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REGISTRANT'S NAME EpiFan Limited

\*CURRENT ADDRESS Level 10  
92 Collins Street  
Melbourne, Victoria 3000

\*\*FORMER NAME \_\_\_\_\_

\*\*NEW ADDRESS \_\_\_\_\_

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Collaboration research progress delivery

2003

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**Notice of Meeting**

The EpiTan Limited Annual General Meeting will be held at:  
Stamford Plaza Melbourne  
111 Little Collins Street Melbourne 3000  
On Friday 31 October 2003 commencing at 10.00am in the  
Edinburgh Room on Level 1.

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EpiTan Limited (ASX ticker: "EPT") is an emerging biotechnology company with a pre-eminent position in the prevention of DNA & skin damage from ultra-violet (UV) radiation exposure through the stimulation of melanogenesis. Based in Melbourne, Australia, EpiTan holds a unique technology platform centred on its leading drug candidate Melanotan®. The company has the exclusive worldwide rights to develop Melanotan which, like sunlight, stimulates the production of melanin (melanogenesis - a unique biochemical process) in the skin resulting in a tan. Simply, it allows a tan to develop without exposure to harmful levels of UV light.

Melanotan is currently concluding its Phase IIb clinical trials at two sites - the Royal Prince Alfred Hospital in Sydney and the Royal Adelaide Hospital. These trials are designed to demonstrate that Melanotan can reduce the incidence of skin damage resulting from harmful exposure to ultra-violet light.

EpiTan has now successfully developed a user-friendly drug delivery formulation of Melanotan in the form of a slow release implant. This will be used in the remaining clinical program and the commercialised product.

EpiTan is also investigating Melanotan as a therapeutic agent for UV-associated skin disorders and diseases such as polymorphous light eruption, vitiligo, solar urticaria, albinism, psoriasis and various other similar afflictions.

Potential markets worldwide for Melanotan for dermatology purposes are estimated at US\$2.5 billion. An even greater market (more than US\$5 billion) exists for Melanotan as a new safe (sunless) tanning drug.

# chairman and managing director's report

Dear Shareholder,

I am particularly pleased to report to you that this year your company has achieved major milestones in the advancement of its clinical trial and drug development programs with Melanotan. Progress has proceeded according to management's schedule and within budget.

## Highlights for the year

- Phase II clinical trials progressed extremely well at the Sydney and Adelaide sites;
- Successful development of a long acting implant, now ready to go into human clinical trials in November 2003;
- Secured the rights through a collaborative agreement signed with CollaGenex and Thomas Sköld to develop a topical formulation;
- Collaborative research agreement signed with Monash University (Melbourne) and the Institute of Medical and Veterinary Science (IMVS) based in Adelaide to fast track development of the topical formulation;
- Additional \$1.3 million capital raised from existing and new shareholders;
- Market capitalisation increased to \$24.5 million (2002 - \$9.5 million).

## Highlights since 30 June 2003

- \$1.5 million cash received from exercise of listed options in July;
- Successful placement of 14.5 million shares raising \$7.4 million in August;
- Volunteer participation in Phase IIb clinical trials concluded on schedule in mid September.

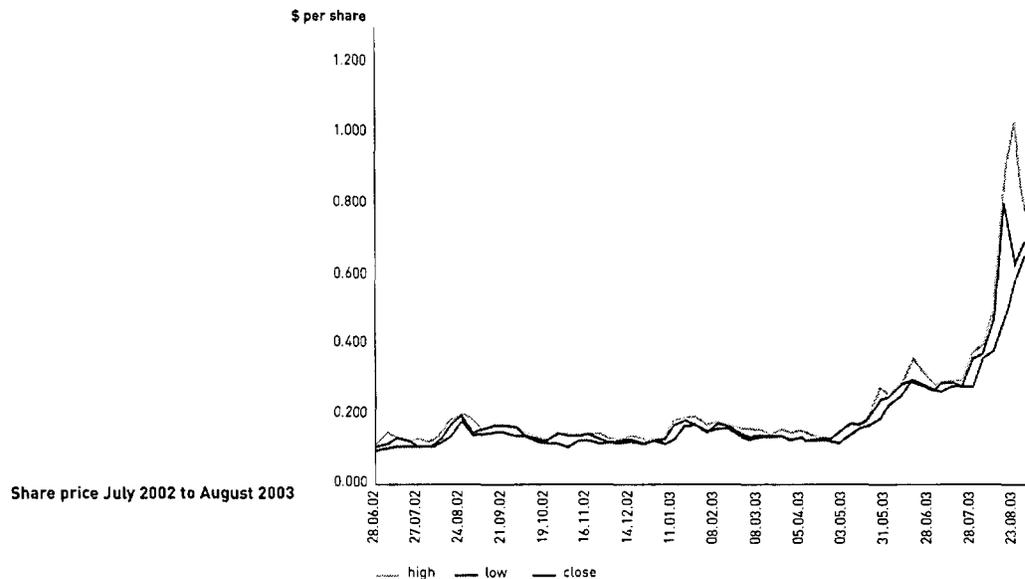
## REVIEW OF OPERATIONS

Expectation for project and corporate development over the next 12-18 months is high in keeping with the current status of Melanotan's progress and its potential global commercial value as a new drug candidate.

### Financial

At the beginning of the year the company's cash resources were \$4 million. During the year the company spent \$3.4 million including \$2.6 million on clinical trials and drug formulation research and development, earned \$136,000 in bank interest and received \$141,000 in GST refunds. A total of \$1.3 million was raised in fresh capital during the year from both the Share Purchase Plan in March and the exercise of listed options in June. At the end of the financial year, the company's financial resources amounted to \$2.6 million; this figure excludes cash of \$1.5 million received in the first week of July from options exercised under an underwriting arrangement in place with Intersuisse Corporate.

In August, EpiTan increased its cash resources to \$10 million after the placement of 14.5 million shares to institutional and sophisticated investors. These resources will enable your company to progress its clinical and pharmaceutical development programs very aggressively during the coming year.



Increase in share price from \$0.11 at 1 July 2002 to \$0.66 cents at 29 August, 2003;

### Clinical trials

The Phase II clinical "sunburn" trial got underway at two sites – Sydney's Royal Prince Alfred Hospital and the Royal Adelaide Hospital. The trial involves eighty healthy volunteers being administered Melanotan. The trial's key objective is to measure the effectiveness of the drug to increase skin melanin density and reduce sunburn injury which results in DNA and skin damage. The subjects, of varying skin types, receive controlled levels of UVA and UVB radiation onto a small area of skin resulting in a level of burning similar to spending 30 – 120 minutes in strong sun without sunscreen. A skin biopsy is taken to measure the level of resulting sunburn injury. The volunteers then receive a regime of Melanotan, the same UV radiation exposure, and another skin biopsy. In May 2003 the company announced that the first group of subjects had completed the three month study and that the results were "excellent". The last group of volunteers has now completed their regime and preliminary results are expected in early November.

### Drug delivery formulations

Two major developments in drug delivery formulations were made during the year. These new formulations both have potential to increase the commercialisation of Melanotan compared to the current daily injection.

In February 2003, EpiTan announced the successful development of a sustained-release formulation for Melanotan. The new formulation was the product of a successful strategic collaborative agreement with Southern Research Institute (Alabama, USA) initiated in May 2002.

The new formulation is a small implant designed to be placed under the skin. It is made of the same material that has been used for many years in "self-dissolving" stitches and is therefore known to be safe and reliable. As the implant is totally biodegradable it does not have to be removed at the end of the treatment.

The formulation is a major improvement on the daily injections being used in the current Phase IIb clinical trial. Melanotan will be released into the body over a period of time so that the subjects participating in the next clinical trial will need only one injection.

Similar implants, such as Zoladex® (AstraZeneca) for the treatment of prostate cancer, have already been approved for use in Australian and worldwide markets.

In May 2003, EpiTan announced the signing of a strategic collaborative agreement with CollaGenex Pharmaceuticals Inc. of Newtown, Pennsylvania, USA and Mr Thomas Sköld of Norrtälje, Sweden to develop a topical formulation. CollaGenex acquired the rights to the novel drug delivery system, known as Restoraderm™ technology, from Mr Thomas Sköld, the inventor of the technology, in 2002. EpiTan has sub-licensed this technology from CollaGenex.

This technology improves the feasibility of developing a topical formulation for Melanotan, as previous technology was unable to achieve this objective. It is envisaged a new formulation may enable Melanotan to be released directly into the skin to the melanin producing cells. This will build on the successful development of a single dose slow-release implant.

In addition, it is important that EpiTan continues to investigate the development of additional delivery mechanisms including lotions and patches. It is expected that Melanotan will be first launched onto the market with the implant. In due course, the successful development of a topical lotion will offer patients and doctors the choice of an alternative user-friendly and convenient delivery for Melanotan.

### Investor relations – communications

Publicity this year on the Melanotan story, has like the previous year, been explosive. Media interest throughout the world has been attracted to this drug and its potential applications for skin protection and therapies.

The story has been covered widely in domestic and international newspapers, TV, radio and professional publications, and extensive interviews have been given by senior company officers.

During the year, EpiTan maintained its program of continuous disclosure to its investors and financial markets. The company also continued its policy of close association with the financial community by undertaking regular presentation briefing programs with institutions and brokers. The frequency of these programs are planned to increase as momentum with the Melanotan project increases this year. A greater awareness of EpiTan has resulted in a total number of shareholders increasing by 82% from 1326 to 2411 over a period from 30 June 2002 to 29 August 2003.

### Outlook

The company will continue to build on its unique melanogenesis platform technology through its leading drug candidate Melanotan. In September, volunteers completed their participation in the Phase IIb clinical trials using the daily injection delivery mechanism. EpiTan is confident that this trial will confirm its earlier, interim progress report of increasing the skin's melanin density and reducing sunburn injury. In November 2003, the company will begin trials using the newly developed sustained release formulation. These Phase I/II trials will be conducted at the Queensland Institute of Medical Research (QIMR) and will involve up to 24 healthy human volunteers. Aside from the usual safety and toxicity data, the trials will confirm the optimal dose of drug to be placed in the long acting implant. This trial is scheduled to take six months.

The company is meeting with the US Food and Drug Administration (FDA) in early October 2003 for the purpose of obtaining approval to begin trials in the USA, via an Investigational New Drug (IND), with Melanotan implants.

During 2004 the company also plans to carry out clinical trials in Europe for polymorphous light eruption and will begin planning for the final Phase III trials expected to take place in the US, Europe and Australia.

As is generally the case with small biotechnology companies with a drug candidate at the Phase II trial level, EpiTan is currently actively seeking a partnership with a larger pharmaceutical company with the view to securing funding for the Phase III trials and commercialisation stages.

The 2003 year saw life science companies worldwide experience very difficult operating environments. As one of the companies, EpiTan has seen the troubled times through thanks to the efforts of its directors, management, staff and consultants who have responded to these taxing circumstances. My personal appreciation goes to them for their endeavours in contributing to the point at which the company now stands.

During this year, shareholder and stakeholder contact with company management has increased considerably. There is always an appeal when this occurs as it affords an ideal mechanism for increasing confidence and positive outcomes between parties.

The 2003 year was one of major progress. With a drug candidate poised to come formally out of a phase II trial, it is anticipated EpiTan will join a select group of companies with an advanced stage drug establishing the springboard for greater potential achievements in the coming year.



**DR WAYNE MILLEN**  
CHAIRMAN AND MANAGING DIRECTOR

directors



\$2.5 million in additional capital raised from existing and new shareholders from

**Dr Wayne Millen** BSc (Hons) PhD  
FRACI C CHEM FAusIMM AFAIM -  
*Chairman and Chief Executive  
Officer*

Dr Millen is the founding Managing Director of EpiTan Limited. He has a PhD in chemistry and biochemistry from the University of Western Australia and is a Chartered Chemist with extensive experience over 30 years operating his own commercial enterprises. In 1967, as a Fulbright scholar, Dr Millen undertook biochemical research in the Molecular Biology Institute at the University of California, Los Angeles, with Nobel Prize laureate Dr Paul Boyer. In 1970, he established his own consultancy business, the Pitbara Group, for the testing and assessment of biological, environmental and mineral materials, which grew to be the largest organisation of its kind in the Australasian region. In 1983, Dr Millen moved into the area of venture and development capital investment with an emphasis on companies involved in technological innovation. He has maintained this focus to the present time and has been the lead investor and strategist in several private and public companies. Dr Millen's scientific and business experience, along with his proven entrepreneurship has been instrumental in maximising corporate opportunities for EpiTan.

**Dr Helmer Agersborg** BS PhD -  
*Non-executive Deputy Chairman*

Dr Agersborg received a PhD in Physiology from the University of Tennessee in 1957 and shortly after was appointed to the position of Clinical Physiologist at Wyeth Laboratories in Pennsylvania, US. In 1975, he was promoted to Vice-President, Research and Development with responsibility for research, chemical, pharmaceutical and biological development, quality assurance and regulatory affairs. In 1985, he was given the additional responsibility for clinical research and made Senior Vice-President. In 1987, American Home Products began to merge its international, Ayerst and Ives and AH Robins research and development activities into one unit, Wyeth-Ayerst Research, an organisation of approximately 3000 people. Dr Agersborg was made President, Wyeth-Ayerst Research in 1987. During his distinguished forty years in the pharmaceutical industry companies under his direction had more than 50 new drug applications approved in the US, many marketing applications approved outside the US and innumerable IND's accepted around the world. Following his retirement from Wyeth-Ayerst in 1990, Dr Agersborg became involved in a series of start-up pharmaceutical development companies. Dr Agersborg is currently Chairman and President of MelanoTan Corp, President of Aferon Corp and director of Virxsys Corporation, all pharmaceutical companies. Dr Agersborg contributes broad international pharmaceutical development experience at the highest level to the company.

