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Welcome

to Remedica Newsletter 2



Mr. Charalambos Pattihis
Group Managing Director

Dear reader,
Welcome to the second issue of Remedica's newsletter. We hope that you enjoyed reading our first issue and we will continue to attempt to keep you more informed in

what goes on in our company. In this issue you will find various interesting topics such as the launch of a new product for breast cancer named Aremed® (Anastrozole), an innovative analytical technique that saves considerable time in the identification of raw materials (the NIR spectrometer), our associates "down under" and many more. We all hope that you will enjoy this issue enough to look forward to the next one.

Charalambos Pattihis
Group Managing Director

Remedica worldwide

Australia – New Zealand



Remedica has been exporting to New Zealand since 2003 and to Australia since 2005. Following a successful GMP inspection from the TGA in 2007, Remedica is allowed to continue its exports to these countries through AFT Pharmaceuticals.

AFT Pharmaceuticals is a privately-owned company with operations in Australia and New Zealand. The company was founded in 1998 by Pharmacist and Pharmacologist, Dr Hartley Atkinson. AFT remains firmly on the Pharmaceutical prescription/Over-The-Counter market, where it holds considerable collective expertise. Since its first product launches in 1998, sales have grown substantially year-on-year. The company has an experienced and qualified

sales team in each country which is currently in the process of being expanded to include additional sales people plus a Key Accounts Manager. The team promotes to doctors, pharmacists and consumers and also participates in the hospital/government tender sectors.

AFT believes that "sales growth is planned which will see the Remedica-AFT business at least double in Australasia in the next year".



Remedica people



Today we introduce Mrs. Andri Aristotelous, the Head of our Accounting

Department and one of our longest-serving associates.

After completing her accounting studies in Greece, she joined our company as a secretary (1973 – 1976) but because of her academic background and hard work she was transferred to the accounting department in 1977. Being a fast learner and full of enthusiasm, she was promoted to accounting supervisor in 1980. Then, having completed 10

years of service with our company and attended many courses such as corporate management and production control, she was promoted to her current position.

Mrs. Aristotelous is also the Secretary of Remedica's Provident Fund Committee and due to her extensive experience, she also takes part in interviews for the recruitment of personnel. She is married with two children, a daughter and a son.

New products

Aremed[®] 1mg Film-coated tablets, is a new anti-cancer product developed by Remedica and registered recently in Cyprus. It will soon be made available in more countries and Remedica has also signed agreements to out-license it to other interested companies.

Aremed[®] offers a better option for the treatment of breast cancer in postmenopausal women and is replacing Tamoxifen as the standard hormonal treatment. It works by the inhibition of aromatase enzyme activity reducing circulating, and possibly intratumoral oestrogen levels, since in postmenopausal women the major source of circulating oestrogens is peripheral conversion of androgens via aromatase enzyme in fat, muscle and liver.

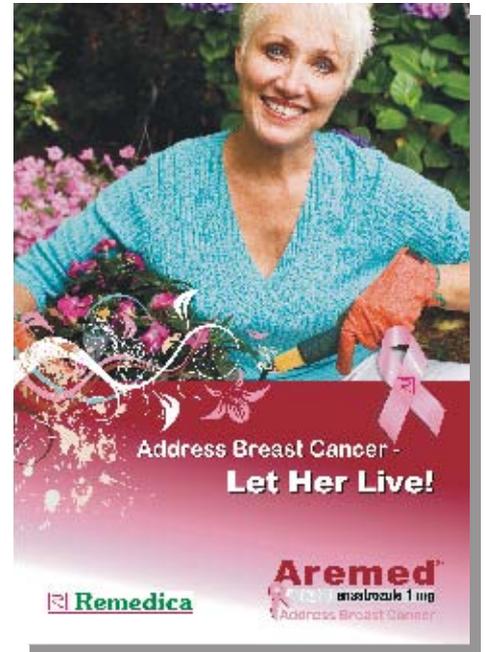
Anastrozole, the active ingredient of

Aremed[®], a third generation aromatase inhibitor, interferes with the body's ability to produce oestrogen from androgens by suppressing aromatase enzyme activity. While first and second generation aromatase inhibitors inhibit oestrogen synthesis in vivo by up to 90%, Anastrozole was shown to cause approximately 98% aromatase inhibition in humans.

