Stimufol® User Guideline

1) Transportation of the lyophilized medicine

For storage, we recommend a classical refrigerator or a cold room (+2 °C to +8 °C).

For air transportation, Stimufol® is placed in large boxes protected with expanded polystyrene layers.

For transportation to the vet or to the farm, it is recommended to place the Stimufol® into a cold box with icepack in order to avoid exposure to extremely high temperature inside the car.

After solubilization of the lyophilized pellet, it is important to store the reconstituted solution into a refrigerator (< 8°C). As an alternative, it is also possible to distribute the doses into small sterile syringes and freeze them (≈ -20 °C).

2) Opening mode of ampoule (One point cut, OPC)

Before opening the bulb, make sure there is no solution left in the top of the bulb.

The bulbs are equipped with an OPC opening system and must be broken in accordance with the following instructions:

1. With one hand, firmly hold the body of the bulb, white dot facing you (Figure 1)

2. On the other side, grip the upper part of the bulb (index finger behind the bulb neck and the thumb on the white point as shown in Figure 2)

3. Holding each part of the bulb tightly, snap the upper part of the bulb out by pressing in the opposite direction to the white dot (Figure 2)

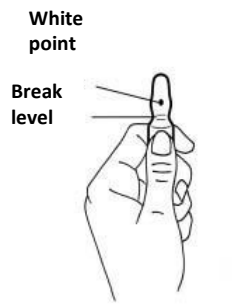

Figure 1

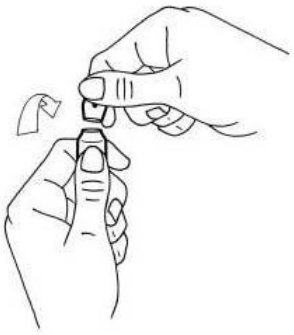

Figure 2

3) Solubilization of Stimufol®

The solvent is conditioned into an ampoule. To inject the solvent into the vial containing the lyophilized powder, do not hesitate to insert a second small needle close to the top in order to extract the nitrogen volume while injecting the solvent. In this way, there is no risk of wasting part of the volume due to the overpressure in the vial.

After adding the solvent to the vial containing the powder, gently shake the vial for a few seconds (20 to 30 seconds are enough). Excessive shakingmay generate foam and may damage the product.

4) Breakage of solvent vials due to transportation

In case the solvent ampoules break during transportation, the solvent can be replaced by sterile physiological solution (0.9% NaCl) of PBS (phosphate buffer saline) without albumin.

5) Treatment of the donor

The general recommendations for selection and handling of donors are to be applied for Stimufol® (beginning of treatment at middle luteal phase, ...).

Concerning the dosage, it is recommended that small females receive smaller doses of Stimufol®. In the leaflet of Stimufol®, doses of 320 to 360 µg

are recommended for heifers. However, according to the results obtained by practitioners, it appears that for small heifers, 2 females can be treated with one single vial of Stimufol® (corresponding to a dose of 250 µg of FSH per animal). When using such a moderate dosage, the percentage of unfertilized ova decreases and the longevity of donors increases (in terms of good response to superovulation treatment).

Moreover, when using low doses of Stimufol®, the time interval between two successive superovulations can be reduced up to 5 or 6 weeks.

6) Injection of Stimufol®

As each female will be treated by 8 successive injections, it is important to fulfill this step in the best conditions. After solubilization, the vial containing Stimufol® must be kept into a refrigerator or into a cold box. The operator is recommended to inject the donor in normal housing conditions (with a minimum of stress). It is also advised to inject by using small thin needles in order to avoid the perception of injection.

When the superovulatory treatment concerns fearful cows or heifers, the surface to be injected with Stimufol® can be treated by a spray or cream containing local anaesthetic (e.g. xylocain) a few minutes before the injection.

7) Complementary treatment

Generally, prostaglandins are injected at the same time as the 5th injection of Stimufol®. However, it is strongly recommended to use distinct syringes for both products. Never prepare in advance a combination ofprostaglandins and Stimufol®. In that case, prostaglandins will lose their activity and the induction of lyteolysis can be altered or delayed.

8) Adverse drug reaction

As with other vet medicines based on gonadotrophins, in rare cases, anaphylactoid incidents may occur after injection of Stimufol® (sometimes after the 1st, 3rd or even the 5th injection). Therefore, it is strongly recommended to monitor the injected females in the first minutes and hours (3 to 4 hours) after the injection.

Adequate monitoring allows identifying cases of anaphylactic shock (directly after injection) or delayed anaphylactic reaction (swelling, salivation, depression, respiratory distress or other behavioral signs indicating discomfort). In such cases, please contact the veterinarian as early as possible in order to initiate a treatment.

In the case of anaphylactic shock, the therapy of choice is based on an injection of adrenaline (1: 1,000) by I.V. or I.M., followed by treatment with corticosteroids and antihistamines. In case of a delayed reaction, corticosteroids with a short half-life (12-36 h) allow a regression of symptoms; according to reported experience, the treatment with Stimufol® can be pursued and embryos can be obtained at the end. Alternatively, the treatment can be replaced by an injection of equine chorionic gonadotropin (eCG about 2,000 IU). However, in any case of adverse reaction, an increased surveillance of the female is strongly recommended.

9) Additional information

In heifers of dairy herd, the treatment of superovulation can induce a perceptible temporary development of mammary glands. This event can be explained by increased levels of estrogens and progesterone issued from multiple follicles and corpora lutea.

In order to comply with pharmacovigilance recommendations, any adverse reaction has to be reported to the manufacturer (Reprobiol SPRL, email: info@reprobiol.be; www.reprobiol.be).