

Basic Principles

The Staccato[®] system comprises the rapid vaporization of a drug to form a small particle aerosol optimal for systemic delivery through inhalation. These aerosols are systemically absorbed very rapidly, with peak plasma blood levels obtained in the first few minutes after administration. Thus, the *Staccato* system enables rapid onset of action for many drugs.

Thermal Aerosols

The key to our proprietary technology is vaporization of drug without thermal degradation, which is achieved by rapidly heating a thin film of the drug. In less than half a second, the drug is heated to a temperature sufficient to convert the solid drug film into a vapor. Because the duration of drug heating is so brief, thermal decomposition is minimal. After vaporization, the drug cools rapidly in air, condensing into pure drug aerosol particles of near ambient temperature. The *Staccato* system consistently creates aerosol particles averaging one to three microns in size, which is the proper size for deep lung inhalation. The *Staccato* system also produces a consistent high emitted dose, regardless of the patient's breathing pattern.

Device Elements

The *Staccato* device consists of three core components: a heating substrate, a thin film of unformulated drug coated on the substrate, and an airway through which the patient inhales. The left panel below shows these core components before patient inhalation. The right panel shows the device components during patient inspiration: the substrate is heated to peak temperature in

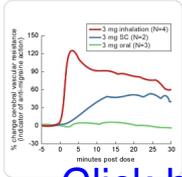


Ease of Use

The *Staccato* system is breath-actuated and a patient simply inhales to administer the drug dose. A special valve in the inhaler airway controls airflow over the vaporizing drug to achieve appropriate aerosol particle size. The aerosol produced with the *Staccato* system is relatively insensitive to patient inhalation rates. To use these inhalers, a patient simply removes an inhaler from its packaging, places the device to his or her lips, and takes a deep breath. Unlike many other inhalation technologies, the patient does not need to learn a special breathing pattern. In addition, the *Staccato* device is small and easily portable.

Pharmacology and Rapid Onset

The aerosol produced with the *Staccato* system is designed to be absorbed rapidly through the deep lung, with a speed of therapeutic onset comparable to IV administration, generally achieving peak plasma levels of drug in two to five minutes, which is much faster than oral tablet delivery. *In vivo* pharmacokinetic studies in an animal model conducted with a commercially available migraine drug show that the *Staccato* system results in more rapid absorption than subcutaneous injection or oral administration. Pharmacodynamic studies with the same migraine drug demonstrate an onset of action of less than one minute as shown in the graph below.



[Click here to see movie of the Staccato [®] aerosolization](#)

Co

nsistent Dose and Particle Size

The *Staccato* system uses rapid heating of the drug film to create consistent and appropriate sizes for deep lung inhalation, rather than mechanics or preformed drug particles, to create drug aerosols. The *Staccato* system produces a consistent high emitted dose regardless of the patient's breathing pattern.

Broad Applicability

Approximately 200 drug compounds have exhibited initial vaporization feasibility with our *Staccato* system. The *Staccato* system can deliver both water soluble and water insoluble compounds while eliminating the need for excipients and additives such as detergents, stabilizers and solvents, enabling the delivery of unformulated drug.

Design Flexibility

The *Staccato* device can incorporate lockout and multiple dose features, potentially enhancing safety, convenience of patient titration and a variety of administration regimens.

We are currently developing two versions of our *Staccat* o device

- **Disposable Single Dose.** The single dose version consists of a metal substrate that is chemically heated through a battery initiated reaction of energetic materials. We have designed the single dose version to meet the specific requirements of our AZ-001, AZ-002, AZ-004 and AZ-007 product candidates. In the current design, the heat package can be coated with up to 10 milligrams of drug compound. The device is portable and easy to carry, with dimensions of approximately three inches in length, two inches in width, and three quarters of an inch in thickness. The device weighs approximately one ounce. A diagram of the single dose device is shown below:



- **Multiple Dose.** The *Staccato* system multiple dose version consists of a reusable controller and a disposable dose cartridge. We have designed the multiple dose technology to meet the specific needs of our AZ-003 product candidate. The dose cartridge contains up to 25 separate metal substrates, coated with the drug, each of which rapidly heats upon application of electric current from the controller. In the current design, up to 100 micrograms of drug compound can be coated on each metal substrate. The device is portable and easy to carry, with dimensions of approximately five inches in length, two and one-half inches in width and one inch in thickness. The controller weighs approximately four ounces and the dose cartridge weighs approximately one ounce.

[Back to top](#)

