Guidance for Industry

NDAs: Impurities in Drug Substances

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
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CMC

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NDAs: Impurities in Drug Substances

This guidance recommends that applicants refer to *Q3A Impurities in New Drug Substances* (January 4, 1996, 61 FR 371) when seeking guidance on identification, qualification, and reporting of impurities in drug substances that are not considered new drug substances. Although Q3A was developed by the International Conference on Harmonisation (ICH) to provide guidance on the information that should be provided in a new drug application (NDA) in support of impurities in ***new*** drug substances that are produced by chemical syntheses, the Agency believes that the guidance provided there on identification, qualification, and reporting of impurities should also be considered when evaluating impurities in drug substances produced by chemical syntheses that are ***not*** considered new drug substances.[2]

This recommendation applies to applicants planning to submit NDAs and supplements for changes in drug substance synthesis or process. It also applies to holders of Type II drug master files (DMFs) that support such applications. Applicants should note that this recommendation would not apply to DMFs cited in an NDA or supplement if the DMF information has been deemed acceptable for that dosage form, route of administration, and daily intake prior to the publication of the final version of this guidance. Examples of NDAs affected by the recommendation include those submitted for new dosage forms of already approved drug products, or drug products containing two or more active moieties that are individually used in already approved drug products but have not previously been approved or marketed together in a drug product.

This guidance does not apply to applications for biological, biotechnological, peptide, oligonucleotide, radiopharmaceutical, fermentation and semisynthetic products derived therefrom, herbal products, or crude products of animal or plant origin, nor does it apply to ANDAs. Guidance on drug substances used for ANDA products is available in FDA's guidance on *ANDAs: Impurities in Drug Substances* (November 1999).

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[1] This guidance has been prepared by the Drug Substance Technical Committee of the Chemistry, Manufacturing, and Controls Coordinating Committee in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration. This guidance represents the Agency's current thinking on reporting impurities in drug substances for certain NDAs and DMFs. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes, regulations, or both.

[2] ICH Q3A defines a *new drug substance* (also referred to as a new molecular entity or new chemical entity) as a designated therapeutic moiety that has not been previously registered in a region or member state. The definition also states that a *new drug substance* may be a complex, a simple ester, or a salt of a previously approved drug substance.