**Dr Terry Winters** BSc PhD -  
*Non-executive Director*

Dr Winters is a director of four private US based companies: MelanoTan Corp, licensor of EpiTan's technology; Alliance Medical Corp, a medical device company and Amplimed, an oncology drug development company. He is CEO and a member of the board of Aferon Corp which is developing vanilloid drugs for incontinence, rhinitis and headache. Dr Winters is also a Special Limited Partner of Valley Ventures, a \$130 million venture capital fund based in Scottsdale, Arizona. Dr Winters was formerly an experimental chemist and licensing manager with Goodyear Tyre & Rubber Co. in Ohio and then licensing manager with Diamond Shamrock and Vice-President of DS Ventures, investing in life science projects. In 1983, he co-founded, and is a General Partner of Columbine Venture Fund which has invested over \$125 million in life science and technology companies in the western US. From the Columbine investments, successful companies have been Orthologic Corp, CollaGenex Pharmaceuticals, Nanophase Technologies, Curis, Neogen (all NASDAQ quoted) and Microgenics. Dr Winters' understanding of US financial markets, particularly capital raising and Nasdaq listing brings an international perspective to the company's global corporate planning.

**Mr Stanley McLiesh** BEd -  
*Non Executive Director*

Mr McLiesh has extensive experience in commercialising pharmaceutical products internationally. Formerly General Manager, Pharmaceuticals at CSL Limited, he was closely involved in the transition of CSL from government ownership through corporatisation to a highly successful listed company. While at CSL, Mr McLiesh brokered numerous in-licensing agreements with international companies which enabled CSL to expand into new markets profitably. The rapid acceleration of growth in sales and marketing associated with this in-license activity resulted in the establishment by Mr McLiesh of new sales and marketing teams. He has also been closely involved in a number of merger and acquisition negotiations; the establishment of partnerships and collaborative relationships; quality control, manufacturing and the negotiation of supply agreements for CSL's export products to international markets. Mr McLiesh's considerable experience in the international pharmaceutical industry will facilitate EpiTan's expansion strategies.



**Mr Michael Kleinig** BAppSc (Chem/Bio) - *Manager-Pharmaceutical Development/New Business Development*

Mr Kleinig's broad knowledge in the fields of process development (from research scale through to commercial scale), project management, immunology and protein chemistry make him well suited to his role as Manager-Pharmaceutical Development. Mr Kleinig was formerly a Senior Research Scientist at CSL Limited where he was employed for 15 years, working in research and development in both the Pharmaceutical and Bioplasma divisions. He graduated from Swinburne Institute of Technology with a double major in Applied Chemistry and Biochemistry. His primary responsibilities at EpiTan are to investigate the best method(s) of delivery for Melanotan and secure a suitable commercial scale manufacturer of the synthetic peptide. Mr Kleinig in his role as New Business Development Manager is actively involved in seeking a partnership with a larger pharmaceutical company.

**Chris Rossidis** - *Manager Pharmaceutical Products Marketing*

Mr Rossidis has broad experience of the pharmaceutical industry after spending 15 years in sales and marketing roles at Eli Lilly, Glaxo Wellcome and latterly CSL. As CSL's Business Development Manager, he was responsible for supporting CSL's growth through identifying and evaluating new prescription medicine business. At EpiTan he will be primarily responsible for the establishment and development of a dermatology products business in Australia and New Zealand by sourcing and in-licensing a range of innovative products within the field of dermatology.

**Iain Kirkwood** MA(Hons)(Oxon), FCPA, FFTP, CA, MAICD *Chief Administrative Officer*

Mr Kirkwood brings to EpiTan extensive financial, commercial and business/strategic experience.

With a successful career spanning over more than 25 years in Australia, Britain and the USA he has held a range of senior financial positions with major public companies including F.H. Faulding & Co. Limited, Santos Limited and Pilkington plc. He is a Chartered Accountant, CPA, former President of the Finance and Treasury Association of Australia and a member of the Institute of Company Directors.

Mr Kirkwood will be integral to the development of the company's financial and commercial profile as the Melanotan project moves towards maturity.

**Dr Stuart Humphrey** BSc (Hons) PhD - *Manager-Clinical Development*

Dr Humphrey brings to the company extensive experience in the management of scientific and clinical development projects within multinational pharmaceutical environments. His clinical development and regulatory background in the field of oncology will be instrumental in progressing the company's clinical trial program. Dr Humphrey has an Honours degree in Biochemistry from the University of Liverpool and a Doctorate of Philosophy from the University of Auckland with 30 years experience in research and pharmaceutical project management. He has held the positions of Regional Operations Manager at Omnicare Clinical Research, a large international Clinical Research Organisation and Regulatory Affairs Manager and Manager Scientific Clinical Development with Bristol-Myers Squibb in Australia and New Zealand.

# management, consultants & collaborative partners



## Consultants

**Professor Robert Dorr** BS MS PhD RPh - *Scientific Consultant*  
Professor Robert Dorr is co-inventor of the Melanotan technology and was the principal investigator in Melanotan's preclinical and clinical studies performed to date in the US. He continues to have an active involvement in the Melanotan project as a consultant. Professor Dorr has a PhD from the College of Medicine at the University of Arizona, and is currently the Professor of Pharmacology and Director of the Pharmacology Research Program at the Arizona Cancer Center. He is a registered pharmacist in Arizona and California, holds twelve US patents for anti-cancer drugs and drug delivery devices, and has authored over 150 scientific articles. Professor Dorr addressed shareholders at the last Annual General Meeting. He advises on trial protocol issues with EpiTan's clinical trial investigators, new patent matters and gives presentations to the financial community, stakeholders, researchers and media groups. His expertise includes new drug formulation, animal models of cancer and toxicity assessment and clinical pharmacokinetics of new agents. He is a member of the American Association for

Cancer Research, the Southwest Oncology Group and the International Society of Oncology Pharmacy Practice, in which he received the Outstanding Biotechnology Award in 1999.

**Professor Terry Dwyer** AM, MB BS MPH MD - *Scientific Consultant*  
Professor Dwyer is Director of the Menzies Centre for Population Health Research managing a staff of 70 and coordinating research projects including those on cancer, heart disease, multiple sclerosis, childhood asthma and diabetes. He has studied at Yale and worked at Baylor College of Medicine, Houston and the CSIRO Division of Human Nutrition, Adelaide. Professor Dwyer has a particular interest in the role that melanin plays in protecting individuals against skin cancer. In carrying out his research, Professor Dwyer has pioneered a method of measuring melanin density in the skin using an instrument called a spectrophotometer. The spectrophotometer shines light on a small section of the skin and, by measuring the amount of light reflected, a very accurate measurement of the melanin density can be made. EpiTan has used this

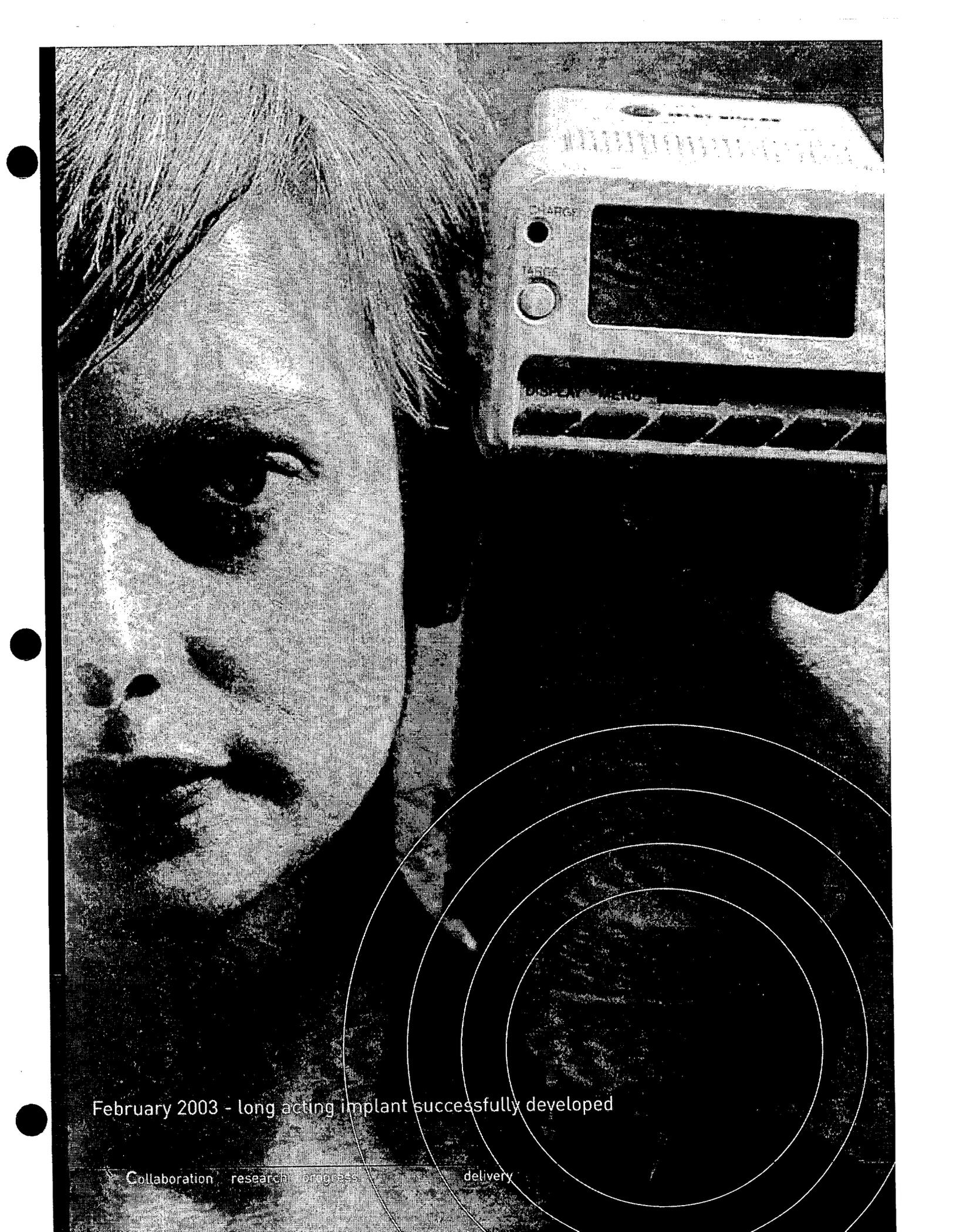
measurement system with success in its clinical trial program to date. As an integral part of his work with EpiTan Professor Dwyer's team is measuring the genotype of clinical trial subjects to obtain an estimate of the genetic risk of developing skin cancer.

**Mr Thomas Laughlin** BA MBA - *In-Licensing Consultant*  
Mr Laughlin has had a distinguished career in the marketing sector of the pharmaceutical industry. He has held positions at the highest level in the world's largest pharmaceutical companies, successfully growing sales through identifying and building new business and revitalizing existing brands. Mr. Laughlin has had positions of increasing responsibility with Pfizer, Procter & Gamble, Pharmacia & Upjohn, and Bayer. As part of its plans to expand its operation base, EpiTan has contracted Mr Laughlin to investigate in-licensing dermatology products for the Australasian region that will complement the company's existing interests in skin care.

## Collaborative partners

To complete the existing loop of expertise, EpiTan has further developed collaborative relationships with renowned Australian and American research organisations. In Australia, these include Monash University, Melbourne, the Institute of Medical and Veterinary Science, Adelaide and the Genetic Epidemiology Unit at the Menzies Centre for Population Health, Tasmania. The company is also working with Southern Research Institute in Alabama, USA to develop a sustained-release delivery formulation for use in the company's clinical trials. In June 2003 a collaborative treatment with Collagenex Inc and Thomas Sköid to develop a topical formulation using Restoraderm™ technology was signed. The innovative technologies being used in this collaborative work have significantly increased the body of information the company has about Melanotan and ongoing studies may provide valuable insights into new therapeutic applications for Melanotan.

\$0.51 per share in August 2003



February 2003 - long acting implant successfully developed

Collaboration research progress delivery

# melanogenesis: a unique biochemical process

**Melanin production - melanogenesis** In the outer layer (epidermis) of the skin, there are specialized melanin-producing cells called melanocytes. These melanocytes form long slender processes that ramify among neighbouring cells called keratinocytes. In this way, each melanocyte makes contact with around 30-40 keratinocytes and this constitutes the so-called epidermal-melanin unit. The melanocyte has receptors on its surface that specifically interlock with a natural hormone called  $\alpha$ -melanocyte stimulating hormone or  $\alpha$ -MSH. These receptors, when activated by  $\alpha$ -MSH trigger the cell to make the dark pigment called melanin.

When a person is in the sun or solarium, ultraviolet (UV) radiation from the sun penetrates the upper layers of the skin and damages it. This gives the tell tale red appearance, which signifies increased blood flow to the area in an attempt to repair the damage. It is believed that signals such as fractured DNA particles from the damaged cells, are responsible for triggering the release of  $\alpha$ -MSH from adjacent cells which migrate to the specialised tanning cells. These cells then produce the tanning molecule melanin. Melanin production takes several days and the melanin is formed into small packages which are transferred to the surrounding keratinocytes via the slender processes. These cells, now filled with the dark brown melanin pigment move towards the surface of the skin and give the skin the "tanned" look. This is the body's way of protecting the skin from subsequent sunburn. The person develops a tan, but only after significant damage has been done to the skin cells. Over several weeks these cells are sloughed off and new cells take their place causing the tan to fade.

