



## Designer Benzodiazepines Panel

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### Introduction

Benzodiazepines are among the pharmaceutical industry's top-selling prescription drugs. Below is a brief history and timeline:

- 1930s: A barbiturate class of compounds were developed by German Scientists as an OTC daytime sedative and sleep aid; however, ongoing use of barbiturates also led to tolerance, dependence, and carried a high risk of overdose.
- 1951: Congress passed a law requiring a doctor's approval for the purchase of barbiturates.
- 1955: Hoffmann-La Roche synthesized the first benzodiazepine, chlordiazepoxide (Librium), which became available in 1960.
- 1958: Hoffmann-La Roche patented diazepam (Valium).
- 1975: Hoffmann-La Roche patented clonazepam.
- 1977: Lorazepam (Ativan) became available by Wyeth.

Numerous benzodiazepine compounds have since followed with many prescribed in the US for treatment. Although benzodiazepines are safer than barbiturates, dependence and addiction are still problematic. Use of benzodiazepines must be monitored given the severe side effects, including possible death, if taken with narcotics and alcohol.

### Designer Benzodiazepine Group

Even though there are many FDA approved benzodiazepines available in the US, there are some compounds called "designer benzodiazepines" which are extremely potent and have not been approved for sale in any country. These compounds are highly addictive or too powerful for routine use, with some that are 10x as potent as Valium. When used in combination with narcotics, muscle



relaxants, or other CNS depressants (such as alcohol) sedation is further deepened and can cause death. The extreme effects of these designer benzodiazepines and their impact on performance is particularly concerning in a workplace setting or for those driving a vehicle. Because these compounds are not part of a benzodiazepine panel, these drugs escape detection.

Many of these designer benzodiazepines are closely related to an FDA approved version. The designer versions were typically kept as research drugs due to the potency and concern over safety. Illicit markets often sell non-FDA-approved benzodiazepines on the dark web under the guise of FDA-approved benzodiazepines names. For example, flubromazolam and etizolam have been detected in fake Xanax tablets instead of alprazolam. The spelling of some of these compounds closely resembles existing benzodiazepines and can be easily confused. The nomenclature distinguishing feature is often "lam" vs "pam".

A recent article (MMWR, August 27, 2021, Vol. 70, No. 34) reported the presence of illicit benzodiazepines and the complications created when consumed with narcotics. Per the study, nearly 15% of ER/fatalities evaluated were positive for at least one illicit benzodiazepine agent, including clonazepam, etizolam, and flubromazolam.

## Testing

CRL has a standard 16 -panel benzodiazepines offering presented in Table 1. These include drugs commonly prescribed in the United States to treat anxiety and alcohol withdrawal, as well as those used as muscle relaxants and for seizure control. Other drugs in the panel are available internationally, such as bromazepam and flunitrazepam, which is associated with date rape. This panel has been available for years and clients choose to include only the commonly prescribed benzodiazepines or the full panel for a more comprehensive test as part of drug treatment program.

More recently CRL has validated an additional 7 designer benzodiazepine drugs (highlighted in Table 1) to expand the standard panel in effort to detect illicit benzodiazepines. Workplace drug testing panels for benzodiazepines have a defined panel of targeted compounds and are designed to report only the employer targeted compounds. If the panel does not specifically include these designer compounds they will not be reported. Please review your panel to maintain safety in the workplace, as these illicit benzodiazepines are not prescribed by a physician for medical treatment.



**Table 1:**

Existing Panel		New Designer Benzodiazepines
Alprazolam	Lorazepam	Bromazolam
Bromazepam	Lormetazepam	Clobazam
Clonazepam	Midazolam	Clonazolam
Diazepam	Nitrazepam	Etizolam
Estazolam	Nordiazepam	Flualprazolam
Flunitrazepam	Oxazepam	Flubromazolam
Flurazepam	Temazepam	Phenazepam
Halazepam	Triazolam	

For further information regarding the inclusion of these designer benzodiazepines, please contact your CRL sales representative.