

KNOWN OPIOID PROCESS IMPURITIES

Urine drug monitoring is widely used by clinicians treating chronic pain patients with opioid therapy medications, in part to ensure patients are abstaining from other drugs or medications.¹ Detection of a drug not prescribed to a patient can result in clinical implications. It is important to be aware that drug manufacturing process impurities can be the cause of an unexpected positive in some cases.

Medicinal opiates used today are produced via semi-synthesis of the naturally occurring opium poppy derivatives and morphine alkaloids.² As a result, the identification of a large amount of one drug and very small amount of a related drug may be due to a pharmaceutical process impurity.³

Detection of impurities which are on the order of 1% or less often occur in cases of high dose prescriptions of opiate medications.³⁻⁵ For example, hydrocodone has been detected in trace amounts in urine among patients prescribed oxycodone.⁶ Additionally, codeine has been detected in trace amounts among patients prescribed morphine.⁷ Table 1 lists common and acceptable impurity levels.

Table 1: Acceptable Opioid Impurities in Commercial Drug Substances ^{5,7-9}

FORMULATION	PHARMACEUTICAL IMPURITIES	ALLOWABLE LIMIT (%)	TYPICALLY OBSERVED (%)
Codeine	Morphine	0.15	0.01-0.1
Hydrocodone	Codeine	0.15	0-0.1
Hydromorphone	Morphine Hydrocodone	0.15 0.1	0-0.025 0-0.025
Morphine	Codeine	0.5	0.01-0.05
Oxycodone	Hydrocodone	1.0	0.02-0.12
Oxymorphone	Hydromorphone Oxycodone	0.15 0.5	0.03-0.1 0.05-0.4

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References:

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