

Pennsylvania Generic Substitution Law

This information is only to provide guidance on the Generic Substitution Law and Narrow Therapeutic Index (NTI) drugs. For official interpretation it is highly recommended practitioners review the law themselves or check with an attorney. You may obtain copies of the Generic Substitution Law at www.health.state.pa.us/ddc .

The law does not prohibit the dispensing of any approved drug. The automatic substitution by a pharmacist of a generic for a brand name is prohibited when a physician prescribes a brand name product and the generic drug is determined to be an NTI drug, non-A rated, or the physician writes brand necessary.

The Pennsylvania Generic Substitution Law states that an NTI drug is not substitutable regardless of bioequivalency rating in the Federal Orange Book or safety/efficacy data. Therefore, if a drug is determined to be an NTI drug it is not substitutable in Pennsylvania.

A current listing of NTI drugs is neither published/provided by the Food and Drug Administration (FDA) nor the Commonwealth of Pennsylvania.

Practitioners should utilize a variety of resources as well as their professional training to determine whether a particular drug is an NTI drug. Some examples of resources available in addition to their professional training are:

1. A 1988 listing of NTI drugs published by the FDA. (See below)
2. Legal Definition of NTI in the Code of Federal Register Section 320.33
According to 21 CFR 320.33©, narrow therapeutic ratio is defined as follows: a. There is less than a 2-fold difference in median lethal dose (LD50) and median effective dose (ED50) values, or b. There is less than a 2-fold difference in the minimum toxic concentrations and minimum effective concentrations in the blood, and c. Safe and effective use of the drug products require careful titration and patient monitoring.
3. FDA approved manufacturer package insert of drug or contact the manufacturer directly for information. NTI information is usually listed under “precautions.”
4. Established Drug Reference

For generic substitutions not involving NTI drugs, practitioners should refer to the Federal Orange Book for bioequivalency ratings to determine if a drug is A-rated. The Federal Orange Book can be accessed free online at www.fda.gov or specifically at www.fda.gov/cder/ob/default.htm .

For generic substitutions not involving NTI drugs but involving biosimilars, practitioners should refer the Federal Purple Book, [Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations](#)

This is a sample list of NTI drugs published by the FDA in 1988.

NOTE: This was only sample list of drugs published by the FDA in 1988. Please still Refer to Official Definition or Contact Specific Drug Manufacturer for Accurate Determination if a drug has a Narrow Therapeutic Index or Range.

Aminophylline	Metaproterenol
Carbamazepine	Minoxidil
Clindamycin	Oxytriphylline
Clonidine	Phenytoin
Digoxin*	Prazosin
Disopyramide	Primidone
Dyphylline	Procainamide
Guanethidine	Quinidine
Isoetharine Mesylate	Theophylline
Isoproterenol	Valproic Acid
Levoxyine	Valproate Sodium
Lithium Carbonate	Warfarin

*Also Pre 1938 Drug