**What is melanin?** Melanin is a generic term that refers to a group of rather complex biopolymers. The chemical composition and physical properties are highly dependent on how and where it was formed. In other words in an analogy to the term 'plastic' - plastic is not a unique term and can be made up of many units of ethylene, propylene for example to make polyethylene and polypropylene. In each case, the plastic exhibits quite different properties and the same applies to melanin. Eumelanins and Phaeomelanins are the two classes of melanins present in human skin. Eumelanin is the dark brown to black pigment and is the form of melanin protective against UV radiation. Phaeomelanin is a red-yellow pigment and is the form of melanin associated most closely with the potential to sunburn easily and to develop skin cancers. Individuals with light coloured skin and brown, blond or red hair tend to have a significant amount of phaeomelanin in our skin whereas darker skinned and black haired individuals have predominantly eumelanin.

**Melanogenesis and photoprotection** The process whereby melanin is provided in the body is termed 'Melanogenesis', a unique biochemical process. The mechanisms proposed for photoprotection by eumelanin include but are not limited to the absorption and scattering of UV light, free radical scavenging and quenching of UV light. There is no doubt that melanin in human skin attenuates the penetration of UV radiation<sup>1</sup>, there is also increasing evidence that melanogenesis represents a major antioxidant defence mechanism in melanocytes neutralizing the deleterious effects of free radicals and active oxygen species<sup>2</sup>.

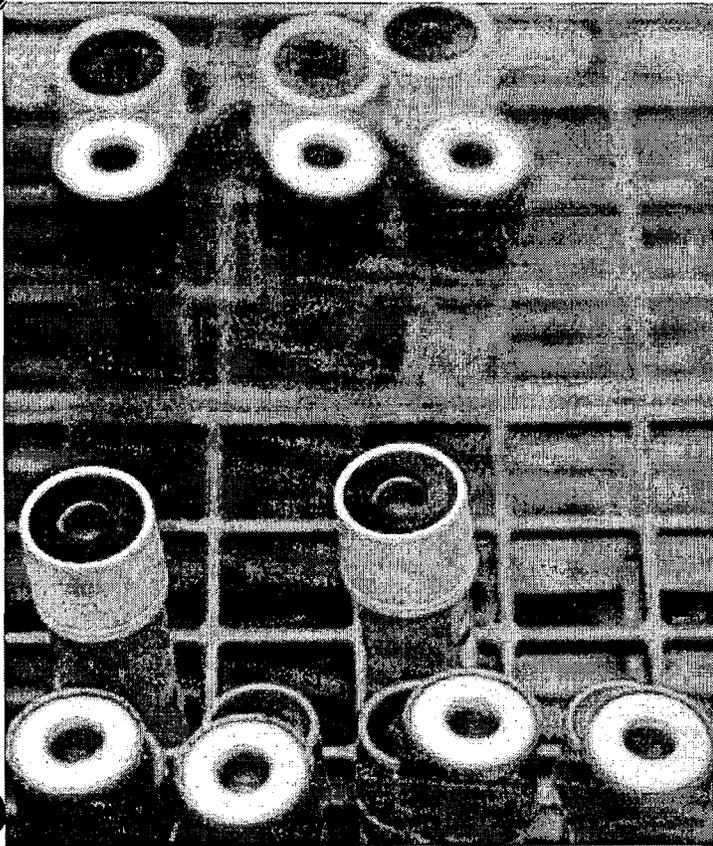
*Professor Ross Barnetson Head of the trial,  
Royal Prince Alfred Hospital*

We are extremely happy with the progress of the trial. I am convinced that people will take a tanning drug, because a certain percentage of the population want to have a tan. The benefit of Melanotan giving a tan is that people don't get the sun damage and that's the great advantage of this. The only way to get a tan today is get the sun damage first. The market for this drug will certainly stretch beyond Australia to places like the United States and Europe. To have a tan is to be beautiful and that holds in Australia, the US and Europe.

*Adrian trial volunteer*

I used to have quite pale skin, especially on my face and my upper chest. But ever since I have been taking Melanotan, I have developed quite a healthy tan. It's been excellent. I would definitely use it if it was commercialised. Sunburn is a big problem for lifesavers, and anything that is going to prevent us from getting sunburn while we are out there doing our job would be excellent.

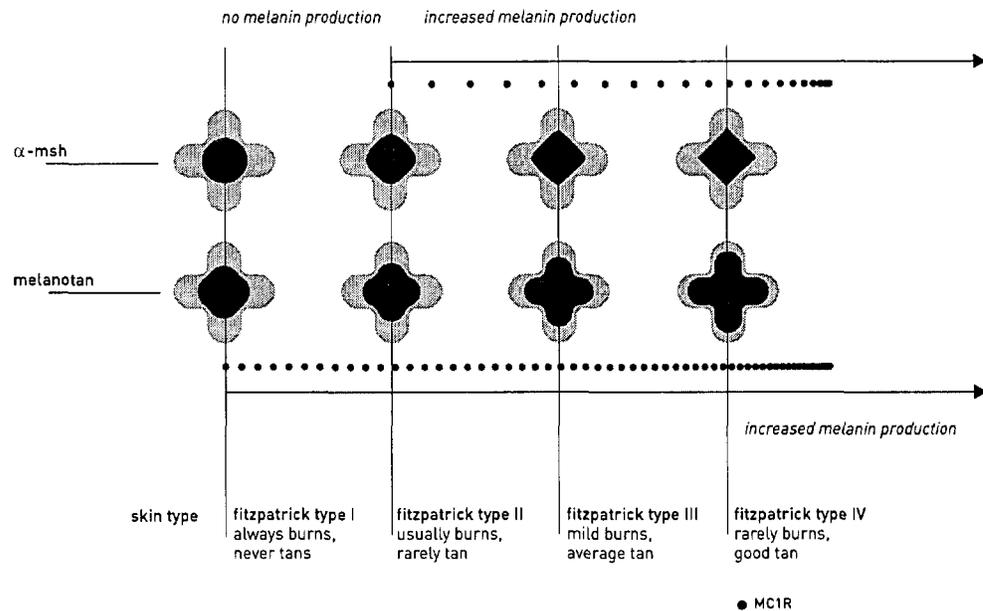
# melanogenesis: a unique biochemical process



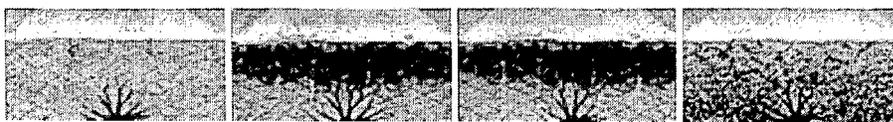
## Skin colour – Evolution and migration

In their analysis of the evolution of humans and early migratory patterns, scientists, Nina Jablonski and George Chaplin concluded that populations evolved particular skin colours in order to better survive in certain environments. The dark skin pigment acts as a natural sunblock – the more you have the better the protection from potentially harmful radiation. Dark skin became an essential human trait at least 1.5 million years ago when our ancestors first attained human-like body proportions and started to live in more exposed habitats. But as later ancestors roamed around the globe, particularly northwards into cooler climatic zones, their tropical skin tones posed a problem. Sunlight penetrating skin spurs production of vitamin D, essential for absorbing the calcium needed to build and support the skeleton. Lighter skin evolved on residents in higher latitudes to ensure sufficient UV light, diminished by the sun's low angle and a thicker blanket of atmosphere, gets through. Conversely, in the hotter tropics, humans needed more melanin to avoid UV damage to the skin and to avoid natural overproduction of vitamin D. Humans living in the middle latitudes or more temperate zones – most of the United States and southern Europe – have moderately pigmented skin but an excellent ability to change their skin tone through tanning. They increase pigment during summer but then lighten the tan during winter, in order to take advantage of shorter, less bright days.

## α-MSH vs Melanotan



June 2003 - collaborative agreement with CollaGenex and Thomas Sköld to develop



## Platform technology

With Melanotan, EpiTan is developing a platform technology for melanogenesis. This is a medically significant advancement out of which is likely to arise protection and treatments for photosensitive skin disorders which occur from solar exposure. These include sunburn injury, polymorphous light eruption (PMLE), actinic prurigo and solar urticaria.

As an example, the market for sufferers of PMLE alone is significant. Research has indicated that approximately 20% of the Scandinavian population and between 10% and 20% of British and Americans suffer in late spring and early summer.

Typically, those affected by it will have been exposed to the sun or two to three days while on holiday, although the complaint does occur between the spring and autumn months in the UK, and sometimes as little as 15 minutes' exposure to sunshine can induce the condition. It can even be brought on by sunlight penetrating through a window or thin clothing.

A delayed-onset, spotty, itchy eruption appears on the skin, and may take between 5 to 10 days to clear. The rash usually consists of small red spots or blisters and can appear on any part of the body that has been exposed to sunshine, although commonly the face and the backs of the hands will be spared. It tends to heal without scarring.

About 10 to 20 per cent of the northern European population is affected by PMLE, which is more common in females than in males. The condition can affect all ethnic groups, and research suggests that 20 per cent of patients have a family history of the complaint. Those suffering from PMLE usually do so by the age of 30.

The cause of PMLE is not completely understood. It's thought by some experts that PMLE may be an allergic reaction following the interaction of sunlight with proteins in the skin.

It has a nuisance value and may restrict lifestyle in the summer months, particularly during holidays. If severe, it may cause significant problems that require more active therapy than simply keeping the affected area out of the sun. Most patients learn to know their skin and can judge how much sunlight exposure they can tolerate.

The global market for PMLE is estimated to be US\$1.0 billion per annum.

Another example is Vitiligo. About 1 to 2 percent of the world's population, or about 50 to 100 million people, have vitiligo and this condition affects about 1% to 2% of the US population, or about 3 to 6 million people. In some countries, the incidence is even higher. Worldwide, there are thought to be more than 100 million people with the condition. For years, many dermatologists have told their patients that vitiligo is untreatable, or have offered only limited treatments such as steroid creams or PUVA. Ninety-five percent of people who have vitiligo develop it before their 40th birthday, most between the ages of 10 and 30. The disorder affects all races, ethnicities and both sexes equally, which suggests that it truly is a human problem.

With respect to the reduction of skin damage from sunburn, as a preventative drug candidate this global dermatology market is estimated to be US\$2.5 billion per annum. Sunburn injury is a pre-cursor of skin cancer and EpiTan envisages that by using Melanotan, skin management programs now will enable the reduction in skin damage, and in times to come, skin cancer.

Since Coco Chanel claimed her 'tan' was fashionable back in the 1930's, whether one approves or not, a 'tan' is universally regarded as fashionable. Respondents in surveys, particularly in places like Britain, confirm that they look 'better' or 'healthier' with a tan.

Independent research has shown that global markets for tanning in a solarium or for 'fake' skin stains are US\$5 billion per annum.

Whilst EpiTan will continue to progress Melanotan for bona fide dermatological or therapeutic reasons, it is highly likely that significant demand for the product will come from people who want a tan, but find it more difficult to get one without more harmful exposure to UV/sun than those with more pigmented skin.

Experts agree that the use of Melanotan, in conjunction with the currently accepted rigorous programs recommended by the SunSmart campaigns will be another positive step in the reduction of skin cancer. EpiTan supports this approach and will direct its marketing programs to work constructively with all relevant anti-cancer councils and equivalent bodies.

### How much melanin do we need in our skin?

Typically Caucasian people have from 0.5% to 4% constitutive skin melanin. Those fair skinned individuals with 1% or less cutaneous melanin usually burn in the sun and do not tan – these are referred to as Fitzpatrick skin type I. Fitzpatrick skin types II and III have melanin densities in their skin ranging between 1% and 3% and type IV skin which always tans and rarely burns contains more than 3% melanin. Dwyer et al<sup>3</sup> recently concluded from measurements of cutaneous melanin density at the upper inner arm of caucasian men living in Australia that those with 0-1% melanin were associated with approximately 7 times greater relative risk of malignant melanoma or basal cell carcinoma than men with > 3% melanin. Therefore, a difference of just 1-2% in the skin content of melanin may provide significant added protection against sun-induced skin cancer.

Melanotan is a more potent synthetic copy of the naturally occurring hormone,  $\alpha$ -MSH. When a person receives Melanotan, the drug is dispersed all over the body through the blood system and acts in the same way as the natural hormone, stimulating the cells that produce melanin. Melanin granules disperse into the epidermal skin cells and form a shield around the cell's nucleus to protect the cell's vital nuclear DNA from being damaged by ultraviolet light from the sun's rays. A protective tan is developed, but without the skin damage.

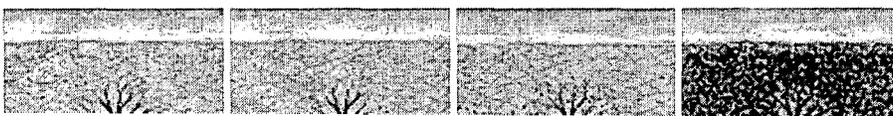
In summary, the natural way we tan is that the UV rays in sunlight damages the skin cells and triggers both keratinocytes and melanocytes to produce  $\alpha$ -MSH. Tanning then occurs in a response to the damage and the skin now has increased protection from sunlight. In nature this protection has come too late to prevent the skin damage (sunburn or skin cancer) that occurred prior to the instigation of tanning. With Melanotan, this takes the place of  $\alpha$ -MSH and so stimulates the skin to produce the protective tan before the sunlight can damage the skin.

