A. PURPOSE:

The quality or the reagents and standards used in the Controlled Substance section must meet the requirements of the procedures they are used for. Reagents and standards must be maintained in a manner as to protect them from contamination and to assure that they work are expected.

B. RESPONSIBILITY:

Analysts assigned to the Controlled Substance Section.

C. SAFETY:

Proper PPE must be used at all times when working with reagents and standards.

1. Chemical hazards: when handling chemicals analysts must observe the safety hazard ratings of the substance
2. Drugs: many of the drug standards can be absorbed through the skin; these include but are not limited to Fentanyl, PCP, LSD and DMT analysts must take caution and were at a minimum gloves and a lab coat when working with drug standards.

D. PROCEDURE:

1. REAGENTS:

a. All reagents must be labeled with a minimum of:

- Reagent name
- Date made (this can act as the lot number with the prepares initials)
- Expiration date as applicable
- Preparer's initials
- Safety Diamond with safety ratings

b. All reagents must be validated as appropriate for use with the method prior to use in reporting case results, the validation process is generally to:

- Use the reagent in the method with appropriate control materials (positive and negative).
- Ensure that the reagent provided acceptable performance with both the positive and negative controls.
  - Acceptable performance: assure both the negative and positive controls have no unexplained peaks by GC/MS. Note that it is rare that a reagent is used for any other procedure than an

extraction were the final product will be analyzed by GC/MS. If this does occur the analyst must demonstrate that the reagent is appropriate in that analytical method.

- A Reagent Validation sticker (below) is completed and added to the analytical data printout (usually the GC/MS TIC), this paperwork is filed in the "Reagent Validation" log book.
    1. Validation data is reviewed by another analyst, section supervisor, Quality Manager or Director prior to acceptance.
    2. When completed this paperwork is filed in the "Reagent Validation" book maintained in the CS Laboratory.
- Accepted reagents are annotated by the addition of a green "validation sticker" to the label. The green sticker will have the method validated for, the date validated and the initials of the person validating the reagent. (example: plant extr. 10/10/10 jmr)
- If appropriate, the stock reagent bottle(s) is appropriately annotated with the new validation information (green validation sticker). When the solution validated is a straight solvent, a validation sticker can be put on all solvent bottles with the same lot number.
- Once validated the reagent is good for one year. After the expiration date the solution need not be destroyed only re-validated for suitability.
    1. At any time within the year of validation if an analysts finds a problem with the reagent (such as significant contamination) the standard will be thrown out.

Solution Name:
_____
Lot number:

Procedure validated for:
Acceptable for use for procedure: **YES** / **NO**
Date Validated by GC/MS:
Analysts Initials:
Reviewed by/Accepted for Use by:
Date:
File paperwork in reagent or solvent log book as appropriate

2. STANDARDS:

I. Standards for Non-Controlled Substances:

1. Standards for non-controlled substances are maintained in the controlled substance laboratory.
2. Such Standards will be analyzed by GC/MS each time of use.
    i. The peak of interest must be present with a good visual spectral match to a published library.
    ii. Other peaks if present must be explainable. An example of this is may be a tablet obtained as a standard will likely have fatty acids present.
    iii. The TIC and Spectra will be printed and reviewed by the analyst. The spectra must match a published library reference. These include but are not limited to the WILEY, SWGDRUG, and PMW libraries and references published in journals such are Micrograms or Journal of Analytical Toxicology, or other reference books such as Clarks or the IDDA.
    iv. The analyst will annotate acceptability of the standard on the GC/MS data sheet, and the TIC with spectra and reference match will be placed in the case file(s). If the standard is validated through FTIR or other method the acceptability will be noted on the data sheet from that instrument.
        1. Annotation of acceptability can be achieved through simply writing ok or acceptable or similar wording on the GC/MS data sheet.

II. Standards for Controlled Substances:

1. Standards for Controlled Substances used as comparison references generally come in two forms “pure”, usually powder, or liquid DEA exempt solutions. In rare occasions manufactured tablets will be used as comparison standards these are generally obtained from drug control.

2. “Pure” Standards: these are maintained within the Controlled Substance safe and locked drug refrigerator and require two people to access them. (See SOP CS-11)

i. When using a Controlled Standard if there is a significant spill, have a second person witness the spill. Gather what can be gathered and weigh the amount spilled. Note on the "Controlled Substance Activity/Inventory Record" accidental spill and the number of milligrams lost both the analyst and witness initial the record. The spilled powder should be destroyed with case material drug waste.

3. DEA exempt standards are maintained in a refrigerator within the section and can be obtained without a witness.

i. DEA exempt standards come with a validation certificate for each lot; this is to be filed in the Standard validation book with in the section. These do not require additional validation.

ii. Once opened, the contents will be transferred to a GC/MS vial or other similar storage vial. This will be labeled with the name and concentration of the compound, date opened, and the initials of the person that opened the vial.

III. **Quantitative Standards**:

1. DEA exempt certified reference materials can be used as quantitative standards using the reference value provided by the manufacturer.

i. When these are used an only a single lot is available the analyst will make the controls and a second analyst will prepare the calibrator.

ii. The lot number of the certified reference material will be noted in the case notes (either as part of the batch information or on the case note sheet), this will allow for traceability of the standard.

iii. The Certificate of Analysis is maintained within the CS section.