Anastrozole is currently the preferred drug for the treatment of breast cancer in postmenopausal, hormone receptor-positive women.

The 5 year-results of the largest international breast cancer trial in the world (ATAC trial) found that, compared to tamoxifen, Anastrozole:

- Prolongs disease-free survival by 13%.
- Reduces the risk of contralateral breast cancer by 53%.
- Reduces the risk of long term



recurrence by 16%.

Furthermore, Anastrozole reduces the risk of breast cancer recurrence by 26% above the 50% already achieved by Tamoxifen.

Corporate Social Responsibility

Blood donations

Remedica is a socially responsible organisation, always searching for ways to enhance public welfare. Taking into consideration society's needs for blood transfusions, Remedica organises blood donations twice a year and thanks to the positive attitude and participation of its

workforce, it has created one of the largest blood banks on the island. Remedica invites all personnel to participate in such blood donations as a gesture of reaching out towards our fellow human beings in need of urgent medical assistance.



Remedica news

Near Infra Red spectrometer

Remedica has recently introduced a new technique in the identification of raw materials. According to the European Union GMP guidelines, "The identity of a complete batch of starting materials can normally only be ensured if individual samples are taken from all the containers and an identity test performed on each sample." This is a very expensive and time-consuming exercise, so in order to improve efficiency, Remedica has acquired a Near Infra Red spectrometer (NIR). This instrument utilises the latest Fibre Optic technology which allows identification of the material in place.

With the NIR spectrometer, it takes only a few seconds to analyse a sample and reveal its identity from a range of possible compounds that have been entered in the processor's memory. It can even carry out this identification without the need to open the plastic bag containing the ingredient! This further safeguards the integrity of the material by minimising handling. In addition it maximises analysis throughput and reduces the turnaround time from reception to analysis, allowing minimisation of production time for our customers. We always strive to keep up-to-date with the latest technological



advances to ensure that our laboratories utilise the best and most suitable analytical techniques available.

Medical congresses

Participation in medical congresses is one of the most important company activities in terms of promoting professional awareness towards health issues. It helps build brand image and enhance Remedica's presence in the market. The Local Sales Team participates in congresses on a variety of issues addressed to cardiologists, dermatologists, general practitioners,



physicians, surgeons and many others. Recently, Remedica attended the 20th Annual Medical Congress of the Nicosia Medical Association where it participated in the pharmaceutical exhibition and presented a number of products including the newly-launched Amlorine 5 and 10 (Amlodipine).

Regulations

New GMP guidelines for dedicated facilities

Remedica's investment in a dedicated facility for high potency products has proved to be the correct decision and other companies would need to follow suit or risk losing a number of marketing authorisations.

A recent concept paper by the EMEA (<http://www.emea.europa.eu/Inspection/docs/1452908en.pdf>) explains the problem that exists with the current wording of sections 3.6 and 5.18 of the Guidelines to Good Manufacturing Practice (GMP) and aims to eliminate the present ambiguity.

Currently, Chapter 3, section 6 of the

GMP guide is as follows:

"In order to minimise the risk of a serious medical hazard due to cross-contamination, dedicated and self-contained facilities must be available for the production of particular medicinal products, such as highly sensitising materials (e.g. penicillins) or biological preparations (e.g. from live microorganisms). The production of **certain** additional products, such as **certain** antibiotics, **certain** hormones, **certain** cytotoxics, **certain** highly active drugs and non-medicinal products should not be conducted in the same facilities. For those products, in

exceptional cases, the principle of campaign working in the same facilities can be accepted provided that..."

However, no guidance is given in the text or anywhere else, to clarify what is meant by "**certain**" and "**exceptional cases**" in this context. In some countries the authorities maintain that dedicated facilities are mandatory but others have a looser approach. There is also no list of products that are described in the GMP text as "certain".

According to some sources, the above-mentioned concept paper will provide

these missing definitions and that the necessary revision of the sections in question should take into account the principles of ICH Q9 (Quality Risk Management). However, it is as yet unclear whether there will be a list of products whose manufacture would require a dedicated facility despite a report by the EMEA that says that the GMP/GDP Inspectors Working Group is

unanimously in favour of such a list.