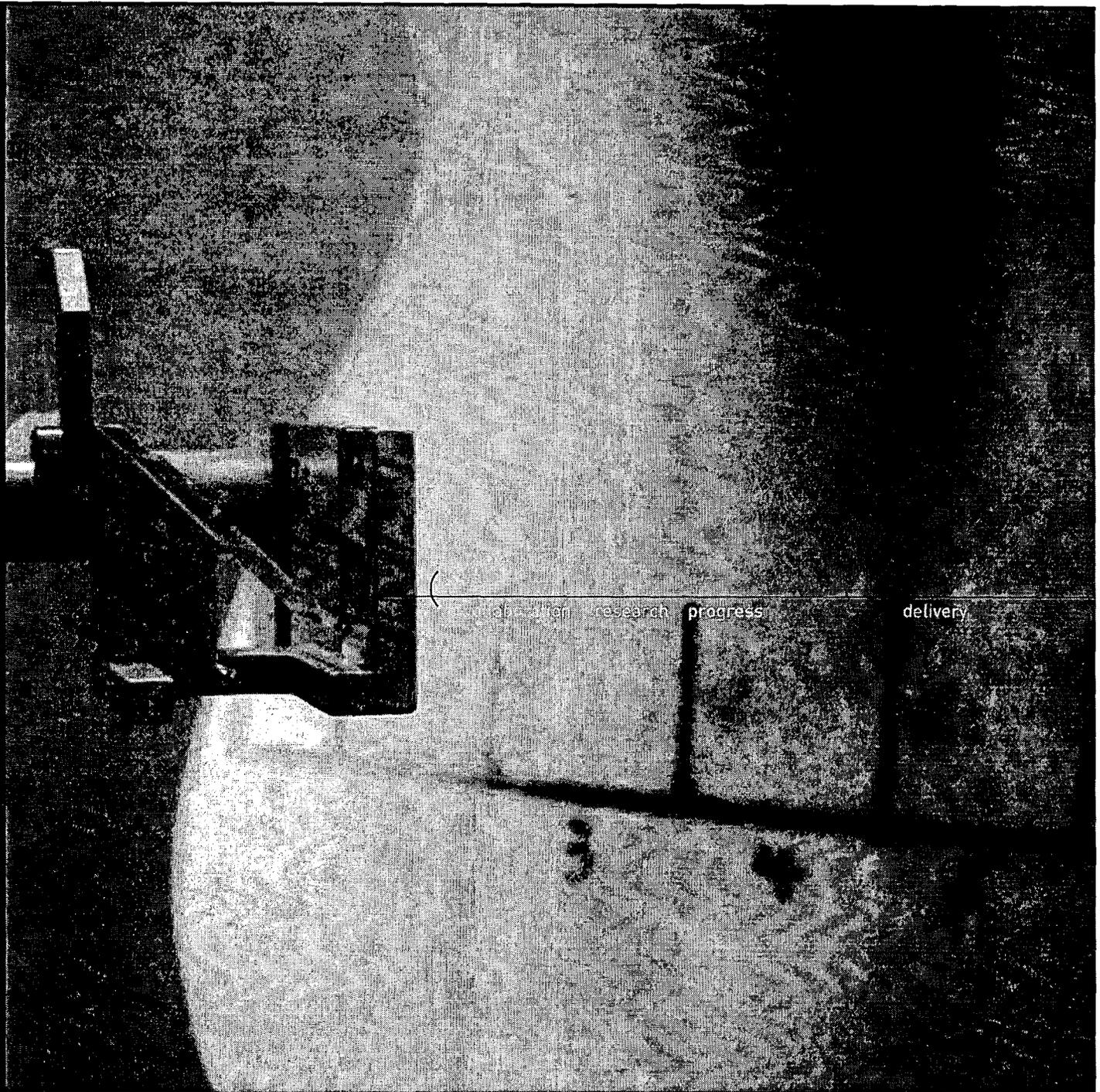
Importantly, when Melanotan initiates melanogenesis, eumelanin is preferentially made.

### Reference list

- 1 Kollias, N., Sayre, R.M., Zeise, L. & Chedekel, M.R. Photoprotection by melanin. *J. Photochem. Photobiol. B* 9, 135-160 (1991).
- 2 Bustamante, J., Bredeston, L., Malanga, G. & Mordoh, J. Role of melanin as a scavenger of active oxygen species. *Pigment Cell Res.* 6, 348-353 (1993).
- 3 Dwyer, T. et al. Cutaneous melanin density of Caucasians measured by spectrophotometry and risk of malignant melanoma, basal cell carcinoma, and squamous cell carcinoma of the skin. *Am. J. Epidemiol.* 155, 614-621 (2002).

a topical formulation using Restoraderm™ technology signed





## technical reports

The 2002/2003 year has been a watershed for EpiTan, with the achievement of major milestones across the spectrum of technical activities from clinical studies pharmaceutical development and R&D programs.

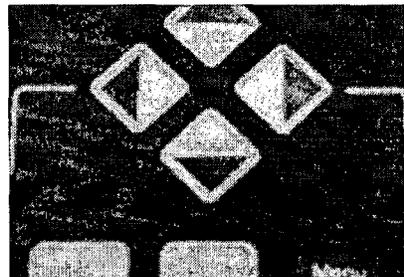
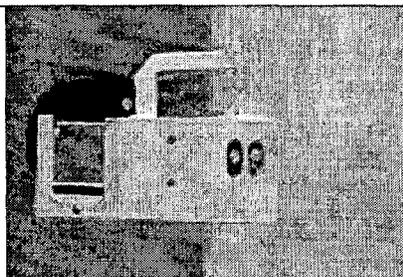
June 2003 – collaborative research agreement with Monash University, based in

# clinical development

2002/2003 saw EpiTan increase the tempo of scientific progress in its clinical trial program. This year saw the commencement of the company's second study, the Phase IIb study to continue investigating the melanogenic properties of Melanotan, and to investigate the potential protective role that this increased melanin pigmentation in the skin may have against the damaging effects of UV radiation. The company also made giant strides towards initiating its third study in Australia using sustained release delivery formulation to further enhance the efficacy of Melanotan and make the clinical trials more attractive to participants and less costly to EpiTan.

## Phase II study - Sunburn study

Following the first successful Phase I/II study at the Royal Adelaide Hospital in November/December 2001, EpiTan commenced this large scale Phase II study at the two sites, the Royal Prince Alfred Hospital in November 2002 and at the Royal Adelaide Hospital in December 2002. Under the direction of Professor Barnetson at the Royal Prince Alfred and Dr Cathy Reid at the Royal Adelaide Hospital a total of 80 volunteers were enrolled. The same subcutaneous dose of 0.16mg/kg/day given in the Phase I study was administered over three separate ten daily periods to subjects with skin types Fitzpatrick, I to IV. This study compared the degree of tanning over a three month period in the different skin types and also the incidence of sunburn cells (defined as apoptotic cells) elicited 24 hours after controlled solar irradiation to a small area of the skin. The amount of skin damage caused before and after Melanotan treatment was compared. The last subjects completed treatment in this study in mid September and preliminary results of this study are now expected in early November 2003. There has been widespread media interest in this study in Australia, UK and Germany.



*Professor Alan Cooper Clinical Associate Professor  
Dermatology Head of the Dermatology Dept - Royal  
North Shore Hospital, Sydney; Clinical Associate  
Professor of Dermatology, University of Sydney*

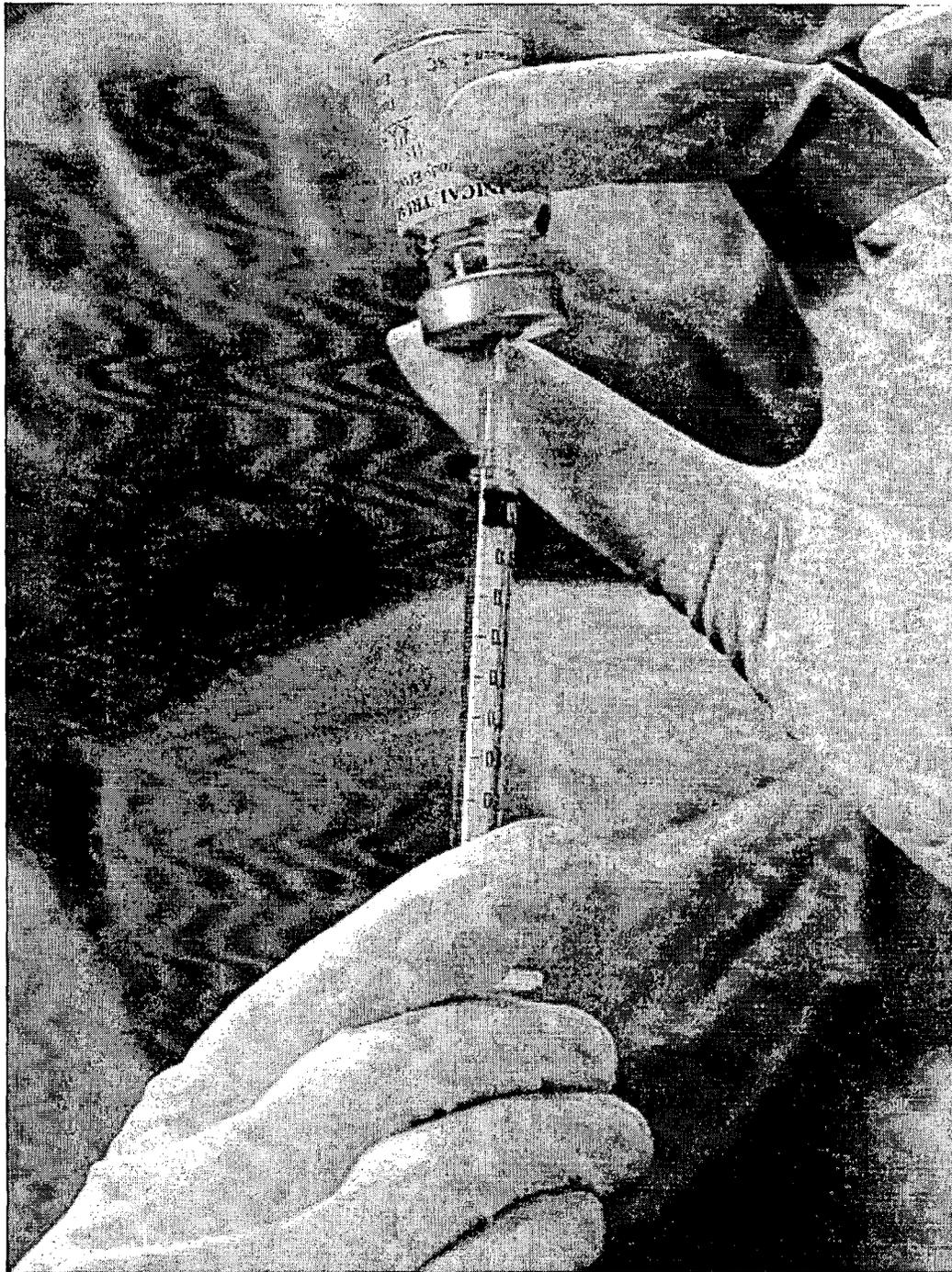
Melanin protects against UV light damage so the more melanin you have the less likelihood of developing skin cancers. If people have natural protection that reduces their likelihood of burning, then they will significantly reduce their likelihood of getting skin cancer. This is a tan that is good. Where you can get a tan without UV radiation, then that tan is a safe tan, and it can have protective benefits.

*Professor Terry Dwyer Director of the Menzies Centre for Population Health Research*

Skin pigmentation is an important predictor of risk of skin cancer in humans. The risk of skin cancer is 6 or 7 times greater in fair skinned population. The number of sunburns in a lifetime is positively associated with skin cancer in a number of studies

Melbourne, and the Institute of Medical and Veterinary Science (IMVS) based in Adelaide signed

## clinical development



*Professor John W Kelly Head of Unit – Dept of Dermatology, Head of Victorian Melanoma Service; Clinical Associate Professor, Monash University Dept of Medicine, Alfred Hospital, Melbourne*

Certainly there is the potential for people who have susceptibility to UV light for one reason or another, to use Melanotan for times when they do need to be in the sun. For example on a holiday, when sailing or windsurfing or playing golf or whatever. It's not going to replace the current methods of sun protection such as clothing and hats and sunscreens, they need to be using all of these as well. If it proves to be safe and efficacious, it will provide another string to our bow, another element in the armamentarium against the deleterious effects of UV light on the skin. Now we may be able to induce a tan, safely that will help protect.

July 2003 - approval to commence Implant clinical trials (Phase I & II) approved at

### **Planned Phase Ib study**

Company strategy is to develop a sustained (or controlled) release delivery system for future studies and for commercialization. EpiTan believes this will overcome the short term side effects associated with bolus daily injections and reduce to one, the number of injections and thus visits to the clinic. By delivering the drug at a very slow but continuous rate from a subcutaneous implant, the amount of Melanotan in the blood can be kept at the minimal level needed to produce the skin pigmentation affect. A Phase Ib dose-escalation study of a single depot injection of Melanotan to determine the most effective and best tolerated dose in healthy adult subjects will now to be conducted at Q-Pharm's purpose-built facility in the new Clive Berghofer Cancer Research Centre at the Queensland Institute for Medical Research (QIMR). The study will evaluate several doses of a small implant, similar in structure to the well-accepted medication Zoladex. The implant is designed to induce pigmentation of the skin during a 3 week period which would last for 3 months or more. This study is expected to commence in October 2003.

