Remedica
FOR A HEALTHIER WORLD

Newsletter 25

Contents

Welcome note

Welcome to the 25th issue of our Newsletter where we present our associates in Singapore and our Logistics Officer.

Under Environmental Issues we report on "global warming" and in Health Matters we feature an article entitled current drug safety and the new challenges.

In Corporate Social Responsibility we describe our financial aid to the Karaiskakio Foundation to support its Cyprus Bone Marrow Donor Registry and the Pattichis Senior Citizens' Centre, participation in the Limassol Marathon, our blood donation session and our Easter gifts.

In Remedica News we report on the visit from an overseas university, the tribute by a local magazine to Remedica's founder, participation in conferences and the publication of an article by our Pharmacovigilance Officer in the magazine of the Cyprus Chemists' Society.

Finally, we "take a dive" to admire the underwater world of Cyprus.

Remedica Worldwide:
GoldPlus Universal Pte Ltd., Singapore.

GoldPlus Universal Pte Ltd is Remedica's partner in Singapore. Located in Southeast Asia, Singapore is a small country with a land area of about 714.3km^2. The mainland of Singapore measures 49km from east to west and 25km from north to south. Through land reclamation, Singapore's land area grew from 585.5km^2 in 1960s to 714.3km^2 today, and may grow by another 100km^2 by 2033.

South East Asia Regional map

Despite being a small island city-state, Singapore is densely populated by about 5.3 million people. Its pharmaceutical expenditure rose from SGD940mn (US$770mn) in 2012 to SGD1.0bn (US$800mn) in 2013. As a consequence of an increased focus on healthcare provision by the government, spending increased from SGD16.3bn (US$13.3bn) in 2012 to SGD18.0bn (US$14.4bn) in 2013.

金昇私人有限公司
GoldPlus Universal Pte Ltd

GoldPlus Universal Pte Ltd was established in April 1998 as a wholesale distributor of pharmaceutical and consumer healthcare products. It has 21 employees, who cover over 1800 GP clinics, private and restructured hospitals and clinics in Singapore. The Singapore pharmaceutical market is mainly prescription-driven. Hence good access and relationships with the medical practitioners are key factors for success. GoldPlus has within its sales team medical representatives with over 40 years of experience in the field who have developed extremely good rapport with its customers.

Sealing the deal in 2009

Remedica has recognised this strength and appointed GoldPlus as its distributor for its products in Singapore in October 2009.

Throughout the last 4 years, the company's products have experienced constant growth both in number of products (now 62) and the value of sales. The introduction of new, stricter stability requirements for pharmaceutical products on 1st July 2010 from the Association of Southeast Asian Nations (ASEAN) had the potential to hamper product registrations but concentrated efforts resulted in more products gaining approval with Health Sciences Authority (HSA) as well as the Brunei market. Several product amendments have also been successfully approved.

Intensive Remedica Product Training Session


Remedica's visit to GoldPlus

GoldPlus has 2 fully air-conditioned, secure warehouses with a total area of over 800 square meters which meet fully the requirements for pharmaceutical goods storage and distribution practice. With a committed sales force and delivery personnel, GoldPlus has an efficient distribution service that ensures orders are delivered within 1 to 2 working days.

Today, GoldPlus is proud to have Remedica as its principal (main supplier) and looks forward to continued expansion of the partnership in years to come.


Goldplus' visit to Remedica

Remedica people

In this issue we present our Logistics Officer, Mr Lambros Demetriades.

After Graduating from Athens University with a degree in Economics and Business he decided that he wished to follow a career in Operation and Logistics Management. He worked for one year as a Demand Planning Assistant in the Greek branch of the multinational company Reckitt Benckiser, specialising in the chemical manufacture of household and cleaning products.

He was then accepted by the University of Nottingham Business School where he was awarded a Master's Degree (with distinction) in Supply Chain and Operations Management. In 2008 he joined Remedica as Logistics Officer with the brief to organise the main logistics operations of the company and the creation of a separate Logistics Department.

As a member of the company's strategic team, he is responsible for the planning and development of the company's basic logistics operations which include: -

a) inbound logistics
b) warehouse operations
c) sales monitoring and planning
d) development of the product and information flows
e) upgrading of local and global outbound logistics.

He has ongoing responsibility for the implementation of the current guidelines of Good Distribution Practices (GDP).

