



LETTERS TO THE EDITOR

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The importance of quality control in raw materials used in pharmaceutical formulations

La importancia del control de calidad de las materias primas empleadas en formulación magistral

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Dear Ms. Director:

During a medicine manufacturing process, compliance with good manufacturing practices (GMP) that guarantee optimal quality, safety and efficacy for the patient is mandatory, and are applicable for both the starting raw materials manufacturing, and for the medicine itself, as well as for the storage and distribution phases that take place between each stage of the process. For this reason, current legislation determines that manufacturers and distributors of pharmaceutical raw materials as well as drug-producing entities are all responsible to guarantee the quality of the raw materials used in accordance with these GMPs^{1,2}.

In pharmacotechnics, raw materials quality is routinely certified through the analytical bulletins provided by suppliers, since currently it is only mandatory to perform a complete quality control according to the Royal Spanish Pharmacopoeia (RFE by its Spanish acronym) when acquired to unauthorized suppliers. However, current legislation recommends that the responsible pharmacist performs at least one identification test even if they come from authorized centers and comply with the RFE specifications³.

However, following the cases of infants who have developed hypertrichosis by taking omeprazole syrup containing minoxidil, and due to the subsequent media impact, it has been inevitable for many of us to analyze the risks of our quality systems in terms of raw materials, despite the fact that pharmaceutical processors have been exempted from liability⁴.

Taking this fact into account and other recent alerts related to raw materials in table 1⁵, we deem it important to recall that manufacturers, importers and distributors of active ingredients used in pharmacotechnics must be registered in the Unified Register of Producers of Active Substances (RUESA by its Spanish acronym), which can be consulted at the Spanish Agency of Medicine and Sanitary Products (AEMPS by its Spanish acronym). In the case of excipients, it is also necessary to guarantee their suitability through a formal risk assessment.

In the light of the foregoing considerations, and being fully aware of the technical limitations and the daily great care burden of pharmacy services, we recommend performing quality controls through simple analytical methods, such as colorimetric tests, determination of pH, solubility, or melting point, and prioritizing these controls when they are going to be used for either preparations of systemic administration, pediatric or geriatric use, or in the case of drugs, with a narrow therapeutic margin. This arrangement would provide analytical results that could be crosschecked with those of the supplier's, and therefore its receipt could be either accepted or rejected during manufacturing.

On the other hand, to procure an integral management program is crucial to assure total traceability of the manufacturing process, as well as rapidly and easily identifying magistral formulas manufactured in each raw material batch.

To have working standards and procedures for handling, preserving, risk management and raw materials inspection is vital, as well as assuring that professionals involved are appropriately trained to detect any change or alteration in the drug's organoleptic and physicochemical properties –in which case the personnel would facilitate its withdrawal or quarantine–.



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Table 1. Alerts and informative notes ratio related to raw materials registered in 2019 by the Spanish Agency of Medicine and Sanitary Products (AEMPS)⁵

Alert/informative note No.	Date:	Registered trademark and branding	Supplier	Description
R_19/2019	July 11, 2019	Omeprazol Ph. Eur.	<i>Distributor:</i> Farma-Química Sur, S.L. <i>Manufacturer:</i> Smilax Laboratories Limited (India)	Potential result out of specifications during identity test. Affected lot: 11072/10/42, expiration date: 03/2021
ICM (MI) 12/2019	August 5, 2019	Omeprazole, orlistat, lidocaine, nystatin, itraconazole, praziquantel, tacrolimus, fluorouracil, dexametasone, finasteride, erytromycin, oxalic acid, tretinoin, meloxicam and fluoxetine	Vencaser, C.B.	Non-compliance by the company of legal obligation to be registered in Unified Register of Producers of Active Substances (RUESA by its Spanish acronym)
R_19/2019 (Extension)	August 6, 2019	Omeprazol Ph. Eur.	<i>Distributor:</i> Farma-Química Sur, S.L. <i>Manufacturer:</i> Smilax Laboratories Limited (India)	Potential result out of specifications during identity test. Affected lots: 11072/10/41, 11072/10/43, 11072/10/44, 11072/10/45, 11072/10/46, 11072/10/47, 11072/10/48, 11072/10/49, 11072/10/50, 11072/10/51, 11072/10/52, 11072/10/53, 11072/10/54, 11072/10/55, 11072/10/56, 11072/10/57, 11072/10/58, 11072/10/59, 11072/10/60, 11072/10/61, 11072/10/62 y 11072/10/63, expiration date: 03/2021

Finally, to enforce quality control on final products is essential. Non conformity of the final product results can derive from a raw material that does not meet the necessary quality standards.

Implementing new quality control standards on raw materials will be a challenge, however we deem it crucial to work on it in order to avoid future incidents such as those that occurred with omeprazole syrup.

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