### **Further planned Phase II studies**

Using the newly developed controlled release formulation, further Phase II studies are designed to establish the safety and degree of tanning in Caucasian subjects with either genetic susceptibility to sunburn and skin cancer or some form of skin sun allergy (such as polymorphous light eruption [PMLE] or solar urticaria). A genotype study to investigate this is planned to be carried out at the QIMR under the direction of Professor Adèle Green, whose group has already published results indicating an increased risk of skin cancer in individuals with abnormal melanocyte receptors in their skin. Other studies to define suitable indications for Melanotan will be performed in the USA and/or Europe where conditions such as PMLE are prevalent. Between 10 and 20 percent of the population in the United States and Europe suffer from PMLE. The Studies will determine the individuals to whom Melanotan can be of most benefit. Subjects will receive the implant and pigmentation will be measured one and two months later using the non-invasive spectrophotometric measurement for melanin. The efficacy endpoint will be the reduction in the manifestation of the symptoms associated with the photosensitive disorder (sunburn; erythematous and/or blistered patches/plaques etc). The first study is planned to begin mid 2004 coinciding with Spring in the Northern Hemisphere.

### **Phase III studies**

A global phase III study (Australia, US and Europe) is expected to be performed in 2005. This will target the indication determined from Phase II studies and comprise 1-2,000 subjects worldwide. The company will seek a partnership with a larger pharmaceutical company to assist with this study.

### **Global studies - IND (US) and CTX (Europe) strategic plan**

EpiTan is working with its consultant company, Kendle, to prepare for a pre-Investigational New Drug (IND) meeting in the last quarter of this year. Opening an IND in the US with the FDA will enable EpiTan to address studies that may need to be done to facilitate a seamless transition into Phase III program conducted under a US IND format. Regulatory affairs experts Kendle International has been assisting EpiTan with its submission to the FDA. An outline of EpiTan's entire clinical program will be presented at the meeting with the FDA to enable feedback on the suitability of current and proposed data acquisition for a valid NDA submission.

In addition to the FDA, meetings with the EMEA (European Regulatory body) are planned to determine any need for additional non-clinical studies required in Europe. This will be carried out following the FDA meeting.

### **Quantitation of Melanotan in blood**

Methodologies to measure Melanotan in the bloodstream have been successfully developed by EpiTan and used in the Phase I study. The company is now engaged in refining the LC/MS/MS and ELISA technology to increase sensitivity so that very small concentrations of Melanotan (< 200pg/mL) in the blood can be measured.

### **Preclinical studies**

Preclinical studies to evaluate the safety and efficacy of several concentrations of Melanotan delivered as a slow-release infusion over 20 to 28 days have been successfully conducted over the past year at Monash University Department of Biochemistry and Molecular Biology, Melbourne and at Firefly Pty Ltd, Sydney. These new preclinical results have allowed EpiTan Ltd to move forward rapidly in the design of implants for the Phase Ib and Phase II human clinical trials outlined in the clinical trials section of this report.



**Dr Stuart Humphrey** Manager – Clinical Development

Collaboration research progress

delivery

2002

2003

2004

2005

2006

2007

#### Alternative delivery mechanism for melanotan

aqueous injection

will not progress into phase III,  
however drug may be sold for  
severe/orphan indications

slow release implant

topical formulation (CollaGenex/Sköld)

"patch" technology (monash university)

oral (monash university)

will accelerate phase I & II trials  
so that impact can be used in phase III (extensive) trials.  
expect this delivery mechanism to be  
first available to market

work has started on  
these alternative  
delivery mechanisms;  
likely to be available  
2006/2008

September 2003 – Eighty volunteers complete Phase IIb "sunburn injury"

# pharmaceutical development

**Drug delivery formulations** During the year two major advancements were made in developing alternative delivery formulations for Melanotan. Whilst the aqueous injection has been making impressive progress in clinical trials to date, this is not the delivery formulation that will be commercialised. The first advancement has been the successful development of a sustained-release, or long acting implant, formulation administered as a single injection. The second advancement secured the rights to develop a topical lotion formulation for Melanotan in conjunction with CollaGenex (Newtown, PA) and the inventor of the Restoraderm™ technology, Mr Thomas Sköld (Björnö, Sweden).

In February 2003, EpiTan announced that it had successfully developed a sustained release implant formulation. This formulation is a result of the strategic collaboration agreement with Southern Research Institute ('Southern') (Birmingham, AL) that was initiated in May 2002. The implants are now in the process of being manufactured to be used in Phase I & II clinical trials, with the first of these implants scheduled to be placed into healthy human volunteers in November 2003. The ability to take an implant concept from the laboratory to the clinic in under two years is a testament of the good working relationship that has been established between Southern and EpiTan.

The new formulation is a small implant designed to be placed under the skin, and is made of the same material that has been used for many years in "self-dissolving" stitches. It is therefore known to be safe and reliable and as the implant is totally biodegradable it does not have to be removed at the end of the treatment. By this means, Melanotan, is slowly released into the body over a period of about 30 days so that the subjects participating in the next clinical trial will need only one injection to develop the appropriate levels of Melanin. Similar implants, such as Zoladex (AstraZeneca) for the treatment of prostate cancer, have already been approved for use in Australian and worldwide markets.

The company is currently progressing a new patent application to cover all intellectual property generated from this development including the formulation studies as it is important to ensure that this new delivery formulation is appropriately protected.

To complement the sustained release implant, EpiTan announced in May 2003, the signing of an agreement with CollaGenex and Mr Sköld, to secure the rights to develop a topical formulation for the delivery of Melanotan. This new and exciting topical delivery formulation technology improves the feasibility of developing a topical formulation for Melanotan. Previously examined topical formulation technologies were considered unable to achieve the delivery of Melanotan through the skin but, it is envisaged that this new formulation will enable Melanotan to be released directly into the skin, delivering it directly to the melanin producing cells. This may also facilitate the use of Melanotan as therapeutic agent for the treatment of various dermatological disorders in which UV radiation plays a part including psoriasis, vitiligo, polymorphous light eruption and solar urticaria.

## Drug manufacture

During the year, EpiTan has received several small-scale batches of Melanotan, manufactured under cGMP (code of Good Manufacturing Practice) specifications, from a supplier located in the USA. This material has been used in the research studies and clinical trials and will be incorporated into the sustained release formulation for use in the first implant clinical trial.

EpiTan has also commissioned a Belgian company to conduct pilot-scale trials on the manufacture of Melanotan using a more economical manufacturing process. By using this technology, the drug can be produced in batch sizes of 100 kg or more. The first pilot-scale batch has been received and preliminary testing indicates the drug to have the same quality properties, (including biological activity), as the initial batches produced by the USA supplier.

To ensure a reliable supply of the drug when the product is released onto the market, EpiTan has also entered into discussions with several other leading peptide manufacturers to also develop large scale manufacturing methods for Melanotan. These methods will allow for commercial scale amounts of the drug to be produced under cGMP specifications at the most commercially competitive price.

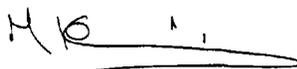
## Research studies

EpiTan continued its close relationship with Australian researchers during the year. In June 2003, EpiTan announced to the market the signing of collaborative agreements with Monash University, Melbourne, and the Institute of Medical and Veterinary Science (IMVS) Adelaide, to aid in the fast track development of the topical formulation using Restoraderm. EpiTan already enjoyed highly productive relationships with Monash University and IMVS, and will continue to work closely with these institutions in the future. The expertise of these research groups in their respective fields will also be exploited to investigate new delivery mechanisms and other mode of actions of Melanotan.

Under the guidance of Associate Professor Tracey Brown in the Department of Biochemistry and Molecular Biology at Monash University, the Monash group will also investigate the delivery of Melanotan using oral formulations. Associate Professor Brown is also world-renowned for her research into transdermal delivery of molecules and her expertise is considered invaluable in this area of Melanotan research.

The work proposed at IMVS, under the management of Dr Tim Kuchel, will support the development of new delivery formulations. IMVS is in the process of establishing a model system to test new drug formulations received by EpiTan.

EpiTan will obtain all of the intellectual and commercialisation rights that are expected to arise from these ongoing research studies, further strengthening EpiTan's strong overall intellectual property position.



**Mr Michael Kleinig**  
Pharmaceutical Development/  
New Business Development Manager

## financial report for year ended 30 june 2003

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## corporate governance statement

The board has the responsibility for ensuring the company is properly managed so as to protect and enhance shareholders' interests in a manner which is consistent with the company's responsibility to meet its obligations to all parties with which the company interacts. The following is a summary of the company's Corporate Governance policies.

### The board of directors

The board is comprised of a majority of non-executive directors to ensure that the board remains independent of day-to-day management.

The terms and conditions relating to the appointment and retirement of non-executive directors are determined on a case-by-case basis and in conformity with the requirements of the ASX Listing Rules and the Corporations Act 2001.

For the purposes of the proper performance of their duties, directors are entitled to seek independent professional advice at the company's expense.

### Audit committee

The current board comprises the members of the audit committee. Dr W.A. Millen is a non-voting member. The principal functions of the Audit Committee include reviewing and making recommendations to the board regarding:

- assisting the board in the discharge of its responsibilities in respect of the preparation of the company's financial statements and the company's internal controls;
- recommending to the board nominees for appointment as external auditors;
- providing a line of communications between the board and the external auditors; and
- examining the external auditors evaluation of internal controls and management's response.

Two meetings of the Audit Committee were held during the financial year.

William Buck was appointed company auditor on 28 November 2000. The Audit Committee is responsible for the terms of the appointment. The external auditor is invited to attend all Audit Committee meetings during the year. Although the appointment of the external auditor is reviewed regularly by the Audit Committee, it is anticipated that the audit engagement partner will be rotated every 5 years.

The auditors do not prepare the primary accounting records nor are they involved in company decision making. The technical expertise of the auditors is called upon from time to time to assist the directors in discharging various statutory responsibilities. The following is a summary of fees paid to William Buck and related entities for non-audit services for the financial year ended 30 June 2003.

- Financial accounting assistance - \$18,352
- Income tax and compliance services including preparation and lodgement of various statutory requirements - \$4,220
- Indirect tax and R&D concession advice \$7,070

### Remuneration committee

The Remuneration and Nomination Committee constitutes the full board and is responsible for determining the appropriate level of remunerations for directors, executives and senior managers details of which are outlined in the directors' report. This committee is also responsible for the nomination of directors and reviewing the balance, nature and experience required of directors to properly fulfil its duties.

### Adoption of a continuous disclosure protocol

The company has adopted a continuous disclosure protocol. The Chief Executive Officer has been appointed the Disclosure Officer and is required to collate and, where appropriate, disclose share price sensitive information.

### Identification and management of significant business risk

The company has prepared a detailed plan for the Melanotan project. The board receives regular reports in order to monitor the progress of the company's major project.

### Ethical standards

The company recognises the need for directors and employees to observe the highest standards of behaviour and business ethics when engaging in corporate activity.

The company intends to maintain a reputation for integrity. The board has adopted a Code of Ethics which sets out the principles and standards with which all officers and employees are expected to comply in the performance of their respective functions.

A key element of that Code is the requirement that officers and employees act in accordance with the law and with the highest standards of propriety. The Code and its implementation are to be reviewed each year.

### Details of options terms and conditions

Details of the Employee Option Plan are included at note 23(b) of the financial statements.

The company engaged Deloitte Touche Tohmatsu ("Deloitte") to prepare a report providing the fair market value of the options issued to directors, Employees and Consultants.

For the purposes of Deloitte's opinion, fair market value is defined as the amount at which the options would change hands between a knowledgeable willing buyer and a knowledgeable willing seller, neither being under a compulsion to buy or sell. The value derived represents a theoretical value as there is not and is not likely to be a market for these options.

The valuation has been undertaken to ensure the company's compliance with the newly published ASIC "Guidelines to valuing options in annual directors' reports" ("ASIC guidelines") and IASB exposure draft "ED2/ED108 share-based payment" ("ED2/ED108"). The methodology utilised incorporates the necessary parameters as specified by the ASIC guidelines and ED2/ED108.

The staff eligible to participate in the scheme may exercise 33.3% of their options after 12 months of being issued, a further 33.3% after 24 months and the remaining options 36 months after issue. The conditions for exercise require the closing sales price of the company's shares on the ASX to equal or exceed a specified price for a period of not less than 5 consecutive trading days. In addition, the staff must satisfy some performance benchmarks specifically related to their area of expertise. The exercise price is determined at the time of the employee joining the company and the term is 5 years.

## directors' report

One of the consultants eligible for the scheme may exercise 33.3% of his options after 12 months of being issued, a further 33.3% after 24 months and the remaining options 36 months after issue. Another consultant may exercise 25,000 options for each month of the service agreement completed. The consultants may only exercise their options when the closing sales price of the company's shares on the ASX equals or exceeds a specified price for a period of not less than 5 consecutive trading days. The exercise price is determined at the time of appointment and the term is 5 years.

One of the directors eligible to participate in the scheme may exercise 33.3% of his options after 12 months of being issued, a further 33.3% after 24 months and the remaining options 36 months after issue. The other directors may exercise 33.3% of their options immediately after issue, a further 33.3% after 9 months and the remaining options after 21 months of issue. If a director ceases to be a director or attends less than 80% of board meetings then a proportion of the options will lapse. The exercise price is \$0.30 and the term is 3.5 or 2.75 years.

