The request for a **SCIENTIFIC EVALUATION** for the auxiliary medical drug “PROAFTOL” spray was submitted by the company “APIMELL”, Ohrid, Republic of Macedonia.

Based on the decision of the Scientific Board at the department of preclinical and clinical pharmacology and toxicology at the Medical Faculty in Skopje, I have been assigned to provide a **SCIENTIFIC EVALUATION** for the auxiliary medical drug “PROAFTOL” spray.

After examining the submitted documentation as well as other relevant information I propose to the Scientific Board at the Institute to accept the following text as a **SCIENTIFIC EVALUATION** for the auxiliary medical drug “PROAFTOL” spray.
1.0 DESCRIPTION AND CONTENTS

Description: Spray

Contents:

100ml solution contains:

- 25 g Propolis dry matter
- Essential oils of:
  - Salviae off. (Sage) 0.4 g
  - Menthae piperitae (Mentha/Mint) 0.6 g
  - Aniseed 0.3 g
  - Menthol (Menthol) 0.6 g
  - Anestezinum 3.0 g
- Alcohol solution ad 100 ml

2.0 GENERAL INFORMATION ABOUT THE DRUG

“PROAFTOL” spray, is an auxiliary medical drug whose function is to alleviate the symptoms of canker sores, herpes simplex infections, gingivitis, stomatitis, alveolit, ulcers, inflammatory processes of the gums and painful abrasions of the mouth.

Proaftol is a combination of propolis and essential oils which carry a number of pharmacological properties. The components of Proaftol possess bactericidal properties against large number of bacteria (mainly Gram-positive), antiviral properties against (herpes simplex and A2 influenza) as well as anaesthetic and antioxidant properties.

In addition, Proaftol possess an anaesthetic properties due present of propolis and anestezinum.

Salviae folium (salviae officinalis - Sage)

Sage (salviae officinalis) is a 30-40 cm tall perennial bush with a pleasant scent. The leaves of the plant (Salviae folium) are picked and used in its second year of growth. The leaves are then dried in a cool place with good air circulation or in a dryer at 35C.

The drug is composed of 1.5-2.5% essential oil, up to 5% of tannins, a bitter principle called picrosalvine(carnesol) diterpentine compound, flavonoids, resin etc.

The Essential oil (Aetheroleum Salviae) is a clear or yellow-green liquid, with a specific scent and aromatic and bitter flavour. In its composition the oil has 50% alpha and beta thujone, about 15% cineol camphor, salvene, borneol etc.

Aetheroleum Menthae piperitae (essential oil of mentha/mint)

Domestic mint (Mentha piperita folia) is a perennial, branched plant with a pleasant characteristic scent, which can grow from 40-60 in height. Leaves are handpicked from the plant when it’s in bloom. The leaves are then dried in a cool place with good air circulation or in a dryer at 35 C.

Domestic mint contains: 1-3% essential oil, tanines, about 5% flavonoids, bitter substances, ferulic and chlorogenic henna etc.
The main component of the essential oil (Aetheroleum Menthae piperitae) is menthol (monocyclic monoterpenic alcohol) which is found in concentrations of 50-68%. 45% of the Menthol is free and 4-12% is esterified with ethanoic acid, isovalerianic and other acids. It also contains ketone-mentone 7-10%, metafuran, therpenes and therpenh derivatives: limonene, cineole etc.

Anisi fructus (essential oil of anis)
Anis is a 20-60 cm tall plant, with characteristic small, white leaves. It possess very pleasant, strong, aromatic adour of anetol.
Anis contains: 1,5-4% essential oil, around 10% fatty oil, 20% proteins and sugar.

Propolis

Propolis is a natural bee product. It is a sappy, yellow-green to dark red substance. By methods of distillation and various solvents it had been determined that propolis contains up to 30% bee wax, about 20% mechanic sub compounds, 40-60% sapp and balsam, 5-10% tannins, pollen etc.
However, from a chemical aspect these compounds remain undetermined and it has been proven that the primary components of propolis are the flavonoids which make up to 25% of the propolis composition.
The following flavonoids are found in propolis: chrizine, galanine, tectochrzine, acacetin, quercetin and many others.
Other then flavonoids, propolis contains significant quantities of minerals, esters of saturated fatty acids, saturated fatty alcohols, 10-15% carbohydrates, free fatty acids, vitamins etc.

3.0 PHARMACODYNAMICS AND MECHANISMS OF ACTION

“PROAFTOL” spray in its composition contain propolis and essential oils well recognized in literature and scientific medicine as compounds which can alleviate the symptoms of ulcers and erosions of mucosa on mouth cavity and throat. Anaesthetic effect of Proaftol is due present of anestezinum and propolis, which decreasing painful abrasions of the mouth, and accelerate regeneration and epitelisation of mucus.

Sage represents one of the oldest plants used in medicine. It is used in the composition of a large number of drugs which are used to wash the mouth and throat in cases of inflammation and, due to it’s harmlessness and properties of strengthening the mucosa (due to the action of tannins) and it’s antiseptic properties (due to the action of the essential oil). Due to it’s spasmylytic and anti-inflammatory properties, sage has a positive effect against inflammatory disease of the stomach, intestines, liver, bladder, and the urinary pathways. Sage also helps in patients with diabetes mellitus due to its hypoglycaemic properties.
Up until the discovery of antibiotics, sage was used centuries as a tea against sweating in patients with tuberculosis because it can reduce the excretion of sweat glands.
The drug is also widely used as a spice for grilling meat in the United States because it improves the smell and taste of meat.
Caution should be practised, especially when the essential oil is used because it contains thujone which is a toxic compound.