After the successful certification of Remedica as a "Known Consignor", he has also been assigned the role of Security Officer.

He is a member of the Cyprus Logistics Association and has, for example, attended seminars on emotional intelligence and Good Distribution Practices (GDP).

Remedica News

1) Bentley University students visit Remedica. (photo 1)
Students from the Bentley University in Massachusetts, USA recently visited Remedica and were given a tour of its facility. They were very impressed by the number of countries to which the company markets its products, the fact that it also invests in product development and its successful business model. They made a specific reference as to how impressed they were with the 'cleanliness' not only of the production areas but also the site in general.


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2) Tribute to Chris Pattichis. (photo 2)
IN BUSINESS, Cyprus' leading business magazine recently published a tribute in the form of an article to Remedica's founder and Chairman, Chris Pattichis, on the occasion of his Lifetime Achievement Award 2013 for his valuable and long-standing contribution to the Cyprus economy and society in general. The article entitled "Make room for vision" begins with some advice offered to new entrepreneurs by Chris Pattichis whom it understandably calls the "father of the Cyprus pharmaceutical industry": An example is "Have a vision. See the draw-backs in every situation as an opportunity to be creative and to evolve". It then carries on with a review of Mr. Pattichis' life from his birth to the founding of the organisation that has evolved today as Remedica. In the last part of the article, Mr Pattichis is quoted as referring to the previous year as "one of the worst in the history of the Cyprus Republic", but was still optimistic about the future saying that "2014 is in front of us" and since for him it began with the IN BUSINESS award, he considers that "the year starts with the best signs and with an award that honours and gives me strength to go on to even greater successes for the company and my colleagues".
As for the economy of Cyprus, he stated that "an important role will be played by developments in the 'Cyprus problem', but also by the local banks, and will have a significant impact, positive or negative, not only for them, but also for the economy as a whole". The directors and employees wish to offer their congratulations for this thoroughly deserved award and to thank him for his inspiration and leadership of the Company.

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3) Conferences. (photo 3,4)
Remedica's local sales team attended 6 conferences where participants (doctors and other health care professionals) had the opportunity to be briefed on both new and existing Remedica products. The conferences were the Pancyprian Dental Conference, 4th Pancyprian Conference of Physiotherapy, 9th Conference of the Medical Society of Ammochostos "Galinos", 1st Pancyprian Diabetic Conference, 1st International Congress of the Cyprus Society of Dermatology and Venereology and the 34th Conference of Limassol Medical Association.

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4) Publication of article.
A scientific article by Remedica's Pharmacovigilance Officer was published in the recent issue of the Cyprus Union of Chemists magazine. The article entitled "Modern-day drug safety and the new challenges ahead" reviews and analyses Pharmacovigilance issues and drug safety in general and an edited version is published above under "Health Matters".


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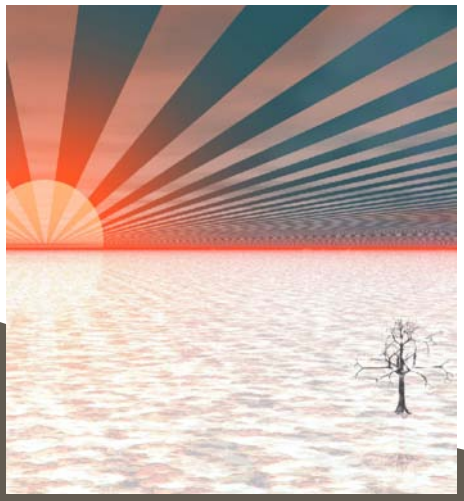

Environmental Issues:
Global warming.

The temperature of the Earth is maintained at habitable levels by the Sun giving off short-wave radiation, most of which passes through the atmosphere to heat the Earth's surface from which it is radiated back as long-wave radiation. A considerable amount of the latter would escape back into space if it was not for its absorption by 'greenhouse gases' (e.g. methane, carbon dioxide) which thus trap heat: this has become known as the greenhouse effect. Control of this phenomenon can only be achieved if the atmosphere contains the correct amount of water vapour and greenhouse gases and if this is disturbed then global warming will occur.

Human activities however, including the burning of fossil fuels on a global scale, have resulted to an unprecedented release of carbon dioxide and other greenhouse gases into the atmosphere. What's more, the alteration of a climatic parameter such as the temperature, has led to the deregulation of the earth's elegant yet chaotic climate system.

