Fentanyl Quantification Procedures

Summary

- Mixture analysis may provide some information about the concentration of fentanyl in a sample, but there are limitations that affect accuracy. If other methods of fentanyl quantification data are available, such as the BCCSU Fentanyl Quant Model, triangulating results can provide the most accurate estimate of fentanyl concentration.
- The fentanyl concentration of a sample does not necessarily convey accurate potency data as other more potent opioids (e.g., carfentanil) may be present and go undetected.
- There are some samples for which quantification information may be unavailable.
- There are inherent limitations to each method of fentanyl quantification.

Description

This document outlines the currently recommended methods for determining the concentration of fentanyl (and other substances) in a drug checking sample.

Progress is still being made to improve methods for determining quantification of fentanyl at point-of-care drug checking. To account for gaps in accuracy, results must forego high precision (i.e., a range of possible values must be provided to service users). If available, technicians should triangulate between different methods to better estimate and narrow the range. The following is a recommended procedure for how to technicians can use FTIR to best determine the concentration of fentanyl in a sample.

How to quantify fentanyl using FTIR

The procedure recommended here should utilize multiple methods to assess quantity of fentanyl and then triangulate those findings to assess the estimated concentration of fentanyl in a sample. However, if only one method (mixture analysis) is available, it is important to be aware of the limitations to avoid assuming an incorrect quantity. As noted in the accompanying SOP on messaging, it is always important to remember the limitations of using an FTIR to quantify results and make sure the service user understands the quantified results and what they mean.

Step 1: Mixture analysis

1. Perform spectrum subtractions to determine the components present. At this point, if fentanyl is not detected, it is not quantifiable. Although it may seem deductive that a

sample without fentanyl detectable by FTIR yet has a positive test strip result may be "below 5% fentanyl," since the detection limit of the FTIR is "about 5%", a positive test strip alone does not indicate that regular fentanyl is present at a low amount. Mixture analysis will not return a reliable 'Fentanyl HCl' value if it was not detected during subtractions. Do not perform a mixture analysis if only one compound was detected during subtractions. A result of "Uncertain match" does not count as a component. For example, if the subtraction results are Fentanyl HCl and Uncertain match, do not perform a mixture analysis to determine the *purity* of fentanyl since the uncertain result will be misattributed.

2. Perform mixture analysis if fentanyl is detectable. When performing a mixture analysis, start with the number of components that were detected during subtractions (e.g., if caffeine, mannitol, and fentanyl were detected, select just the BCCSU Library and 3 components). This step limits the chance that false results will be returned by the mixture analysis algorithm. False results take concentration away from other components since the result will always sum to 100%.
3. Restrict libraries to yield best results during mixture analysis. If all the components are contained with the BCCSU FTIR-ATR Library, using that library alone tends to provide the best mixture analysis results. Using more than one library may slow down process and/or yield duplicate results.
4. Look at the level of fentanyl in the composite (purple) spectrum of mixture analysis to help determine if fentanyl was over- or underestimated compared to the query (red) spectrum.
5. If the mixture analysis fails to return fentanyl as a result, try to use more than the determined number of components (e.g., three components plus one extra). Remember that doing this increases the chance that false results will be returned by the mixture analysis algorithm. False matches are those which are returned by mixture analysis but were not detected during subtractions.
6. If multiple analogues are returned in mixture analysis results, they are likely false matches and cannot be used to calculated fentanyl concentration. For example, if fentanyl HCl is returned at 12% and acetylfentanyl HCL at 22%, do not report 34% fentanyl. Fentanyl analogues are not interchangeable when calculating percentages. In this example, acetylfentanyl is almost certainly a false match. It is up to the technician to determine if the mixture analysis results returned are useful or must be discarded since the algorithm failed to produce useful results.

Step 2: BCCSU Fentanyl Quant Model (if available)

If the OPUS software has been augmented with the QUANT 2 add-on from Bruker, then proceed with running a QUANT 2 analysis with the BCCSU Fentanyl Quant Model.

1. After completing a mixture analysis, run the model to return a percent estimation of fentanyl. Take note of the difference between the mixture analysis result and the model estimate. Is the model estimate significantly lower? Perhaps mixture analysis overestimated.

2. Remember that even if the two methods (mixture analysis and Fentanyl Quant Model) align very well on a percent estimation, it does not necessarily accurately represent the sample as the mixture may have been heterogeneous when sampled on the spectrometer (a further example of the chocolate chip cookie effect or hot/cold spots of uneven mixtures).

Step 3: Assess fentanyl content in light of test strip result

1. Conduct fentanyl test strip as normal.
2. When the test strip results are positive but the FTIR was fentanyl-negative or inconclusive, it does not immediately suggest that fentanyl is present below 5%. There could always be a separate analogue (e.g., carfentanil) present that is tripping the strip.
    a. If fentanyl was not detected by FTIR, there are multiple reasons these results could happen:
        i. There is no fentanyl or analogue present. In this case there could be no opioid present at all (i.e., bunk) or another opioid (e.g., heroin, a nitazene).
        ii. Carfentanil is the only opioid present but there is not enough to trigger a positive strip. Refer to the BCCSU Drug Checking Webinar Series Fentanyl Test Strip Module (#2) for further details.
3. When the test strip is negative:
    a. If the FTIR was fentanyl-positive, these are conflicting results. First, repeat the fentanyl test strip analysis with a new (second) strip. If the negative result persists, then confirm that fentanyl was truly detected and that the fentanyl signal was not misattributed to something else (carbon dioxide is a common mistake). Seek assistance if conflicting results persist.

See Table 1 for a summary.

Step 4: Assess in light of knowledge of local supply

1. Consider what is known about the local supply. Are the results in line with this knowledge or do they seem strange?
2. Did the service user report that the sample was particularly strong, knocked them out, or caused an overdose? Do these results support the possibility of there being carfentanil or benzodiazepines?

Complete Analysis and formulate quantified result

Once the analysis is complete, review the available sources of information and determine how to share these findings with the service user. It is recommended that technicians provide quantified information in a range and clearly indicate that the result is an estimate. Until more precise methods are available, it is recommended to provide results within a 5% range (or more if required). See “SOP for Quantification and Messaging” for more information.

Test results	Interpretation	Other contributing factors	Quantification information
FTS pos, FTIR pos	Fentanyl is present, confidence is very high.	Does not rule out presence of other opioids such as carfentanil, which may co-occur with fentanyl.	Can attempt quantification using FTIR methods.
FTS neg, FTIR neg	Fentanyl is not present, confidence is high.	Does not rule out presence of other opioids such as carfentanil which may not trip the FTS, or nitazenes which don't react with FTS.	No quantification is available if no fentanyl is detected.
FTS pos, FTIR neg	Fentanyl is present, confidence is moderate.	Other opioids may be co-occurring with fentanyl but in amounts too small to be picked up by FTIR (below detection limit). Fentanyl is present likely below the detection limit of the FTIR but saying "present below 5%" is vague and may not be true.	Cannot quantify using FTIR methods.
FTS neg, FTIR pos	Unlikely that fentanyl is present. Re-do FTS and review FTIR.	Conflicting results. Test strip should be repeated. If conflicting results persist, review FTIR spectrum and ensure signal was not misattributed to something else. If conflicting results persist after thorough review (very rare if at all possible), see assistance from another technician. This finding is inconclusive for fentanyl.	Cannot quantify using FTIR methods.

Table 1. Summary of fentanyl detection results and their interpretation.