Annales Pharmaceutiques Françaises (2017) 75, 446—454

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

ORIGINAL ARTICLE

Multivariate statistical process control in product quality review assessment — A case study

Évaluation de la revue qualité produit par la maîtrise statistique du procédé multivariée — étude de cas

M. Kharbach[a,b], **Y. Cherrah**[a], **Y. Vander Heyden**[b], **A. Bouklouze**[a,*]

[a] *Pharmaceutical and toxicological analysis research team, laboratory of pharmacology and toxicology, faculty of medicine and pharmacy, university Mohammed V. Souissi, avenue Med Belarbi El Alaoui, BP 6203, 10000 Rabat, Morocco*
[b] *Department of analytical chemistry and pharmaceutical technology, CePhaR, Vrije Universiteit Brussel (VUB), Laarbeeklaan 103, 1090 Brussels, Belgium*

Received 29 November 2016; accepted 3 July 2017
Available online 7 August 2017

KEYWORDS
Annual product review;
Statistical process control;
Multivariate statistical process control;
Principal component analysis;
Hotelling's T^2

Summary According to the Food and Drug Administration and the European Good Manufacturing Practices (GMP) guidelines, Annual Product Review (APR) is a mandatory requirement in GMP. It consists of evaluating a large collection of qualitative or quantitative data in order to verify the consistency of an existing process. According to the Code of Federal Regulation Part 11 (21 CFR 211.180), all finished products should be reviewed annually for the quality standards to determine the need of any change in specification or manufacturing of drug products. Conventional Statistical Process Control (SPC) evaluates the pharmaceutical production process by examining only the effect of a single factor at the time using a Shewhart's chart. It neglects to take into account the interaction between the variables. In order to overcome this issue, Multivariate Statistical Process Control (MSPC) can be used. Our case study concerns an APR assessment, where 164 historical batches containing six active ingredients, manufactured in Morocco, were collected during one year. Each batch has been checked by assaying the six

* Corresponding author.
E-mail addresses: a.bouklouze@um5s.net.ma, yvanvdh@vub.net.be (A. Bouklouze).

http://dx.doi.org/10.1016/j.pharma.2017.07.003
0003-4509/© 2017 Académie Nationale de Pharmacie. Published by Elsevier Masson SAS. All rights reserved.

active ingredients by High Performance Liquid Chromatography according to European Pharmacopoeia monographs. The data matrix was evaluated both by SPC and MSPC. The SPC indicated that all batches are under control, while the MSPC, based on Principal Component Analysis (PCA), for the data being either autoscaled or robust scaled, showed four and seven batches, respectively, out of the Hotelling T^2 95% ellipse. Also, an improvement of the capability of the process is observed without the most extreme batches. The MSPC can be used for monitoring subtle changes in the manufacturing process during an APR assessment.

© 2017 Académie Nationale de Pharmacie. Published by Elsevier Masson SAS. All rights reserved.

MOTS CLÉS
Revue annuelle produit ;
Maîtrise statistique du procédé ;
Maîtrise statistique du procédé multivariée ;
Analyse en composante principale ;
T^2 de Hotelling

Résumé Selon la FDA et les bonnes pratiques de fabrication européennes (BPF), la revue annuelle produit (RAP) est une exigence réglementaire. Elle consiste à évaluer des données qualitatives ou quantitatives dont l'objectif de vérifier la fiabilité d'un procédé de fabrication existant. Selon le Code de la régulation fédérale partie 11(21 CFR211.180), la qualité des produits finis doit être documentée annuellement afin de déceler si un changement dans les spécifications ou la fabrication du médicament est préconisée. La maîtrise statistique du procédé classique (MSP) évalue le procédé de fabrication pharmaceutique en variant uniquement un seul facteur à la fois à l'aide de la carte de contrôle de Shewart. Cette méthode ne prend pas en considération les interactions qui peuvent exister entre les variables. Ce phénomène peut être mis en évidence par l'application de la maîtrise statistique du procédé multivariée (MSPM). Notre travail consiste en une étude de cas d'une revue qualité produit basée sur 164 lots historiques d'une spécialité pharmaceutique contenant six principes actifs fabriqués au Maroc durant un an. Chaque lot a été contrôlé par le dosage des six principes actifs par la chromatographie liquide de haute performance selon la monographie de la pharmacopée européenne. La matrice de données (164×6) a été évaluée à la fois par la MSP et Par MSPM. La MSP a montré que tous les lots sont sous contrôle, alors que la MSPM basée sur l'analyse en composante principale appliquée aux données avec préalable prétraitement adéquat a révélé que sept lots sont en dehors de l'intervalle de T^2 de Hotteling 95 %. Une amélioration de la capabilité a été observée en éliminant les sept lots supposés aberrants. La MSPM peut être recommandée pour déceler des faibles variations dans le procédé de fabrication sur la base de l'évaluation d'une revue annuelle produit.

© 2017 Académie Nationale de Pharmacie. Publié par Elsevier Masson SAS. Tous droits réservés.

According to the Food and Drug Administration (FDA) and the European Good Manufacturing Practices (EU-GMP) guidelines, Annual Product Review (APR) or Product Quality Review (PQR), respectively, is a mandatory requirement [1]. It should be conducted by the quality unit with the objective of verifying the consistency of the process. Such reviews are documented at least annually. The results of this review should be evaluated and an assessment made of whether corrective action or any revalidation should be undertaken. When corrective actions are required, the reason should be documented. Agreed corrective actions should be completed in a timely and effective manner. The PQR is an evaluation tool that is integrated into the quality management system. It offers a high level of confidence in the quality of the resulting product, which establishes a strong customer supplier mutually beneficial relationship and it reduces the risk to public health.

The integration of the Annual Product Review in the International Conference on Harmonization (ICH) Q7 [2], ICH Q10 [3] and in the GMP European guidelines [4] indicates a genuine desire by the regulatory authorities to increase the level of confidence in the product, manufactured by the pharmaceutical industries.

Conventional Statistical Process Control (SPC) (see Theory section) which is defined as the ability of a process to produce output within specification limits is often performed to verify the performance of the manufacturing process. This is inappropriate for many process applications where several variables are generated that are mutually not independent. However, in reality the process is governed by a large number of variables, which can be dependent, which increases the risk of missing an out-of-control situation due to an interaction between two variables [5,11]. Hence, they all should be treated simultaneously in multivariate approach to ensure the success of the implementation process and obtaining good results [7].

In order to overcome this problem, Multivariate Statistical Process Control (MSPC) has been used in detecting variations due to given factors [6—9].

Download English Version:

https://daneshyari.com/en/article/5546950

Download Persian Version:

https://daneshyari.com/article/5546950

Daneshyari.com