According to the 2013 Climate Change report published by the Intergovernmental Panel on Climate Change, '*the warming of the climate system is unequivocal, and since the 1950s, many of the observed changes are unprecedented over decades to millennia'*. Taking this into account, global warming has triggered a chain of events including the shifting of the precipitation patterns, the melting of glaciers and polar icecaps which in turn resulted to the rising of sea level, threatening coastal regions and even whole islands.

It should be noted that the European Environment Agency is expecting that changes in natural patterns will continue to occur, resulting in a higher frequency and intensity of extreme weather events. These events could give rise to hurricanes, flooding or droughts, depending on the geography of the affected region. In addition, it is expected that many animal and plant species would not have the necessary time to adapt to the fast changing climate conditions. As a result, a considerable proportion of biodiversity is facing a high risk of extinction.

Taking into consideration the interrelated environmental and socioeconomic effects of uncontrolled climate change, the European Union has played a leading role in tackling of climate change on a global scale. According to the Institute of Environmental Management and Assessment, the European Union became the leader in global environmental initiative, mainly due to the fact that although it is responsible for the production of 14% of the global greenhouse gases, it has agreed to reduce its emissions by 8%.

In order to maintain this global leadership by example, the EU has approved the 2009 EU climate and energy package which includes legislative measures to achieve specific targets by 2020. According to the European Environment Agency, these targets include a reduction in greenhouse gases emissions by 20% below 1990 levels, the production of 20% of the total energy by renewable means, and a 20% reduction in primary energy use against projected figures. In addition, the EU has introduced legislative measures to control the use and emissions of fluorinated greenhouse gases which have a major impact on global warming.

Although the EU has set the benchmark for tackling climate change, a more decisive global action is needed to safeguard climatic stability, so that life will continue to exist as we know it. ■

Corporate Social Responsibility:
Remedica Cares

1) Financial aid to the Karaiskakeio Foundation. (photo 1)

As part of its corporate social responsibility activities, Remedica has made a donation to the Karaiskakeio Foundation. During the annual charity dinner held at the Presidential Palace, under the auspices of the President of the Cyprus Republic Mr. Nicos Anastasiades, Remedica's Managing Director, Mr. Emilios Savvides presented the Foundation's President Dr. Popi Kanari with a cheque for €2,000. The Karaiskakeio Foundation is a charity organisation set up with the aim of organising and running a donor's bank of bone marrow in order to offer the hope of life to fellow human beings. It is worth pointing out that many Remedica employees as well as making regular donations of blood are also bone marrow donors.

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2) Donation to the Pattichis Senior Citizens' Centre. (photo 2)

Once more, Remedica provided financial support to the Pattichis Senior Citizen's Centre, which is unique in Cyprus and can count 13 years of valuable support to senior citizens of Limassol. Its main aims are to provide recreation, productive occupation and other wide ranging services to its members so that they may continue lead fulfilled lives as active citizens. Remedica's Marketing Manager, Mr Andreas HadjiPanayis, presented the Centre's Treasurer, Mr. Dinos Kafkalias, with a donation of €2,000.

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3) Limassol Marathon. (photo 3)

Remedica supported the 8th Limassol International Marathon GSO held on the 16th March with a corporate entry of 20 colleagues thereby making a significant contribution to the fund-raising effort. In total about 7000 runners took part and thousands more participated in the student run, the charity run or as mere spectators. In addition to raising valuable funds for various charities, the Marathon aims to spread the spirit of sportsmanship, participation and volunteerism.

4) Blood donation. (photo 4, 5)

"Millions of people owe their lives to people they will never meet". Using this message, Remedica organised a blood donation session where more than 80 employees made this altruistic gesture. The purpose of the blood donation was to boost the stocks of the blood bank of Limassol General Hospital. Remedica organises yearly blood donation and encourages all its employees to participate.

5) Easter donations. (photo 6)

At Easter, as in previous years, Remedica assisted several charitable organisations by purchasing Easter candles, which were then given free of charge to its staff. This year the 3 associations to benefit were: the Day Centre for People with Special Needs (Prosvasi), the Theotokos Foundation and the Cyprus Association of Cancer Patients and Friends. ■

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Health Matters:

Safety of medicinal products in these days and the new challenges

Andreas Vasiliou, Head of Drug Safety and Pharmacovigilance Department, Remedica Ltd.