The main component of the essential oil of mint (Aetheroleum Menthae piperitae) is menthol. Menthol, when applied on the skin and mucus causes a scent of coldness, followed by an easy anaesthetic activity and a pleasant refreshing scent. When used in light concentrations, menthol can
inhibit the transport of calcium ions from the thermo-receptors. The sense of coldness is caused because Menthol evaporates easily. It has an antiglogistic action. It stimulates the nerve ends of the skin and mucosa. Menthol also has spasmolytic action on the smooth muscle of the intestines; it decreases the transmission of the extra-cellular calcium in the cells.

When applied orally, mentol acts as a holagogue and holoteric. Due to its refreshing scent and flavour, it is often used for improving the flavour of other oral preparations.

In addition, the domesticated mint (Menthae piperitae) has a wide usage both in scientific and home medicine. Mint is a well known spice which has been used for a long time and is quite popular nowadays.

The infusion mint (Mint tea) acts as carminative, stomahic, spasmolytic and a light sedative. It is also used as aholagogume and antidiaroeicum due to the presence of tannins in its composition.

Due to its spasmolytic properties the tea made of mint leaves is a recognized and well appreciated medicament against inflammatory diseases in the stomach and intestines (gastritis, gastroduodenitis, cholitis, peptic ulcerations), flatulence and diarrhea.

Besides that, Mentha piperita stimulates the function of the liver by increasing the production of bladder juice and its flow through the bladder canals; it can also aid in the dissolution of bladder stones. This action occurs probably due the presence of menthol and flavonoids. The relaxing properties of mint are also well known; it aids in decreasing and relive of nervous tension and neurosis.

Other than the infusion, the essential oil is used for preparing galenic preparates such as: Aqua, Spiritus, Pastilli, Etosaccharum etc.

The essential oil is also added to toothpaste, mouthwash, as an aromatic, deodorant and a disinfectant. It is also used as supplement in various pharmaceutical preparates as well as scent corrector.

Essential oil of aniseed: Its application is very often like ecspectorans , karminativ, spasmolytic,,and like corrector of adour and taste of very anpleasent drugs. It stimulate a secretion of bladder juice and saliva. Action of essential oil on the neuromuscle system, explain its successful properties against cholics and gastralgie.

Propolis has bacteriostatic, bactericidal, and gungicidal properties. Theantimicrobial substances is propolis are thermostable. Gram positive bacteria are more sensitive to propolis in comparison with gram negative bacteria. This properties of propolis are mainly due to the action of flavonoids. The propolis flavonoid-acacetine decreases inflammation and increases resistance of the capillary wall.

Propolis is used in treatment of various diseases in dentistry, othorhinolaryngology, gastroetherology and diseases of the skin. Propolis has antibacterical, antiseptic, as well as anaesthetic and trophic-granular effect which decreases pain and stimulates healing of the wounds.

4.0 BENEFITS OF USAGE

“PROAFTOL” spray , is an auxiliary medical drug whose function is to alleviate the symptoms of canker sores, herpes simplex infections, gingivitis, stomatitis, alveolit, ulcers, inflammatory processes of the gums and painful abrasions of the mouth.

5.0 DOSAGE AND USAGE INSTUCTIONS

Proaftol spray: 2-3 sprays, 3 -4 times per day, half an hour prior to consumption of food.
6.0 PRECAUTIONARY MEASURES AND WARNINGS

“PROAFTOL” spray and throat drops are not to be taken by patients sensitive to any of the ingredients of the drug.

Pregnancy and breastfeeding: the usage of Proaftol should be avoided during pregnancy due to the properties of some of the essential oils which can have an abortive effect and also have an effect on the menstrual cycle.

Notice: The preparate can leave stains on cloth which are difficult to remove.

7.0 PACKING

Proaftol spray: 20 ml solution in a spray bottle

8.0 STORAGE
To be kept in a dry place on a temperature up to 25C.
TO BE KEPT AT A PLACE WHICH IS NOT ACCESSIBLE TO CHILDREN.

9.0 DATE OF EXPIRY
3 (three) years after date of production.
Not to be used passed the date of expiry!!

10.0 CONCLUSION
“PROAFTOL” spray, is an auxiliary medical drug whose function is to alleviate the symptoms of canker sores, herpes simplex infections, gingivitis, stomatitis, alveolitis, ulcers, inflammatory processes of the gums and painful abrasions of the mouth.
Proaftol is a combination of propolis and essential oils which carry a number of pharmacological properties. The components of Proaftol possess bactericidal properties against large number of bacteria (mainly Gram-positive), antiviral properties against (herpes simplex and A2 influenza) as well as anaesthetic and antioxidant properties.
In addition, Proaftol possess an anaesthetic properties due present of propolis and anestezinum.
Based on the literature data about the properties and actions of the essential oils which are present in the combination of “PROAFTOL” spray, it can be expected that the drug, or it’s components possess the properties which have been attributed by the producer.
Based on everything which has been presented in this SCIENTIFIC STUDY, I conclude that “PROAFTOL” spray – a product made by “APIMELL”, Ohrid, Republic of Macedonia, satisfies the auxiliary medical drug conditions in lieu of it’s composition and properties, and as such it can be registered in the Republic of Macedonia as an auxiliary medical drug.

The Scientific Study was concluded by
Prof. Dr. Stojmir Petrov
The Scientific Board at the Institute of Preclinical and Clinical Pharmacology and Toxicology, at the meeting held on 18.04.2001 reviewed and approved the scientific evaluation for the auxiliary medical drug “PROAFTOL” spray – a product of the company “APIMELL”, Ohrid, Republic of Macedonia.

Director
Prof. Dr. Stojmir Petrov