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Impurity profiles of API validations and challenges for GMP inspection

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Validation of impurity profile of API always poses a challenge for the GMP auditors and many times the decisions taken are not the true reflections of the prevailing conditions of the audited company, due to possibility of multiple sources for impurities as contaminants. Specification of impurities in the API, residual solvents, validation of analytical procedures impurity profile does not provide reasonable assurance for the accuracy and precision, not only the product quality but also the process and systems of the organizations' ability to reproduce. For validation of a process to prepare a new API, the impurity profile should be comparable to or better than the profile determined during process development. Identification of process parameters that could affect the critical quality attributes of the API. Critical parameters should be determined by scientific judgment and typically should be based on knowledge derived from research, scale-up batches, or manufacturing experiences. Sometimes the inspectors reject the product based on the facts that the approved protocol failed to establish inter-laboratory acceptance criteria for impurities in the drug product; the approved method for executing the above protocol failed to establish a single integration parameter for analyzing the concentration of oligomictic peaks for the entire sequence. The firm re-integrated the sequence using different integration parameters for these peaks. This resulted in independent selection of desired peak width. Many potential toxins as impurities are not directly analyzed. The inspector's dilemma all the way increases when the site visited is biotech product manufacturing area like insulin production area (the cause for immune response isn't the insulin itself, but often impurities in the insulin) or contract manufacturing of API/formulations unit. Growth of medical devises and implants all over the world added additional areas challenges like metallic and polymer components and their cross contaminants assembled in different locations widens auditors scope more complicated. Several factors like process, environmental influences, Technology transfers, non-coordination between R&D/FP&D/ plant personals, usage of high reactive toxins like cyanides/PCA etc. in the process influence the impurity profiles of the product and some of the related key issues of impurity validations are discussed.

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