And whilst it may be possible to manufacture other products based on a risk analysis approach, substances that may pose a great risk both due to their physico-chemical characteristics and their pharmacological/toxicological properties will also have to be manufactured in dedicated facilities

unless the manufacturer can demonstrate their case by means of Quality Risk Management and suitable risk-reducing measures.

At present it is anticipated that a text will be submitted to the European Commission at the end of 2008 / beginning of 2009 for public consultation.

Cyprus

10,000 year-old history

Cyprus, according to Mythology, is the birthplace of the goddess of love and beauty, Aphrodite. The island is both an ancient land, with a ten thousand year-old history and civilisation as well as a young, independent republic since 1960. Its geographic location at the crossroads of three continents – Europe, Asia and Africa – and at the meeting point of great civilisations, has been one of the factors influencing the path of the island's history throughout the centuries. Cyprus is the third biggest island and a popular tourist destination in the Mediterranean, attracting more than 2 million tourists every year.

Brief history

Neolithic Age (app. 8200 – 3900 BC)

The oldest known settlement in Cyprus dating from this period can be seen in Khirokitia.

Chalcolithic Age (app. 3900 – 2500 BC)

Small-scale settlements and activity-areas were in use all over the island. The copper from local mines begins to be exploited and used.

Bronze Age (app. 2500 – 1050 BC)

Copper trade was expanded to the Near East, Egypt and the Aegean. After 1400 BC, ancient Greeks reached the island bringing with them the Greek language, their religion and customs. During this period they built new cities like Paphos, Kourion and Salamis.

Geometric Period (app. 1050 – 750 BC)

Ten Kingdoms in the island.
Archaic & classical period (750–325 BC)
The island came under the domination of Assyria, Egypt and Persia, and finally

became part of the empire of Alexander the Great.

Hellenistic period (325 – 58 BC)

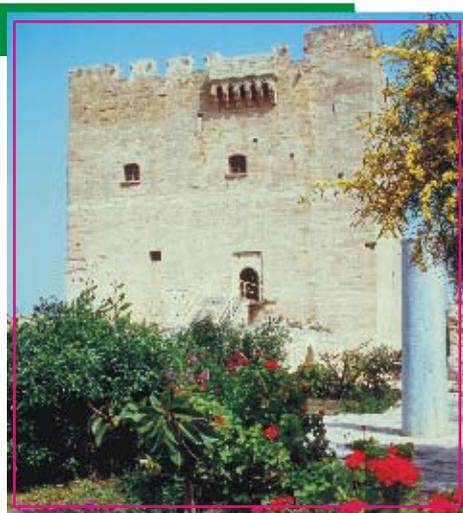
A period of wealth for Cyprus. Paphos was the capital of the island.

Roman period (58 BC – 330 AD)

Cyprus became part of the Roman Empire. During the missionary journeys by Saints Paul and Barnabas, the Proconsul, Sergius Paulus is converted to Christianity and Cyprus became the first country to be governed by a Christian ruler.

Byzantine period (330 – 1191 AD)

Richard the Lionheart and the Templars (1191-1192 AD)



Kolossi Castle

Frankish (Lusignan) period (1192-1489 AD)

Venetian period (1489-1571 AD)

Ottoman period (1571-1878 AD)

British period (1878-1960 AD)

Republic of Cyprus (1960 AD)

According to the Zurich-London Treaty,



Kourion Theatre

Cyprus became an independent republic on 16th August 1960.

1974 Turkey invaded Cyprus and ever since, 37% of the island is under Turkish military occupation whilst 200,000 Greek Cypriots, 40% of the total Greek Cypriot population, were forced to leave their homes in the occupied area and were turned into refugees. Many Greek Cypriot civilians and soldiers disappeared during this period.

1975 – present modern era

Even though the political problem remains unresolved, the free market economy in the government-controlled area has made a remarkable recovery since 1974. Tourism, financial services, real estate and industrial products are some of the main sectors. Cyprus joined the European Union in 2004, joined the European Exchange Rate Mechanism (ERM2) in May 2005 and adopted the euro as its national currency on 1st January 2008. As a member of the European Union, Cyprus has a prosperous economy with a per – capita GDP slightly lower than that of France, Germany, Italy and the UK but higher than the European Union average. Cyprus can be characterised as a modern country with a highly developed infrastructure that attracts many international and offshore companies to expand their activities or to locate their head offices here.