



JRF GLOBAL



GLP 5-Batch Analysis

The mirror of your technical grade product and the backbone of your dossier

"Analysis of five representative manufacturing batches of technical grade material for the percentage of main AI and impurities"

Why it is required?

The five batch analysis is required for the registration of new product and generic product by the manufacturer. By doing five batch analyses manufacturer proves the chemical equivalence to the reference specifications as per FAO and WHO. The aim of the analysis is to quantify significant impurities $\geq 0.1\%$ w/w, borderline impurities $\geq 0.06\%$ w/w and toxicological relevant impurities. All other impurities which are $< 0.06\%$ w/w, possibly need to be identified and characterized.

Selection of 5 manufacturing batches

The random selection of true five batches has to be at a point in the production process, after which no further chemical reaction (designed to produce or purify the substance) is intended. A number of guidelines are available to be followed for the enforcement of analytical method. To name a few are ABNT, US-EPA, SENASA, COFEPRIS etc. FAO and IUPAC provide information on toxicological relevant impurities. There is a little variation in the requirements of the regulatory bodies in different countries, with a common objective of quality and safe product in the market.

Analytical Method Development

Details of manufacturing process, with enough information on key starting materials, their impurities and intermediates play an important role in selection of appropriate techniques for method development process. Even a laboratory with state of the art facility is prone to shoddy analysis unless they are armed with correct information from the manufacturer. Careful study of the manufacturing process will help in identifying the nature of impurities and selection of suitable analytical technique for analysis. The presence of non-chromophoric impurities would need RI/ELSD detector if they are not heat labiles and non-volatiles. Analysis of volatiles would need GC-FID/NPD/ECD detectors depending upon attached moieties or functional groups. Before initiating the method development, the analytical chemist has to think about the country of submission of dossier for which five batch analyses is intended. Compliance with the country centric guidelines will ease the process of registration. If a manufacturer wishes to submit a dossier to Brazilian authorities for one of the thiocarbamates, will have to confirm to the Brazilian requirements of the 3D analysis, but thiocarbamates do not have any chromophore, so 3D HPLC analysis is not feasible using as such molecule. Development of a selective derivatization procedure for the chromophore to the molecule can make 3D analysis feasible.

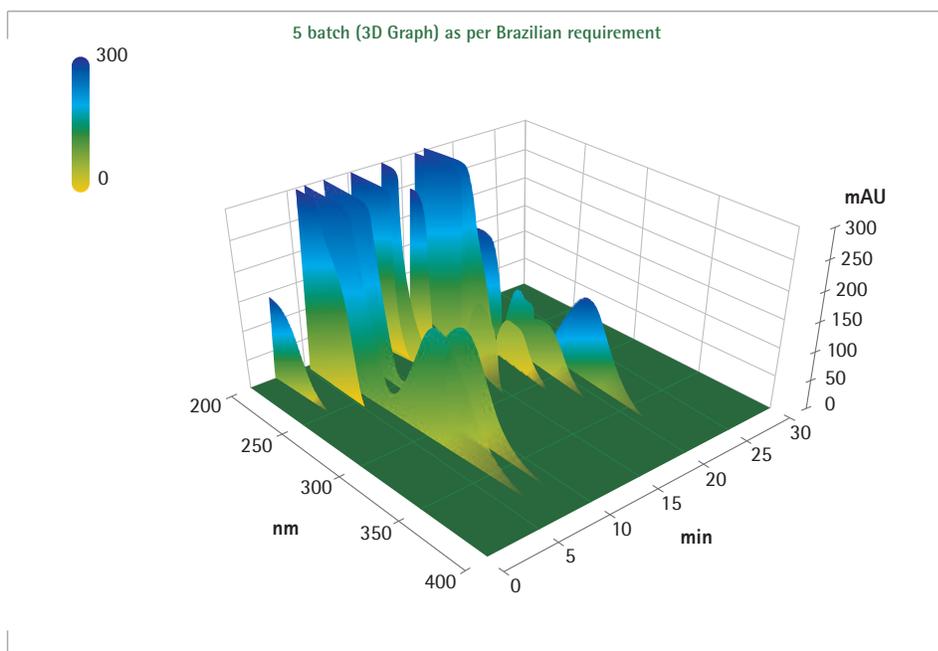


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Once the technique/s is/are selected, the optimization of various parameters like the polarity of a column or phase of column, column temperature, mobile phase composition, flow rate, monitoring wavelength etc. completes the method development path. The combined set of optimized parameters which gives desired resolution of all impurities, proper peak shapes, peak purities and acceptable run time will be defined as a suitable method for the next step of preliminary screening of five batches.

Preliminary Screening of five batches for the %age of AI and impurities (by products, carry over, salts etc.)

This screening of samples could be Non-GLP. It includes qualitative or semi quantitative analysis of active ingredient and impurities in the technical grade material. If the molecule is organic and has a chromophore LC-MS & / or GC-MS is/are right techniques for the screening purpose. The outcomes of this analysis are a % Area of all identified and resolved peaks along with their retention times, m/z ions and fragmentation Pattern. The mass balance has to meet 98-102% criterion. Before going for method validation, characterization of Active ingredient for all known and unknown impurities using ¹H NMR, Mass and FTIR would certify the respective structures.



Method Validation

The method validation has to be performed to satisfy SANCO 3030/99 rev 4, ABNT NBR 14029:2005, 2016, OCSPP 830.1800 in accordance to 40 CFR part 158.

For method validation parameters need to be covered are linearity, LOQ, LOQ, accuracy and precision. Once method is validated, the method is used to analyze the target five batches which are randomly selected and are true representatives of manufacturing process.

JRF Capabilities

At JRF we have completed more than 350 five batch analysis. The reports generated for 2D or 3D analysis are accepted by all regulatory authorities. With a team of experienced five batch analysts. One of them has completed more than 100 five batch analysis. JRF stands with 39 years of history in supporting manufacturers for data generation to submit their dossiers. JRF is capable of handling inorganic compounds for five batch analyses like phosphides, sulfates etc, which completes the bandwidth of existing molecules.

References: Guidelines (ABNT, OCSPP, SANCO, SENASA, COFEPRIS) and EC regulations

JRF India

JRF America

JRF Europe

JRF Japan

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