Your directors present their report on the company and its controlled entity for the financial year ended 30 June 2003.

### Directors

The names of directors in office at any time during or since the end of the year are:

Dr W.A. Millen  
 Dr H.P.K. Agersborg  
 Dr T.E. Winters  
 Dr A.J. Cooper (resigned 30 April 2003)  
 Mr S.R. McLiesh (appointed 12 September 2002)

Directors have been in office since the start of the financial year to the date of this report unless otherwise stated.

### Principal activity

The principal activity of the consolidated entity during the financial year was to further develop, 'Melanotan', the company's drug candidate in the field of melanogenesis, the process whereby melanin is produced in the body.

### Operating results

The consolidated loss of the consolidated entity after providing for income tax amounted to \$3,976,770

(2002 - \$3,141,224).

### Dividends paid or recommended

No dividends were paid or declared during the financial year.

### Review of operations

Highlights for the year

- Phase II clinical trials progressing extremely well and scheduled to be completed in September 2003;
- Successful development of a long acting implant and now ready to go into human clinical trials in November 2003;
- Secured the rights through a collaborative agreement signed with CollaGenex and Thomas Sköld to develop a topical formulation;
- Collaborative research agreement signed with Monash University (Melbourne) and the Institute of Medical and Veterinary Science (IMVS) based in Adelaide to fast track development of the topical formulation;
- Additional \$1.3 million capital raised from existing and new shareholders;
- Market capitalisation increased to \$24.6 million (2002 - \$9.5 million).

### Financial

At the beginning of the year the company's cash resources were \$4,414,100. During the year the company spent \$3,412,046 including \$2,642,767 on clinical trials and drug formulation research and development, earned \$136,404 in bank interest and received \$140,828 in GST refunds. During the year a total of \$1,316,380 was raised in fresh capital from both the Share Purchase Plan in March and the exercise of listed options in June. At the end of the financial year, the company's financial resources amounted to \$2,611,853; this figure excludes cash of \$1,527,341 received in the first week of July from options exercised under an underwriting arrangement in place with as at 30 June 2003.

### Clinical trials

The Phase II clinical "sunburn" trial got underway at two sites – Sydney's Royal Prince Alfred Hospital and the Royal Adelaide Hospital. The trial involves eighty healthy volunteers being administered Melanotan. The trial's key objective is to measure the effectiveness of the drug to increase skin melanin density and reduce sunburn injury which results in DNA and skin damage. The subjects, of varying skin types, receive controlled levels of UVA and UVB radiation onto a small area of skin resulting in a level of burning similar to spending 30 – 120 minutes in strong sun without sunscreen. A skin biopsy is taken to measure the level of resulting sunburn injury. The volunteers then receive a regime of Melanotan, the same UV radiation exposure, and another skin biopsy. In May 2003 the company announced that the first group of subjects had completed the three month study and that the results were "excellent". The last group of volunteers are now nearing the completion of their regime and preliminary results are expected in early November.

### Drug delivery formulations

Two major developments in drug delivery formulations were made during the year. These new formulations both have potential to increase the commercialisation of Melanotan compared to the current daily injection.

In February 2003, EpiTan announced the successful development of a sustained-release formulation for Melanotan. The new formulation was the product of a successful strategic collaborative agreement with Southern Research Institute (Alabama, USA) initiated in May 2002.

The new formulation is a small implant designed to be placed under the skin. It is made of the same material that has been used for many years in "self-dissolving" stitches and is therefore known to be safe and reliable. As the implant is totally biodegradable it does not have to be removed at the end of the treatment.

The formulation is a major improvement on the daily injections being used in the current Phase IIb clinical trial. Melanotan will be released into the body over a period of time so that the subjects participating in the next clinical trial will need only one injection.

Similar implants, such as Zoladex (AstraZeneca) for the treatment of prostate cancer, have already been approved for use in Australian and worldwide markets.

In May 2003, EpiTan announced the signing of a strategic collaborative agreement with CollaGenex Pharmaceuticals Inc. of Newtown, Pennsylvania, USA and Mr Thomas Sköld of Norrtälje, Sweden to develop a topical formulation. CollaGenex acquired the rights to the novel drug delivery system, known as Restoraderm technology, from Mr Thomas Sköld, the inventor of the technology, in 2002. EpiTan has sub-licensed this technology from CollaGenex.

This technology improves the feasibility of developing a topical formulation for Melanotan, as previously examined technology was unable to achieve this objective. It is envisaged a new formulation may enable Melanotan to be released directly into the skin to the melanin producing cells. This will build on the successful development of a single dose slow-release implant.

In addition, it is important that EpiTan continues to investigate the development of additional delivery mechanisms including lotions and patches. It is expected that Melanotan will be first launched onto the market with the implant. In due course, the successful development of a topical lotion will offer patients and doctors the choice of an alternative user-friendly and convenient delivery for Melanotan.

### Outlook

The company will continue to build on its unique melanogenesis platform technology through its leading drug candidate Melanotan. In mid September, volunteers participating in the Phase IIb clinical trials using the daily injection delivery mechanism will complete their regime. EpiTan is confident that this trial will confirm its earlier, interim progress report of increasing the skin's melanin density and reducing sunburn injury. In November 2003, the company will begin trials using the newly developed sustained release formulation. These Phase I/II trials will be conducted at the Queensland Institute of Medical Research (QIMR) and will involve up to 24 healthy human volunteers. Aside from the usual safety and toxicity data, the trials will confirm the optimal dose of drug to be placed in the long acting implant. This trial is scheduled to take six months.

The company is meeting with the US Food and Drug Administration (FDA) in early October 2003 for the purpose of obtaining approval to begin trials in the USA, via an IND, with Melanotan implants.

During 2004 the company will begin planning for the final Phase III trials for Melanotan which are expected to take place in the US, Europe and Australia.

The company is currently actively seeking a partnership with a larger pharmaceutical company with the view to securing funding for the Phase III trials and commercialisation stages.

### Significant changes in the state of affairs

There have been no significant changes in the state of affairs.

### Significant events after the balance date

Directors are not aware of any significant events that may have occurred subsequent to balance date, except that:

- i. a further 5,485,909 ordinary shares were issued in July 2003 as a result of the exercise of listed options which were the subject of an underwriting agreement in place as at 30 June 2003. Total cash received after 30 June as a result of this issue was \$1,527,341.
- ii. a placement of 14,500,000 ordinary shares was completed on 25 August 2003 to institutional and sophisticated investors pursuant to s.708 of the Corporations Act. Total proceeds amounted to \$7,395,000 before expenses.

### Likely developments and expected results

The directors anticipate that the company will continue its clinical trial and drug development program.

### Environmental regulation and performance

The consolidated entity's operations are not regulated by any significant environmental regulation under a law of the Commonwealth or of a State or Territory.

**directors' report continued**

**Information on directors**

**Dr Wayne A. Millen** *Chairman and Managing Director*  
Age: 62

**Qualifications:** BSc(Hons) PhD  
FRACI C CHEM FAusIMM AFAIM

**Experience:** Dr Millen is the founding Managing Director of EpiTan Limited.

He has a PhD in chemistry and biochemistry from the University of Western Australia and is a Chartered Chemist with extensive experience over 30 years operating his own commercial enterprises.

Dr Millen has extensive experience in venture and development capital investment with an emphasis on companies involved in technological innovation and has been the lead investor and strategist in several private and public companies.

He has considerable experience in establishing and managing start-up enterprises and brings to the company operational skills embracing corporate, technological and marketing disciplines.

**Interest in shares and options:**  
19,666,144 ordinary shares.

**Dr Helmer P.K. Agersborg**  
*Non-executive Deputy Chairman*  
Age: 74  
**Qualifications:** BSc PhD

**Experience:** Dr Agersborg is Chairman and President of MelanoTan Corp, President of Afferon Corp and director of Virxsys Corporation, all pharmaceutical companies. He has been *President of Wyeth-Ayerst Research.*

During his distinguished forty years in the pharmaceutical industry, more than 50 new drug applications were approved in the United States, countless marketing applications were approved outside the United States and innumerable IND's were accepted around the world by companies under his direction.

Dr Agersborg contributes broad international pharmaceutical development experience at the highest level to the company.

**Interest in shares and options:**  
750,000 options to acquire ordinary shares.

**Dr Terry E. Winters**  
*Non-Executive Director*  
Age: 61  
**Qualifications:** BSc PhD

**Experience:** Dr Winters is a director of four private US based companies and a Special Limited Partner of Valley Ventures, a \$50 million venture capital fund based in Scottsdale, Arizona.

In 1983, he co-founded, and is a General Partner of, Columbine Venture Fund which has invested over \$125 million in life science and technology companies in the western USA.

*From the Columbine investments, successful companies have been Orthologic Corp, CollaGenex Pharmaceuticals, Nanophase Technologies, Curis, Neogen (all NASDAQ quoted) and Microgenics.*

**Interest in shares and options:**  
15,315,415 ordinary shares and 750,000 options to acquire ordinary shares.

**Mr Stanley Roy McLiesh**  
*Non-Executive Director*  
Age: 66  
**Qualifications:** BEd

Mr McLiesh has extensive experience in commercialising pharmaceutical products internationally. Formerly General Manager, Pharmaceuticals at CSL Limited, he was closely involved in the transition of CSL from government ownership to corporatisation to a highly successful listed company.

While at CSL, Mr McLiesh brokered numerous in-licensing arrangement with international companies which enabled CSL to expand into new markets profitably. Mr McLiesh has considerable experience in the international pharmaceutical industry.

**Interest in shares and options:** 750,000 options to acquire ordinary shares.

**DIRECTORS' AND EXECUTIVE OFFICERS' EMOLUMENTS**

The emoluments of each director are as follows:

	Salary \$	Fees \$	Superannuation Contributions \$	Allowances \$	Options \$	Total \$
Dr W.A. Millen	205,800	-	19,200	12,631	-	237,631
Dr H.P.K Agersborg	-	30,000	-	-	26,890	56,890
Dr T.E. Winters	-	30,000	-	-	26,890	56,890
Mr S.R. McLiesh	-	21,951	2,097	-	26,814	50,862
Mr A.J. Cooper	-	22,861	2,193	-	24,371	49,371

At the date of this financial report, there are no executive officers that are not directors of the company.

**MEETING OF DIRECTORS**

During the financial year, 9 meetings of directors were held. Attendances were:

<b>Directors</b>	<b>No. eligible to attend</b>	<b>Directors' meetings No. attended</b>
Dr W.A. Millen	9	9
Dr H.P.K. Agersborg	9	9
Dr T.E. Winters	9	9
Dr A.J. Cooper	8	8
Mr S.R. McLiesh	7	7

**INDEMNIFICATION AND INSURANCE OF DIRECTORS AND OFFICER**

During or since the end of the financial year the company has given an indemnity or entered an agreement to indemnify, or paid or agreed to pay insurance premiums as follows.

The company has paid premiums to insure each of the directors against liabilities for costs and expenses incurred by them in defending any legal proceedings arising of their conducts while acting in the capacity of director of the company, other than conduct involving wilful breach of duty in relation to the company. The amount of the premium was \$72,150.

**EMPLOYEES**

The consolidated entity employed 6 employees as at 30 June 2003 (2002: 5 employees).

**SHARE OPTIONS**

At the date of this report, unissued ordinary shares of the company under option are:

<b>Expiry date</b>	<b>Exercise price</b>	<b>Number of options</b>
30 September 2004	\$0.30 / share	1,935,937
30 September 2005	\$0.30 / share	428,958
31 March 2006	\$0.30 / share	750,000
3 April 2006	\$0.10 / share	1,250,000
22 October 2006	\$0.10 / share	1,300,000
30 May 2007	\$0.12 / share	300,000
2 February 2008	\$0.16 / share	750,000
13 June 2008	\$0.29 / share	500,000

During the year 3,089,825 shares were issued as a result of the exercise of the company's listed options ("EPTO"). A further 5,485,909 shares were issued after 30 June 2003 as a result of the exercise of listed option which were the subject of an underwriting arrangement.

**PROCEEDINGS ON BEHALF OF THE COMPANY**

No person has applied for leave of Court to bring proceedings on behalf of the company or intervene in any proceedings to which the company is party for the purpose of taking responsibility on behalf of the company for all or any part of those proceedings.

The company was not party to any such proceedings during the year.

