

MRO Advisory: Critical Pre-Publication Information for MROs on Opiate Interpretations

An important poster was presented at a recent pain management meeting that showed there are known impurities found in prescription opiates that can lead to misinterpretations of opiate drug test results. In the gross manufacture of commercial opiates there are low levels of "impurities" that include other opiate drugs. The relevant impurities are shown in the table below.

Acceptable Opioid Process Impurities In Commercial Drug Substances

NB: New Methods Eliminate These Impurities for Hydrocodone and Hydromorphone; Both Varieties Are Currently Available

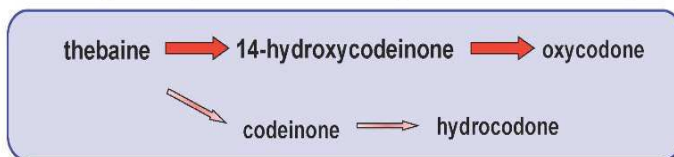
| Commercial Active Pharmaceutical Ingredient (API) | Process Impurities | Allowable Limit (%) | Typical Observed (%) |
|---|--------------------|---------------------|----------------------|
| Codeine | Morphine | 0.15 | 0.01 – 0.1 |
| Hydrocodone | Codeine | 0.15 | 0 – 0.1 |
| Hydromorphone | Morphine | 0.15 | 0 – 0.025 |
| | Hydrocodone | 0.1 | 0 – 0.025 |
| Morphine | Codeine | 0.5 | 0.01.– 0.05 |
| Oxycodone * | Hydrocodone | 1.0 | 0.02 – 0.12 |
| Oxymorphone | Hydromorphone | 0.15 | 0.03 – 0.1 |
| | Oxycodone | 0.5 | 0.05 – 0.4 |

Information from API Manufacturers' Certificates of Analysis

An important manufacturing flow chart is shown in Figure 2 which shows the side line production of low levels of hydrocodone in the manufacture of oxycodone.

It is important to understand that these impurities have no clinical significance, and are allowed by the FDA, but may show up in laboratory analysis when testing for an extended panel of opiates with low detection levels. This has recently been observed by an MRO who had a patient on oxycontin for severe back pain (vertebral cage). The patient had a urine drug test positive for significant levels of oxycodone, expected oxymorphone, and unexpected but low level of hydrocodone. A pattern consistent with Figure 2.

* Figure 2. Hydrocodone from Oxycodone Manufacturing



References

This is very new but important information that I felt should be brought to your attention as soon as possible. The topic will be covered in more detail in the next MROAlert. It is anticipated this work will be expanded and published in the near future.

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Clinical Considerations for Interpretation of Unexpected Results from Urine Drug Testing

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