Flexineb™

SIMPLE & INTEGRATED:
Easy set-up and operation with no hoses, cords or awkward valves.

RAPID
For example, 10 millilitres of saline is aerosolized in less than 10 minutes.

SILENT
Unlike most nebulizers.

ADAPTABLE
For use with metered dose inhalers (MDIs).

SAVINGS
On drug costs and administration time.

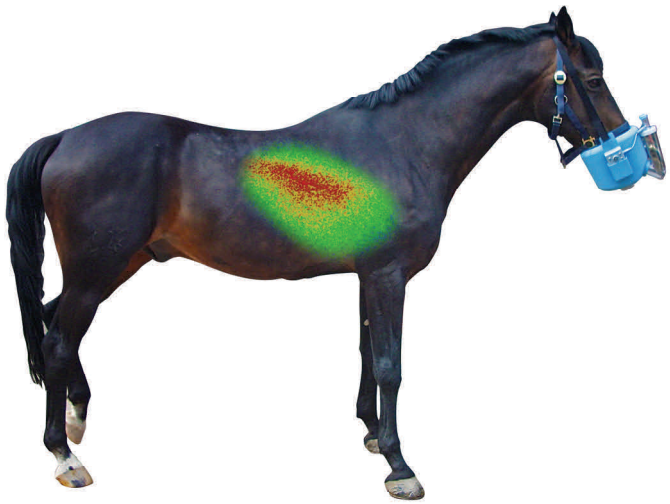
To get an aerosolized drug into the lower airways, where it is required to treat the associated respiratory problems, the size of the particles being produced is very important. These particles must be 5 microns or less in diameter to get into the lower airways. To put the size of these particles into context, a human hair is between 50 and 150 microns in diameter. As you see below, on average the total of particles produced by Flexineb of a diameter of 5 microns or less is approximately 68%. This means, on average, when using the Flexineb system, 68% of the drug or liquid will be aerosolized directly into the lower airways. This is very competitive compared to other portable nebulizers.

Test Solution	*Dv50 (µm)	% < 5µm
0.9% Saline	4.303	66
0.9% Saline	4.114	67
Liposomal Antibiotic	3.105	71

* Dv50 (µm) means 50% of droplets are below this value and 50% are above this value.

Nortev droplet size testing is carried out by independent laboratory @ Melbourn Scientific UK.

To give a further example of how the aerosol from a Flexineb deposits in the lungs, Nortev carried out a Nuclear Imagery study at Hagyard Equine Medical Institute in Lexington, Kentucky under the supervision of Dr. Nathan Slovis. Flexineb was used to nebulize radiopharmaceuticals, which were then inhaled directly into the lungs. Using nuclear imagery the dispersal of these radiopharmaceuticals via nebulization can clearly be seen to penetrate deep into the lung field.



nortev

*The nuclear image picture above is of the right lung during a study on October 25, 2013 at the Hagyard Equine Medical Institute in Lexington, Kentucky.

HAGYARD
Equine Medical Institute

How the technology works:

The Flexineb aerosol generator technology converts liquids into a fine aerosol for inhalation into the lungs of the horse.

The **medication cup** incorporates a wafer thin metallic membrane with micro holes *(Figure 1)*. It is a high quality alloy but it can be damaged if contacted by hard or sharp instruments.

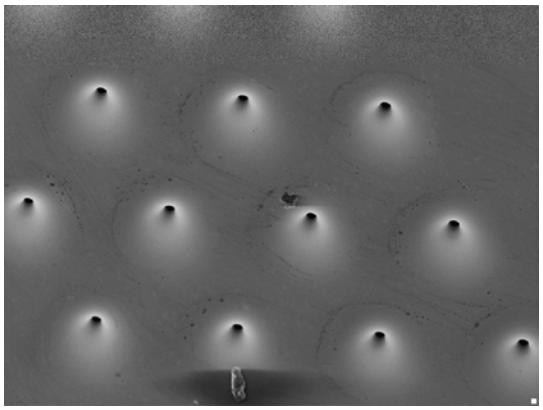


Figure 1: Magnified picture of membrane showing micro holes

It is the vibration of this membrane that acts like a micro pump and converts the liquid drug into a fine aerosol.