Signed in accordance with a resolution of the board of directors:



**S.R. MCLIESH** DIRECTOR  
Dated this 8th day of September, 2003.



**W.A. MILLEN** DIRECTOR

**statement of financial performance**

The accompanying notes form part of these financial statements

	Note	Consolidated		EpiTan Limited	
		2003 \$	2002 \$	2003 \$	2002 \$
Revenues from ordinary activities	2	136,404	257,507	136,404	257,507
Total expenses from ordinary activities	2	(4,113,174)	(3,398,731)	(4,113,174)	(4,269,171)
<b>Profit(loss) from ordinary activities before related income tax expense</b>		<b>(3,976,770)</b>	<b>(3,141,224)</b>	<b>(3,976,770)</b>	<b>(4,011,664)</b>
Income tax expense (benefit) relating to ordinary activities	3	-	-	-	-
<b>Profit(loss) from ordinary activities after related income tax expense</b>		<b>(3,976,770)</b>	<b>(3,141,224)</b>	<b>(3,976,770)</b>	<b>(4,011,664)</b>
Net profit(loss)		<b>(3,976,770)</b>	<b>(3,141,224)</b>	<b>(3,976,770)</b>	<b>(4,011,664)</b>
<b>Net profit(loss) attributable to members of EpiTan Limited</b>		<b>(3,976,770)</b>	<b>(3,141,224)</b>	<b>(3,976,770)</b>	<b>(4,011,664)</b>
Total changes in equity other than those resulting from transactions with owners as owners		<b>(3,976,770)</b>	<b>(3,141,224)</b>	<b>(3,976,770)</b>	<b>(4,011,664)</b>
Basic earnings per share - cents per share	15	<b>(4.6)</b>	<b>(3.6)</b>		

## statement of financial position

The accompanying notes form part of these financial statements

	Note	Consolidated		EpiTan Limited	
		2003 \$	2002 \$	2003 \$	2002 \$
<b>Current Assets</b>					
Cash assets	16(a)	2,611,853	4,414,100	2,611,859	4,414,092
Receivables	4	30,832	29,602	30,832	29,602
Other	5	105,643	39,391	105,643	39,391
<b>Total Current Assets</b>		<b>2,748,328</b>	<b>4,483,093</b>	<b>2,748,334</b>	<b>4,483,085</b>
<b>Non Current Assets</b>					
Receivables	4	-	-	5,110,098	5,857,410
Property, plant and equipment	6	147,176	141,535	147,176	141,535
Intangible assets	7	5,170,662	5,895,734	60,560	38,334
Other financial assets	8	-	-	169	169
<b>Total Non Current Assets</b>		<b>5,317,838</b>	<b>6,037,269</b>	<b>5,318,003</b>	<b>6,037,448</b>
<b>Total Assets</b>		<b>8,066,166</b>	<b>10,520,362</b>	<b>8,066,337</b>	<b>10,520,533</b>
<b>Current Liabilities</b>					
Payables	10	465,826	156,874	465,826	156,874
Provisions	11	69,625	53,954	69,625	53,954
<b>Total Current Liabilities</b>		<b>535,451</b>	<b>210,828</b>	<b>535,451</b>	<b>210,828</b>
<b>Total Liabilities</b>		<b>535,451</b>	<b>210,828</b>	<b>535,451</b>	<b>210,828</b>
<b>Net Assets</b>		<b>7,530,715</b>	<b>10,309,534</b>	<b>7,530,886</b>	<b>10,309,705</b>
<b>Equity</b>					
Contributed equity	12	16,580,441	15,382,490	16,580,441	15,382,490
Accumulated losses	13	(9,049,726)	(5,072,956)	(9,049,555)	(5,072,785)
<b>Total Equity</b>		<b>7,530,715</b>	<b>10,309,534</b>	<b>7,530,886</b>	<b>10,309,705</b>

**statement of cash flows**

The accompanying notes form part of these financial statements

	Note	Consolidated		EpiTan Limited	
		2003 \$	2002 \$	2003 \$	2001 \$
<b>Cash flows from operating activities</b>					
Refund from ATO		140,428	106,207	140,428	106,207
Payments to suppliers and employees		(3,334,729)	(2,856,716)	(3,248,946)	(2,807,831)
Interest received		152,992	260,346	152,992	260,346
Net cash provided by (used in) operating activities	16(b)	(3,041,309)	(2,490,163)	(2,955,489)	(2,441,278)
<b>Cash flows from investing activities</b>					
Payments for property, plant and equipment		(48,727)	(63,551)	(48,727)	(63,551)
Loans to related parties		-	-	(85,769)	(48,824)
Payments for trademarks		(17,012)	(9,468)	(17,012)	(9,468)
Payments for patents		(9,087)	(3,268)	(9,087)	(3,268)
Net cash provided by (used in) investing activities		(74,826)	(76,287)	(160,595)	(125,111)
<b>Cash flows from financing activities</b>					
Proceeds from issue of ordinary shares		1,197,950	-	1,197,950	-
Proceeds from ordinary shares not yet issued		118,429	-	118,429	-
Payment of share issue costs		(2,491)	-	(2,491)	-
Net cash provided by (used in) financing activities		1,313,888	-	1,313,888	-
Net increase/(decrease) in cash held		(1,802,247)	(2,566,450)	(1,802,233)	(2,566,389)
Cash at beginning of the year		4,414,100	6,980,550	4,414,092	6,980,481
Cash at end of the year	16(a)	2,611,853	4,414,100	2,611,859	4,414,092

**notes to and forming part of the financial statements**

**1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

The financial report is a general purpose financial report that has been prepared in accordance with Accounting Standards, Urgent Issues Group Consensus Views, other authoritative pronouncements of the Australian Accountancy Standards board and the Corporations Act 2001. The financial report has been prepared on an accruals basis and is based on historical costs and does not take into account changing money values or, except where stated, current valuations of non current assets. Cost is based on the fair values of the consideration given in exchange for assets. The accounting policies have been consistently applied, unless otherwise stated.

The following is a summary of the significant accounting policies adopted by the economic entity in the preparation of the financial report.

**(a) Principles of consolidation**

The consolidated accounts comprise the accounts of EpiTan Limited and its controlled entity. A controlled entity is any entity controlled by EpiTan Limited. Control exists where EpiTan Limited has the capacity to dominate the decision-making in relation to the financial and operating activities of another entity so that the other entity operates with EpiTan Limited to achieve the objectives of EpiTan Limited. A list of controlled entities is contained in Note 9 to the financial statements.

All inter-company balances and transactions between entities in the economic entity, including any unrealised profits or losses, have been eliminated on consolidation.

Where controlled entities have entered or left the economic entity during the year, their operating results have been included from the date control was obtained or until the date control ceased.

**(b) Income tax**

The consolidated entity adopts the liability method of tax effect accounting whereby the income tax expense is based on the profit from ordinary activities adjusted for any permanent differences.

Timing differences which arise due to the different accounting periods in which items of revenue and expense are included in the determination of accounting profit and taxable income are brought to account as either a provision for deferred income tax or as a future income tax benefit at the rate of income tax applicable to the period in which the benefit will be received or the liability will become payable.

Future income tax benefits are not brought to account unless realisation of the asset is assured beyond any reasonable doubt. Future income tax benefits in relation to tax losses are not brought to account unless there is virtual certainty of realisation of the benefit.

The amount of benefits brought to account or which may be realised in the future is based on the assumption that no adverse change will occur in income tax legislation and the anticipation that the company will derive sufficient future assessable income and comply with the conditions of deductibility imposed by the law.

**(c) Cash**

For the purpose of the statement of cash flows, cash includes cash on hand and at call deposits with banks or financial institutions.

**(d) Property, plant and equipment**

Property, plant and equipment are brought to account at cost or at independent or directors' valuation, less, where applicable, any accumulated depreciation or amortisation. The carrying amount of property, plant and equipment is reviewed annually by directors to ensure it is not in excess of the recoverable amount from these assets. The recoverable amount is assessed on the basis of the expected net cash flows which will be received from the assets' employment and subsequent disposal. The expected net cash flows have not been discounted to their present values in determining recoverable amounts.

The depreciable amount of all fixed assets is depreciated over the assets' useful lives to the economic entity commencing from the time the asset is held ready for use.

The depreciation rates used for each class of depreciable assets are:

<b>Class of fixed asset</b>	<b>Depreciation rate</b>
Office equipment	20 - 40%
Furniture and fittings	20%

## notes to and forming part of the financial statements continued

### 1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES CONTINUED

(e) **Investments**

Non-current investments are brought to account at cost or at directors' valuation. The carrying amount of investments is reviewed annually by directors to ensure it is not in excess of the recoverable amount of these investments. The recoverable amount is assessed from the underlying net assets in the particular entities. The expected net cash flows from investments have not been discounted to their present value in determining the recoverable amounts.

(f) **Research and development expenditure**

Research and development costs are charged to profit from ordinary activities before income tax as *incurred or deferred where it is expected beyond any reasonable doubt that sufficient future benefits will be derived so as to recover those deferred costs*. No research and development costs have been deferred during this financial year.

Deferred research and development expenditure is amortised on a straight line basis over the period during which the related benefits are expected to be realised, once commercial production has commenced.

(g) **Intellectual property**

*(i) Sub-licence*

The sub-licence to develop and commercialise Melanotan has been recorded at cost. Cost is based on the fair value of the consideration given in exchange for the assets.

The consideration given for the acquisition of the sub-licence was the issue of 11,167,000 ordinary shares and attaching options in the company. Hence the cost of the sub-licence has been determined by assessing the fair value of net assets of the economic entity immediately after the sub-licence was acquired. For the purpose of valuing the assets of the company, an independent valuation of the sub-licence was performed. The valuation was based on discounted future cash flows expected to flow from the right to the sub-licence. The valuation was adjusted for the probability of success.

The directors have determined that it is appropriate to record the sub-licence at cost rather than revalued to market value at this time.

*(ii) Amortisation of Sub-licence*

The sub-licence to develop and commercialise Melanotan is amortised on a straight-line basis over 10 years. The directors have assessed this to be the period over which the future economic benefits of the sub-licence are expected to be realised. The period approximates the remaining life and likely extensions of the patents subject to the sub-licence.

*(iii) Amortisation of trademarks*

Trademarks are amortised on a straight line basis over their expected useful lives.

(h) **Payables**

Liabilities are recognised for amounts to be paid in the future for goods and services received, whether or not billed to the economic entity.

**1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES CONTINUED**

**(i) Employee benefits**

Provision is made for the economic entity's liability for employee benefits arising from services rendered by employees to balance date. Liabilities arising in respect of salaries and wages, annual leave and any other employee benefits expected to be settled within twelve months of the reporting date are measured at their nominal amount based on remuneration rates which are expected to be paid when the liability is settled. All other employee benefit liabilities are measured at the present value future cash outflow to be made.

Employee benefits expenses and revenues arising in respect of the following categories; wages and salaries, non-monetary benefits, annual leave, long service leave, sick leave and other leave benefits are charged against profits on a net basis in their respective categories.

The value of the employee option scheme described in note 23 is not being charged as an employee benefit expense.

Contributions are made by the economic entity to employee superannuation funds and are charged as expenses when incurred.

**(j) Directors' remuneration**

Directors' remuneration includes all remuneration in connection with the management of the company and means any money, consideration or benefit. Remuneration includes the value of share options granted. Options over shares have been valued at grant date using an option pricing model in accordance with current ASIC guidance, Australian Exposure Draft ED 108 and International Exposure Draft ED 2. The value of options issued to directors has been included in the determination of directors' remuneration during the period from grant date to vesting date. In accordance with Australian Accounting Standards, share options have not been expensed.

**(k) Revenue**

Interest revenue is recognised on a proportional basis.

**(l) Share capital**

Ordinary share capital is recognised at the fair value of the consideration received by the company.

Any transaction costs arising on the issue of ordinary shares are recognised directly in equity as a reduction of the shares proceeds received.

**(m) Earnings per share**

*(i) Basic earnings per share*

Basic earnings per share is determined by dividing net profit after income tax attributable to members of the company, excluding any costs of servicing equity other than ordinary shares, by the weighted average number of ordinary shares outstanding during the financial year, adjusted for bonus elements in ordinary shares issued during the year.

*(ii) Diluted earnings per share*

Diluted earnings per share adjusts the figures used in the determination of basic earnings per share to take into account the after income tax effect of interest and other financing costs associated with dilutive potential ordinary shares and the weighted average number of shares assumed to have been issued for no consideration in relation to dilutive potential ordinary shares.

**(n) Goods and Services Tax (GST)**

Revenues, expenses and assets are recognised net of the amount of GST, except where the amount of GST incurred is not recoverable from the Australian Tax Office. In these circumstances the GST is recognised as part of the cost of acquisition of the asset or as part of an item of the expense receivables and payables in the statement of financial position are shown inclusive of GST.

**(o) Leases**

Leases payments for operating leases, where substantially all the risks and benefits remain with the lessors, are charged as expenses in the periods in which they are incurred.

