5.1.3 The Validation Protocol must document the validation parameters being evaluated, acceptance criteria for each parameter and if known, Test method numbers/SOPs.

5.1.4 The Validation Report must document what was accomplished during protocol execution and provide a summary of results. This report must be approved by the QA Manager or Designee and a representative from the Site Quality Authority, independent of the Laboratory Manager where the validation work was conducted.

5.1.5 For legacy methods, the acceptability of existing data is determined on a case by case basis. Supplementary data may be required. There must be a documented justification for appropriate sections not being performed. Legacy Methods may require validation according to local regulatory requirements. A Concurrent Validation approach may be used to support the analytical method validation.

5.1.6 The following factors must be considered when selecting an analytical method for use in equipment cleaning validation studies and for determining acceptable criteria:

- Type of residue being measured (e.g. organic, inorganic)
- Sampling method (e.g. swab or rinsate)
- RAL (Residue Acceptance Limit) in the analytical sample.

5.1.7 The validation of a cleaning validation analytical method for product residue must be based on the RAL calculated for that material as defined in cleaning validation plan.

5.1.8 The method may be considered valid for any RAL within the validated RAL recovery range. If the RAL is outside this recovery range the method must be re-validated with respect to the affected parameters / characteristics (refer to **Section 5.2 – 5.4**).

5.1.9 **Sections 5.2 – 5.6**, must be considered for each validation. A description of how these parameters will be performed such as experimental design, sample concentrations, swabbing materials should be outlined in the protocol. Parameter consideration may be dependant on the type of assay/ method being validated or its intended use. Where appropriate, provide a rationale as to why a parameter may not be included in the validation.

5.2 Cleaning Validation Analytical Method

5.2.1 System Suitability (Instrument Precision)

System suitability limits should be established to demonstrate the instrument is working satisfactorily. A solution at LOQ (or lower if required) should be analysed to ensure the instrument is able to detect at this level. Blank samples should be prepared using same batch of swab/ rinsate as the samples.

Where applicable, precision should be validated at the 100% RAL level, as this is the most critical concentration at which the sample recovery is validated. Precision at recovery concentrations around 100% of the RAL determine whether the sample passes / fails where as precision at sample recoveries less than or greater than 100% levels give information on the extent of the pass / fail.

5.2.2 Method Precision

three replicate samples at each of the three concentrations. The accuracy and precision of sample recovery is performed spiking the primary surface with known amounts of the product of interest and allowing it to dry for a predetermined minimum period as stated in the protocol.

The recovery sample concentrations should be prepared at, above and below the expected residue limit. Ensure the recovery range accommodates the critical limits e.g. a higher level 150% of the expected residue level and a suitable low level, LOQ or 50% of the expected residue level and the expected residue level are spiked. The spike is recovered as per the relevant swabbing procedures. In addition, a blank solution is dried onto the surface. Three successful runs are required.

5.2.13 **Sample Recovery Accuracy and Precision Acceptance Criteria**
Typical acceptance criteria are that the recovery from the surface is not less than 50% and that the RSD of the swab sample preparation at 100% of the cleaning validation acceptance limit is not more than 12%. The acceptance criteria may change depending on the nature of the product.

If the recovery is greater than or equal to 50% but less than 90% a correction factor should be used with all samples recovered using this method (swab / rinse). The correction factor is obtained by dividing the percentage recovery into 100%. The recoveries are then multiplied by the correction factor.

5.2.14 **Rinse Sampling Solutions and Solubility**
Composition of solution and solvent must be considered. Solvent selection for rinsate should be based on product solubility in the rinsate solvent.
Solvent handling practices, safety and environmental requirements must be considered when selecting the rinsate solvent.

5.2.15 **Recovery at More Than One Acceptance Limit**
In some instances, validation of cleaning cycles may be performed on more than one piece of equipment and therefore there may be more than one RAL or expected residue limit. Validation of recovery may be performed on a minimum of three different concentration levels that covers of all the expected residue limits. However, if the expected residue limits are of similar concentration, recovery validation may be combined. In this case, the lowest, highest (or equivalent figures) levels are used to validate recovery below and above the expected residue acceptance limits. The accuracy and precision of each expected residue limit is validated.

5.2.16 **Stability**
Stability of the standard and the sample (swab and rinse solutions) must be determined or referenced, if previously performed. Standard and swab solutions should be analysed initially at time 0 and days as is appropriate. A minimum twenty four hour study must be completed for all validations.
A typical acceptance criteria is 12%. This should be carried out in duplicate.

5.3 **Sampling Method**

5.3.1 The sampling technique (e.g., swab / rinse) must address the following relevant factors:

- Swab type (including wipes) and size