The performance and life of the **medication cup** is highly dependent on the type of drug or liquid used as the technology has to pump the drug or liquid through these tiny holes to form the aerosol. Its life is also very dependent on how well it is maintained between uses.

If a liquid with a high viscosity (*e.g. like honey*) is placed in the medication cup it may not nebulise. Dilution may help if the liquid is water based. If a liquid is oil based dilution will not help.

Another factor that will affect performance is if the drug or liquid used is a ***Solution*** or ***Suspension***.

Solution type drugs have their active agent completely dissolved in the liquid *(like sugar in coffee)*. An example of a solution type drug is the bronchodilator Atrovent®.

Suspension type drugs have their active agent suspended in the liquid in the form of tiny solid particles *(like sand in water)*. An example of a suspension type drug is the corticosteroid Flixotide™.

Reasons why the medication cup may not nebulise:

Given the nature of the technology as explained it is reasonable to understand that if a drug or substance has a high viscosity or has big solid particles suspended then they may not nebulise and may clog the tiny holes in the membrane.

Suspensions are more erosive because they have tiny solid particles jetting through the holes in the membrane therefore the life of the medication cup may be reduced if suspensions are used. If the drug tends to leak through the membrane it is an indication that the holes have eroded and a replacement is required.

Natural therapies that are not finely filtered may also clog the holes in the membrane.

Drugs that have been successfully nebulised using the Flexineb are listed on the Nortev Drug Table.

In some cases it is advisable to dilute the drug with saline to improve nebulisation performance.

If water or moisture gets into the internals of the medication cup mechanism it will stop working because a short circuit will occur.

Maintenance:

To maintain the performance and life of the medication cup it is very important to check if the drug or liquid you intend to use is suitable for the Flexineb technology.

If it is not listed on the Nortev published Drug Table please contact Nortev before putting it in the medication cup.

If the drug is deemed suitable and nebulises successfully it is very important to rinse the medication cup with clean warm water and a few drops of washing up liquid after each use. Alternatively nebulise a few drops of **distilled vinegar** to break down any oil based residue on the membrane.

If the holes are clogged with solid particles it will prove difficult to clean without damaging the membrane and the medication cup will require replacement.

Do not immerse the medication cup in water when cleaning.

It is not advisable to use any chemicals in the medication cup as they may corrode the metallic membrane or remain as a residue in the drug path and may pose a hazard to the horse and caregiver.

Flexineb and Nuclear Scintigraphy

Nuclear scintigraphy is a helpful diagnostic modality generally used, in horses, to look at radioisotope uptake in bone. A radiopharmaceutical is injected (or in this case, inhaled) into the horse and the radiation emitted by the animal is captured by external detectors (gamma camera) to create the image. The radiopharmaceutical is attached to a drug that travels to a specific area of the body. When you assess the image from the scan, you want to look at the distribution as well as the concentration of the "uptake" of the radiopharmaceutical. The amount and distribution of the uptake gives you an indication of how that specific organ is functioning. In the case with the Flexineb, it was important to demonstrate how well the nebuliser can deliver medication to the lower airway.

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Medication delivery is very important, of course, because many airway diseases involve the lower airway and cannot be properly treated if the size of the nebulised particle is too large to reach the small airways deep in the lung. The particle size required to reach the lower airway is 5 microns or less in diameter. For perspective on size, a human red blood cell is approximately 5 microns in diameter. So, the technology to create a particle that size is necessary to be able to treat the lung properly.

The Flexineb has been extensively tested and we know that up to 71% of the medication inhaled is 5 microns or less. So, this means that potentially 71% of the drug will reach the lower airways and the rest will likely not get further than the upper airway and trachea. With today's technology, that is a very competitive and successful percentage. With this data, Flexineb wanted to visually show how well the nebuliser can deliver medication to the lower airway. With the use of the scintigraphy (see image above), it is clear that the lung field achieves full exposure to the medication.

We are very grateful to Dr. Nathan Slovis and Hagyard Equine Medical Institute in Lexington, KY for performing the imaging to reiterate the effectiveness and quality of therapy that the Flexineb nebuliser can achieve.

Go to **www.nortev.com** for further information.