceutical forms (one is the discovered product and another generic) was validated using accuracy profile (total error) in the sender laboratory A. The results showed that the receiver laboratory B masters the test dissolution process, using the same HPLC analytical procedure developed in laboratory A. In conclusion, if the sender used the total error to validate its analytical method, dissolution test can be successfully transferred without mastering the analytical method validation by receiving laboratory B and the pharmaceutical analysis method state should be maintained to ensure the same reliable results in the receiving laboratory.

1. Introduction

The transfer of analytical methods of pharmaceuticals plays important roles within the pharmaceutical industry. Transferring the methods is now a challenging step during the life cycle of the analytical method. It is considered the last step before the routine use of the method at the receiving laboratory. The receiver must therefore guarantee of their capacity to implement the method and importantly being able to obtain reliable results (Rozet et al., 2009).

An analytical transfer is a complete process that consists in transferring a validated analytical method from a sending laboratory (called sender) to a receiving laboratory (called receiver) after experimentally demonstrating the capability to master the method (Dewé et al., 2007). Verification of a test method's acceptability should be performed for all methods. When a test method is transferred to an alternative testing site requires evidence that the test procedure is functioning correctly (Stephen et al., 2002).

The transfer protocol or test plan should include suitable acceptance criteria relevant to the tests and specific dissolution profiles where dissolution is a characterization test commonly used by the pharmaceutical industry to guide formulation design. Also, it is used to control product quality and it is considered a key parameter in assessing the uniformity at the formulation stage as well as throughout the shelf-life of the product (Cohen et al., 1990).

Due to lack of formal guidance or regulatory requirements, several approaches are possible to select the experimental design, for choosing the statistical data treatment and hence for the decision process namely the dissolution test (Fontenay, 2008). The success of an analytical method transfer is tested by comparing results or their summary parameters such as the means and variances of the participating laboratories obtained after analyzing similar samples. Therefore, it is important for the researchers to search ways to validate the analytical transfer.

Several terms and statistical approaches for the transfer of analytical methods have been described and designed. The USP (2009) described the transfer of analytical procedures: A proposal for a new general information chapter 1224. Also the FDA (2006) has released an official guidance on how to conduct and document method transfer. The ISPE (The International Society for Pharmaceutical Engineering) design provides adequate probabilities to accept successful method transfers correctly only for relatively small error amounts (Schepers and Wätzig, 2005; Kaminski1 et al., 2010). Also the conventional statistical approaches generally were used in the transfer of quantitative methods namely bioanalytical applications associated with risk evaluation of this transfer (Rozet et al., 2008). On the other hand, the United States Pharmacopoeia concept (1010) was used as the equivalence test for analytical method transfer (Schepers and Wätzig, 2006) and it uses total error as a decision criterion for transfer of HPLC–UV method (Rozet et al., 2006). The best way to estimate the characteristics of dispersion of an HPLC method and a powerful tool for analytical transfers was studied (Vial and Jardy, 2001).

The objective of this work is to demonstrate the applicability of the total error approaches with certain statistical models to a more variability domain pharmaceutical namely dissolution test and in the interpretation of acceptance criteria of transfer of dissolution profiles of solid pharmaceutical form.

2. Materials and methods

2.1. Standard and placebo

The reference standard (*RF*) for diclofenac sodium (DS) (98.2%) was obtained from Drugs Quality Control Laboratory as certified by external secondary standard. The product A as originator was obtained from Novartis for pharmaceutical industries and product B as generic was obtained from Galanica for pharmaceutical industries (Morocco). The placebos used in validation of the analytical method were the fallowing: calcium phosphate tribasic, sodium starch glycolate, magnesium stearate, polyvinylpyrrolidone, microcrystalline cellulose, sucrose, purified talc, disperse red, lactose, selenium dioxide, cellulose acetophthalate, titanium dioxide, ethanol, polyethylene glycol, iron oxide red, iron oxide yellow, maize starch, silica colloidal anhydrous, silicone antifoam, sodium methyl carboxyl and polysorbate 80.

2.2. Reagents

At the sending and receiving sites, methanol was of HPLC grade from Sigma–Aldrich (Germany). Hydrochloric acid and phosphoric acid were supplied by Merck KGaA (Germany). Sodium phosphate tribasic was obtained from Riedel-de Haen (Germany).

2.3. Apparatus

At the sending site, the chromatographic system consisted of Waters 2695 pump, auto sampler and Waters 2998 photodiode-array detector (PDA). Data acquisition was performed by the Empower Software data registration TM. Dissolution test of Erweka DT 600, Frankfurt (Germany). pH meter of Concort (Belgium). Balance of Precisa (Switzerland).

At the receiving site, Dissolution test of Hanson SR8-Plus™ (USA), the chromatographic system consisted of Waters 2695 pump, auto sampler and Waters 2998 photodiode-array detector (PDA). Data acquisition was performed by the Empower