Published in Cyprus Union of Chemists magazine (Issue 13, March 2014).

Introduction:

The safety of medicinal products is among the first issues to be considered when medicinal products are discussed nowadays but it is not a new topic. In modern history, there are numerous examples of doctors and national competent authorities questioning the safety of specific medicinal products. For example, in 1912, the American Medical Association examined deaths associated with the use of chloroform as an anaesthetic in surgical operations [1]. Also, during the late 50's and early 60's thalidomide was marketed in more than 46 countries and researchers were setting the alarm for its safety. In 1961, most countries decided to withdraw thalidomide from their market whilst about 10000 children were born with phocomelia (small or non-developed limbs) [2]. Some would say that thalidomide was the trigger of the creation of a strong framework for verifying drug safety.

Actions taken over time in order to ascertain drug safety

1. More stringent protocols for clinical studies

Increasingly stringent protocols for clinical studies are required by national competent authorities in order to gain a marketing authorisation for a new medicinal product or use. Some principles that are included in the protocols (besides those covered by the Helsinki declaration of 1964) are the following:

- Large number of participants including those from a range of phyletic origins, must be recruited in clinical trials
- Researchers conducting clinical studies are required to record in detail all data regarding product safety, even if presented by a single participant or even if the investigator believes that is not drug-related
- Use of advanced mathematical and statistical models for analysing the results.

Moreover, research centres that conduct the study must be approved and adhere to the guidelines of Good Laboratory Practice and Good Clinical Practice issued by the relevant competent authorities. The protocol of the study must be approved by an ethics committee of the relevant country according to the location of the study.

During the conduct of the study, national competent authorities have the right to inspect the research centre in order to confirm that it meets the requirements and conditions set out in the protocol of the specific clinical study. At the same time, the European Union has approved and applied the Council Directive 2001/20/EC which provides guidelines on how a clinical study must be carried out in order to be acceptable by European Authorities.

Around 12 years of pre-clinical studies (studies on animals) and clinical trials [3] are needed in order for a new medicinal product to be marketed and the estimated cost is around 1.3 billion dollars[4].

In the case of generic medicinal products, their equivalence with innovator medicinal products should be demonstrated through bioequivalence studies in order to be authorised. Bioequivalence studies are conducted in a smaller number of patients or healthy volunteers than would be required for a new active compound. The two medicinal products are considered to be bioequivalent if the concentration of the drug or its metabolites in volunteers' blood can be shown (through mathematical and statistical analysis of haematological results) to be the same at equivalent time points, following administration of both the test and reference product.

2. Pharmacovigilance

All of the above actions have not only helped to reduce the number of reported adverse drug reactions but also to increase drug efficacy. However, they cannot provide a complete or permanent solution that some might expect. On some, thankfully rare, occasions, medicinal products were marketed for several years after they had been suspected of being ineffective or suspected adverse drug reactions had been reported. Therefore, it is legal requirement that data/information regarding drug effectiveness and adverse drug reactions be recorded both during clinical trials as well as after authorisation.

In 2001, European Union officially introduced the term pharmacovigilance (the science and actions related to detection, assessment, understanding and prevention of adverse events or any other medical related problems), through Council Directive 2001/83/EC. As a result pharmaceutical companies, European national competent authorities and the European Medicines Agency were obligated to create and maintain a pharmacovigilance system aiming to protect patients and public health.

Today, the European Medicines Agency is connected electronically with national competent authorities and pharmaceutical companies in European Union, through an electronic database (Eudra Vigilance) and can thus collect centrally all safety information. If a product is raised to the level of concern, it is investigated and an assessment is made based on benefit and risk and the appropriate action is taken, rapidly if the risk to patient health is considered serious.

One of the recent pharmacovigilance measures taken is the introduction of the inverted black triangle added in the instructions of use, accompanied by the indication that this product is subject to additional monitoring. The black symbol will allow patients to identify these medicinal products and to be aware that product safety has not been completely elucidated.

