

Title: Cleaning Validation - Calculations of Residue Limits for Drug Product Therapeutic and Non-therapeutic Materials for Equipment Cleaning					
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**Cleaning Validation - Calculations of Residue Limits for Drug Product Therapeutic and Non-therapeutic Materials for Equipment Cleaning**

**Introduction**

This guideline provides equations and examples for calculating the Maximum Allowable Residue (MAR), and Residue Acceptability Limits (RAL) for Drug Products and Non-Therapeutics.

Examples are provided for determining the acceptable equipment cleaning residue limits for therapeutic drug products (MAR<sub>T</sub> and RAL<sub>T</sub>) and for non-therapeutic ingredients (MAR<sub>N</sub> and RAL<sub>N</sub>). For the therapeutic drug products both single product combination (Product A to B) and multiple products combination examples are given.

**Recommendations & Rationale**

The attached Appendices give equations and example calculations for therapeutic drug product cleaning limits for a solid oral dosage form (tablet), creams/ointment and ophthalmic product. In Case-1 therapeutic example it is included the calculation of Maximum Allowable Residue (MAR) limits using two formulas; dose MAR<sub>T</sub> and toxicity MAR. It also includes an example for determining the worst case limit for shared equipment using multiple products. Example for residue limits calculation of CIP® 100 detergent, a non-therapeutic ingredient is also given.

**Background Information and Equations:**

The Maximum Allowable Residue for Therapeutics (MAR<sub>T</sub>) and Residue Acceptability Limit for Therapeutic Dose (RAL<sub>T</sub>) should be calculated based on each product that is to be processed in a specific equipment train and determined by the formulas and equations provided in Appendix A. A common default MAR<sub>T</sub> is not more than ten (10) ppm.

The calculated MAR<sub>T</sub> and the default MAR<sub>T</sub> should be compared and the lower of the two (2) used. A Toxicity limit may also be calculated and compared to the default MAR<sub>T</sub> and the NMT 10 ppm, and the lower of the three limits chosen.

The Maximum Allowable Residue for Non-Therapeutics (MAR<sub>N</sub>) and Residue Acceptability Limit for Non-Therapeutic Materials (RAL<sub>N</sub>), such as materials used for equipment cleaning, is a function of toxicity, and should be determined by use of the formulas and equations provided in Appendix B. A default MAR<sub>N</sub> is not more than one hundred (100) ppm. The calculated MAR<sub>N</sub> and the default MAR<sub>N</sub> should be compared and the lower of the two (2) used. Residue