2. Standards used for quantitative purposes that are not certified reference standards (DEA exempt) are prepared using the pure standards. Note that any controlled substance standard (CI or CII) made in a concentration of greater than 1 mg/ml must have a disposition record. (See CS-11:2).

i. Note that most "pure" standards will come with documentation from the manufacturer; this will be stored with the drug disposition records within the section.

ii. The lot number of the reference material will be noted in the case notes (either as part of the batch information or on the case note sheet), this will allow for traceability of the standard.

iii. Once prepared in the desired concentration the standard must be validated by UV to determine its true concentration when ever possible. (See SOP CS-9 UV.)

iv. If UV data is not available the value used will be the concentration prepared, analysts must be very careful in these cases to perform accurate quantitative transfers.

1. In these cases a second analyst will make up a control using a different lot of standard when available.

v. Note in a few cases the standard will need to be made from pharmaceutical preparations; in these cases the standard concentration must be validated by UV. If the substances UV data can not be found the section supervisor or Director must be consulted.

vi. Once validated by UV the solution will be given a green validation sticker with the concentration, standard name, initials, and date annotated. In general, UV validations are validate from one year from the date validated.

3. Non-Controlled Substances: The standards maintained for many of the non-controlled substances are not "pure" standards. If a quantitative standard of a non-controlled substance is required the analysts must assure the starting standard is pure.

i. UV in conjunction with GC/MS can be used to determine the "purity" of these standards. (See SOP CS-8 and SOP CS-6)

ii. If UV data is not available the analyst must consult the section supervisor or Laboratory Director as to the best standard to use.

IV. **Qualitative Standards**:

1. DEA exempt standards can be used directly.

i. DEA exempt standards come with a validation certificate for each lot; this is to be filed in the Standard validation book with in the section.

ii. Each time of use the GC/MS or other instrumental data sheet will be printed. The TIC and Spectra will be printed and reviewed by the analyst. The spectra must match a published library reference. These include but are not limited to the WILEY, SWGDRUG, and PMW libraries and references published in journals such are Micrograms or Journal of Analytical Toxicology, or other reference books such as Clarks or the IDDA.

1. For “new” compounds where published references are not available the certificate of analysis data sheet can be used to compare the spectra obtained by the laboratory to that of the provider of the compound. In these cases a copy of the COA will be filed in the case jacket.

iii. The analyst will annotate acceptability of the standard on the GC/MS data sheet, and the TIC with spectra and reference match will be placed in the case file(s). If the standard is validated through FTIR or other method the acceptability will be noted on the data sheet from that instrument.

1. Annotation of acceptability can be achieved through simply writing ok or acceptable or similar wording on the GC/MS data sheet.

iv. Once opened the standard will be transferred to a GC/MS or other similar sealable vial and labeled with the Name of the compound, date opened, lot number and initials of the person opening the vial.

1. An expiration date are not assigned to qualitative standards since they are evaluated at each use.
2. Analysts noting a significant amount of extraneous peaks in the TIC will evaluate the fitness of the standard. In general if extraneous peaks are present at approximately half the peak height of the target compound the standard will be discarded.

2. Pure standards will be run by GC/MS or other instrument as appropriate and evaluated upon each use.

For GC/MS:

i. The peak of interest must be present with a good visual spectral match to a published library.

ii. Other peaks if present must be explainable. An example of this is may be 6-MAM in a heroin standard.

iii. The TIC and Spectra will be printed and reviewed by the analyst.

iv. Each time of use the GC/MS instrumental data sheet will be printed. The TIC and Spectra will be printed and reviewed by the analyst. The spectra must match a published library reference. These include but are not limited to the WILEY, SWGDRUG, and PMW libraries and references published in journals such are Micrograms or Journal of Analytical Toxicology, or other reference books such as Clarks or the IDDA.

1. For "new" compounds where published references are not available the certificate of analysis data sheet can be used to compare the spectra obtained by the laboratory to that of the provider of the compound. In these cases a copy of the COA will be filed in the case jacket.

v. The analyst will annotate acceptability of the standard on the GC/MS data sheet, and the TIC with spectra and reference match will be placed in the case file(s). If the standard is validated through FTIR or other method the acceptability will be noted on the data sheet from that instrument.

1. Annotation of acceptability can be achieved through simply writing ok or acceptable or similar wording on the GC/MS data sheet.

vi. Standards (whether DEA exempt or "pure") shown to be acceptable as qualitative standards by GC/MS may be used in different methods without validation on that instrument (example: caffeine is used as an internal standard for LC, it need not be validated by LC first if it is validated by GC/MS).

V. **Traceability of Standards**:

1. When working with standards either "pure" or DEA exempt standards the analyst must maintain the traceability of the standard.
2. Most standards used are for GC/MS lot number will be recorded on the GC/MS paperwork, which is stored in the case file, so that the standard can be traceable to its source. For non-controlled standards if a lot number is not available the standard ID number will be used.

E. **REFERENCES**:

1. Clark's Isolation and Identification of Drugs in Pharmaceuticals, Body Fluids, and Post-Mortem Materials, The Pharmaceutical Society of Great Britain