3. Campaigns against counterfeit medicinal products

In recent years, the trend of purchasing medicines over the internet has increased, either due to low prices, or because of the fear of social stigmatization (e.g. sexual dysfunction). However, only 2% of online "pharmacies" are legal, and more than 50% of drugs purchased online are counterfeit [6] (in formulations purchased from online 'pharmacies' were found to contain rodenticides which led to illness and even death). Between 20th and 27th September 2011, Interpol, assisted by police authorities and post offices of 81 countries, seized 2.4 million counterfeit drugs[7]. Directive 2011/62/EC is trying to put the brakes on the frantic increase in the purchase of medicinal products over the internet with the introduction of a Pan-European logo that will help patients to identify licensed online pharmacies. An attempt is also being made through this Directive to control the entire pharmaceutical supply chain in order to reduce the possibility of importing counterfeit medicinal products in the European market. In addition to the certificate of Good Manufacturing Practice that all pharmaceutical manufacturers must hold, should also ensure that raw material manufacturers have the corresponding certificates recognised by the European Union, and that they only distribute their medicinal products to licensed wholesalers.

Finally, new measures concerning the outer package have also been introduced and are expected to be used. These include the introduction of a special adhesive tape, which once removed cannot be reapplied and as a result the patient will be able to recognise if the supplied medicinal product has been tampered with or not.

"▼ This medicine is subject to additional monitoring.

This will allow quick identification of new safety information.

You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects."

The inverted black triangle with its explanation, as it will be added to the product information leaflet of selected medicinal products[5].

Example of adhesive tape on the outer package of the medicinal product.

Conclusions - New Challenges

Several actions have been taken to date in order to ensure the safe use and administration of medicinal products. However, in a rapidly developing arena such as medicines production and supply, it is certain that new safety issues will continuously need to be addressed. A topic that has concerned scientific community for a number of years but will need its serious attention in the immediate future is the misuse and abuse of antibiotics. It is estimated that each year in Europe 400 thousand citizens are hospitalised due to becoming infected by resistant microorganisms, whereas over 25000 lose their lives from such infections [8]. Sweden has already prepared written instructions for antibiotic use, whereas it is also expected to be followed by the rest European countries.

Finally, the biggest challenge that the pharmaceutical world has to deal with is to impress upon patients and healthcare professionals (doctors, pharmacists, nurses etc.) of their responsibility to report any adverse drug reactions that they observe or experience. Although some efforts have been made they need to be intensified by national competent authorities and pharmaceutical companies and must include education and campaigns to increase awareness. It needs to be understood that reporting an adverse drug reaction does not indicate the manufacturing company as 'guilty', but helps them and the entire health care community to better understand their medicines, thus aiming to protect all patients through preventive measures. Adverse drug reaction reporting should be considered as a contribution of patients and healthcare professionals to the public health.

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A glimpse of Cyprus: a view from the seabed: A Stunning Underwater World.

From intriguing sea caves to silent shipwrecks, and from magnificent ruins of once-thriving ancient city-kingdoms to a beautiful and rich marine life, the underwater world of Cyprus is as mysterious as it is spectacular. Natural wonders and submerged man-made structures combine in numerous locations around the island to create a stunning artwork that, sadly, can rarely be seen.

Widely popular among divers from around the world who spend hours exploring their unique features and tunnels, the many sea caves around Cyprus are a truly breathtaking sight. Sea caves can be found at Alaminos, Pegeia, Akamas, and Ayia Napa. Yet, perhaps the most notable example are the majestic Amphorae Caves off the coast of Paphos which, according to an American team of archaeologists, was created by movements in the seabed over the last two thousand years, and owes its name to one remarkable and iconic cave with a roof encrusted with amphorae.

The seabed around the island is home to a number of shipwrecks, which have been lying silently for decades while fish swim through their dark, foreboding labyrinths. Perhaps the most famous of all is the wreck of the MS Zenobia; a Swedish-built ferry launched in 1979 that capsized and sank on her maiden voyage in June, 1980. Approximately 180 metres long, the wreck now rests on her port side at a depth of approximately 42 metres and 2 nautical miles off the coast of the town of Larnaca where it provides one of the best wreck diving sites in the world. Fortunately, there were no lives lost when it sank which was due to a software error.

The underwater world of Cyprus also comprises the ruins of a number of ancient cities, some of which can easily be detected from the shore. Near the town of Famagusta lie the fascinating ruins of the ancient Roman city of Salamis, whereas just off the coast of Limassol the harbour of the ancient Amathus attracts guests on a daily basis. Dating back to 1100BC, Amathus was one of the most significant ancient city-kingdoms of Cyprus and is believed to have been the first inhabited city of Limassol. Lying underwater, its harbour is to be found next to a number of other parts of the ancient city, which include the acropolis and agora, the stoae (covered walks), the baths, the basilicas, as well as a sanctuary of the goddess Aphrodite.

Due to its geographic location, Cyprus also boasts the rich marine life of the Mediterranean Sea. Though a diversity of fish and rare plants decorate the underwater world around the island, the sea world of the Akamas peninsula in the northwest and the associated national park in particular offers a glimpse into an underwater environment teeming with life. According to the European Environment Agency, it is one of only 22 areas of endemism in Europe as it portrays both the beauty and the abundance of Cyprus marine life.

Here, the stunning rock formations and coastal reefs are inhabited by a variety of colourful fish, octopus, mussels, eels, cuttlefish and sea urchins, as well as sponges, coral, and spectacular sea anemones. Finally and perhaps most importantly, it offers a haven and breeding ground to two of the most exquisite and rare examples of marine life, namely the green sea turtle (Chelonia mydas) and the loggerhead sea turtle (Caretta caretta), both of which are endangered species and are the subject to protection.

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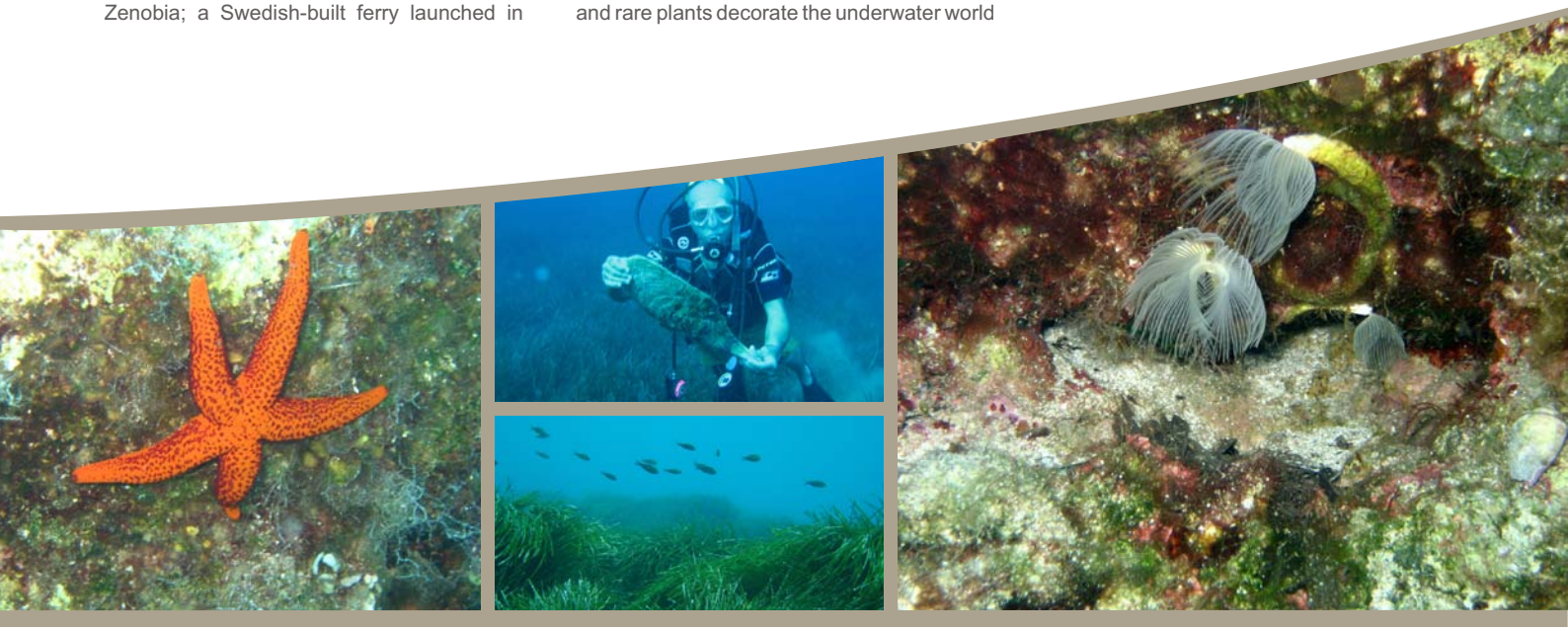

Photos by George Alexandrou, Electrician - Remedica

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