**(p) Comparatives**

Where necessary, comparatives have been reclassified and repositioned for consistency with current year disclosure.

notes to and forming part of the financial statements continued

	Note	Consolidated		EpiTan Limited	
		2003 \$	2002 \$	2003 \$	2002 \$
<b>2 PROFIT/(LOSS) FROM ORDINARY ACTIVITIES</b>					
(a) <b>Revenues from ordinary activities</b>					
Interest revenue – other persons		136,404	257,507	136,404	257,507
<b>Total revenues</b>		<b>136,404</b>	<b>257,507</b>	<b>136,404</b>	<b>257,507</b>
(b) <b>Expenses from ordinary activities</b>					
Clinical development costs		1,693,328	1,871,867	946,030	1,124,569
Drug delivery research costs		949,439	372,758	949,439	372,758
Occupancy costs		75,080	81,252	75,080	81,252
Marketing costs		118,275	108,437	118,275	108,437
Finance & administration costs		1,277,052	964,417	2,024,350	2,582,155
<b>Total expenses from ordinary activities</b>		<b>4,113,174</b>	<b>3,398,731</b>	<b>4,113,174</b>	<b>4,269,171</b>
(c) <b>Profit/(loss) from ordinary activities before income tax has been determined after:</b>					
Depreciation		43,086	38,405	43,086	38,405
Amortisation of sub-licence		747,298	747,299	-	-
Amortisation of trademarks		3,873	319	3,873	319
Research & development costs		1,895,496	1,497,326	1,895,496	1,497,326
Doubtful debts – wholly owned subsidiary		-	-	833,082	1,666,625
Operating lease expense		-	-	-	-
- minimum lease payments		83,964	78,205	83,964	78,205
<b>3. INCOME TAX EXPENSE</b>					
(a) The prima facie tax on profit(loss) from ordinary activities before income tax is reconciled to the income tax expense(benefit) as follows:					
Prima facie tax payable on profit(loss) from ordinary activities before income tax at 30%		(1,193,031)	(942,367)	(1,193,031)	(1,203,499)
Add:					
Tax effect of permanent differences					
- non deductible amortisation		1,162	96	1,162	96
- other non allowable items		-	1,455	-	1,455
Write off FITB due to lack of virtual certainty		1,191,869	940,816	1,191,869	1,201,948
		-	-	-	-
(b) Future income tax benefits arising from unconfirmed tax losses and net timing differences not brought to account at balance date as realisation of the benefit is not regarded as virtually certain. The benefits will only be obtained if the conditions set out in note 1(b) occur:					
Tax losses		2,086,038	1,411,312	1,928,464	1,000,694
Net timing differences		618,975	104,652	776,620	512,450
		<b>2,705,013</b>	<b>1,515,964</b>	<b>2,705,104</b>	<b>1,513,144</b>

	Note	Consolidated		EpiTan Limited	
		2003 \$	2002 \$	2003 \$	2002 \$
<b>4. RECEIVABLES</b>					
<b>Current</b>					
Sundry debtors		30,832	13,014	30,832	13,014
Accrued income		-	16,588	-	16,588
		<b>30,832</b>	<b>29,602</b>	<b>30,832</b>	<b>29,602</b>
<b>Non-Current</b>					
Receivable from wholly owned entity	20	-	-	7,609,805	7,524,035
Provision for non-recovery		-	-	(2,499,707)	(1,666,625)
		-	-	<b>5,110,098</b>	<b>5,857,410</b>
<b>5. OTHER ASSETS</b>					
<b>Current</b>					
Prepayments		105,643	39,391	105,643	39,391
<b>6. PROPERTY, PLANT AND EQUIPMENT</b>					
Office equipment					
At cost		192,483	157,376	192,483	157,376
Less: Accumulated depreciation		(95,163)	(62,301)	(95,163)	(62,301)
		<b>97,320</b>	<b>95,075</b>	<b>97,320</b>	<b>95,075</b>
Furniture and fittings					
At cost		77,358	63,738	77,358	63,738
Less: Accumulated depreciation		(27,502)	(17,278)	(27,502)	(17,278)
		<b>49,856</b>	<b>46,460</b>	<b>49,856</b>	<b>46,460</b>
Total property, plant and equipment		<b>147,176</b>	<b>141,535</b>	<b>147,176</b>	<b>141,535</b>

**Movements in Carrying Amounts**

Movements in the carrying amounts for each class of property, plant and equipment between the beginning and the end of the financial year

	Office Equipment \$	Furniture and Fittings \$	Total \$
<b>Consolidated &amp; EpiTan Limited - 2003</b>			
Carrying amount at the beginning of year	95,075	46,460	141,535
Additions	35,107	13,620	48,727
Depreciation expense	(32,862)	(10,224)	(43,086)
Carrying amount at the end of year	<b>97,320</b>	<b>49,856</b>	<b>147,176</b>

notes to and forming part of the financial statements continued

	Note	Consolidated		EpiTan Limited	
		2003 \$	2002 \$	2003 \$	2002 \$
<b>7. INTANGIBLE ASSETS</b>					
Sub-licence to develop and commercialise Melanotan – at cost		7,472,983	7,472,983	-	-
Less: Accumulated amortisation		(2,362,881)	(1,615,583)	-	-
		<b>5,110,102</b>	<b>5,857,400</b>		
Trademarks		47,567	30,555	47,567	30,555
Less: Accumulated amortisation		(4,192)	(319)	(4,192)	(319)
		<b>43,375</b>	<b>30,236</b>	<b>43,375</b>	<b>30,236</b>
Patents		17,185	8,098	17,185	8,098
		<b>5,170,662</b>	<b>5,895,734</b>	<b>60,560</b>	<b>38,334</b>
<b>8. OTHER FINANCIAL ASSETS</b>					
<b>Non-Current</b>					
Investments at cost comprise:					
Shares in unlisted controlled entity	9	-	-	169	169
<b>9. INTERESTS IN SUBSIDIARIES</b>					
Melanotan (Australia) Pty Ltd Incorporated in Australia. Percentage of equity interest held by the consolidated entity: 100% (2002: 100%)					
<b>10. PAYABLES</b>					
<b>Current</b>					
Trade creditors		235,929	69,458	235,929	69,458
Sundry creditors and accrued expenses		111,468	87,416	111,468	87,416
Ordinary shares yet to be issued		118,429	-	118,429	-
		<b>465,826</b>	<b>156,874</b>	<b>465,826</b>	<b>156,874</b>
(a) Aggregate amounts payable to:					
- directors and director-related entities		47,401	55,554	47,401	55,554
(b) Australian dollar equivalents of amounts payable in foreign currencies not effectively hedged:					
- Swedish krone		14,423	-	14,423	-
- US dollars		96,991	11,046	96,991	11,046
(c) Terms and conditions: Trade and sundry creditors are non- interest bearing and normally settled on 30 day terms.					
<b>11. PROVISIONS</b>					
<b>Current</b>					
Employee benefits		69,625	53,954	69,625	53,954
<b>12. CONTRIBUTED EQUITY</b>					
(a) Issued and paid up capital fully paid ordinary shares		16,580,441	15,382,490	16,580,441	15,382,490

	No.	2003 \$	No.	2002 \$
(b) Movements in shares on issue				
At the beginning of the financial year				
Issued during the year	86,414,254	15,382,490	86,414,254	15,382,490
- share purchase plan	1,935,753	271,005	-	-
- options exercise	3,089,825	926,946	-	-
Less: transaction costs	-	-	-	-
	91,439,832	16,580,441	86,414,254	15,382,490

(c) Share Options

As at 30 June 2003 the following share options existed which if exercised, would result in the issue of fully paid ordinary shares.

Expiry Date	Exercise price	Number of options
30 September 2004	\$0.30 / share	1,935,937
30 September 2005	\$0.30 / share	428,958
31 March 2006	\$0.30 / share	750,000
3 April 2006	\$0.10 / share	1,250,000
22 October 2006	\$0.10 / share	1,300,000
30 May 2007	\$0.12 / share	300,000
2 February 2008	\$0.16 / share	750,000
13 June 2008	\$0.29 / share	500,000

During the year the following share options were issued which if exercised, would result in the issue of fully paid ordinary shares.

Expiry Date	Exercise price	Number of options
31 March 2006	\$0.30 / share	750,000
30 May 2007	\$0.12 / share	150,000
2 February 2008	\$0.16 / share	750,000
13 June 2008	\$0.29 / share	500,000

(d) Terms and conditions of contributed equity

Ordinary Shares

Ordinary shares have the right to receive dividends as declared and, in the event of winding up the company, to participate in the proceeds from the sale of all surplus assets in proportion to the number of and amounts paid up on shares held. Ordinary shares entitle their holder to one vote, either in person or by proxy, at a meeting of the company.

A further 5,485,909 ordinary shares were issued in July 2003 as a result of the exercise of listed options which were the subject of an underwriting agreement in place as at 30 June 2003. Total cash received after 30 June as a result of this issue was \$1,527,341.

notes to and forming part of the financial statements continued

	Note	Consolidated		EpiTan Limited	
		2003 \$	2002 \$	2003 \$	2002 \$
<b>13. ACCUMULATED LOSSES</b>					
Accumulated losses at the beginning of the year		(5,072,956)	(1,931,732)	(5,072,785)	(1,061,121)
Net loss attributable to the members of EpiTan Limited		(3,976,770)	(3,141,224)	(3,976,770)	(4,011,664)
Accumulated losses at the end of the financial year		(9,049,726)	(5,072,956)	(9,049,555)	(5,072,785)
<b>14. LEASE COMMITMENTS</b>					
<b>Operating lease commitments</b>					
Non-cancellable operating leases Contracted for but not capitalised in the accounts:					
Payable					
- not later than 1 year		90,354	48,951	90,354	48,951
- later than 1 year but not later than 5 years		150,590	-	150,590	-
		240,944	48,951	240,944	48,951

**15. EARNINGS PER SHARE (EPS)**

	Consolidated	
	2003	2002
(a) Basic earnings per share – cents per share	(4.6)	(3.6)
(b) The Weighted Average Number of Ordinary Shares (WANOS) used in the calculation of Basic Earnings Per Share	86,923,303	86,414,254
(c) The numerator used in the calculation of Basic Earnings Per Share.	(6,714,895)	(3,141,224)
(d) Since 30 June 2003 a further 5,485,909 ordinary shares were issued in July 2003 as a result of the exercise of listed options which were the subject of an underwriting agreement in place as at 30 June 2003.		
(e) Potential Ordinary Shares not considered Dilutive As at 30 June 2003 the company had on issue 6,714,895 options over unissued capital. The details of which are included in Note 12(c) and 23 (b). These options are not considered dilutive as they do not increase the net loss per share.		

	Note	Consolidated		EpiTan Limited	
		2003 \$	2002 \$	2003 \$	2002 \$
<b>16. CASH FLOW INFORMATION</b>					
(a) Reconciliation of Cash					
For the purposes of the Statement of Cash Flows, cash includes cash on hand and with banks.					
Cash at the end of the financial year as shown in the Statement of Cash Flows is reconciled to the related items in the balance sheet as follows:					
Cash on hand		31	250	31	250
Cash at bank		2,611,822	4,413,850	2,611,828	4,413,842
		2,611,853	4,414,100	2,611,859	4,414,092
(b) Reconciliation of cash flows from operating activities with operating profit(loss)					
Operating profit(loss) after income tax		(3,976,770)	(3,141,224)	(3,976,770)	(4,011,664)
Non cash flows in operating (loss):					
Depreciation expense		43,086	38,405	43,086	38,405
Amortisation expense		751,171	747,619	3,873	319
Doubtful debt expense		-	-	833,082	1,666,625
Changes in assets and liabilities:					
(Increase)/decrease in receivables		(1,230)	5,316	(1,230)	5,316
(Increase)/decrease in prepayments		(66,252)	(26,502)	(66,252)	(26,502)
Increase/(decrease) in payables		193,015	(140,112)	193,014	(140,112)
Increase/(decrease) in provisions		15,671	26,335	15,671	26,335
Net cash used in operating activities		(3,041,309)	(2,490,163)	(2,955,526)	(2,441,278)

notes to and forming part of the financial statements continued

	Note	Consolidated		EpiTan Limited	
		2003 \$	2002 \$	2003 \$	2002 \$
<b>17. REMUNERATION OF DIRECTORS</b>					
Income paid or payable, or otherwise made available, in respect of the financial year, to all directors of each entity in the consolidated entity, directly or indirectly, by the entities of which they are directors or any related party:		451,644	355,382		
Income paid or payable, or otherwise made available, in respect of the financial year, to all directors of EpiTan Limited, directly or indirectly, from the entity or any related party:				451,644	355,382
The number of directors of EpiTan Limited whose income (including superannuation contributions) falls within the following bands is:				No.	No.
\$0 - \$9,999				-	1
\$10,000 - \$19,999				-	1
\$30,000 - \$39,999				-	3
\$40,000 - \$49,999				1	-
\$50,000 - \$59,000				3	-
\$230,000 - \$239,999				1	-
\$240,000 - \$249,999				-	1
<b>18. REMUNERATION OF EXECUTIVES</b>					
All executives are directors of EpiTan Limited.					
<b>19. AUDITORS' REMUNERATION</b>					
Amounts received or due and receivable by William Buck for:					
- audit services		20,000	12,500	20,000	12,500
- other services		29,642	57,875	29,642	57,875
		49,642	70,375	49,642	70,375

**20. RELATED PARTY DISCLOSURES**

**Directors**

The directors of EpiTan Limited during the financial year were:

W. A. Millen	A.J. Cooper (resigned 30 April 2003)
H. P. K. Agersborg	S.R. McLiesh (appointed 12 September 2002)
T. E. Winters	

**Wholly-owned group transactions**

*Loans*

The loan receivable by EpiTan Limited from Melanotan (Australia) Pty Ltd is non-interest bearing. Repayment of the loan will commence upon commercialisation of the company's drug candidate. A provision for non-recovery has been raised in the accounts of EpiTan Limited to the extent that a deficiency in net assets exists in Melanotan (Australia) Pty Ltd.

**Equity instruments of directors**

*Interests at balance date*

Interests in equity instruments of EpiTan Limited held by directors of the reporting entity and their director-related entities:

	Ordinary shares fully paid		Options over ordinary shares	
	2003 Number	2002 Number	2003 Number	2002 Number
W. A. Millen	19,706,144	19,591,144	-	11,979,638
H.P.K. Agersborg	-	-	750,000	750,000
T. E. Winters	15,315,415	15,288,154	750,000	9,982,185
S.R. McLiesh	-	-	750,000	-
A.J. Cooper	-	-	428,958	750,000

On 30 June 2003, the entity's listed options to acquire ordinary shares lapsed. As a consequence, options held by Dr W.A. Millen and Dr T.E. Winters and their respective director related entities amounting to 12,061,246 and 9,624,911 respectively lapsed.

During the year Mr S.R. McLiesh was issued 750,000 non-tradeable options to acquire ordinary shares. Due to the resignation of Professor A.J. Cooper 321,042 options to acquire ordinary shares were forfeited.

All equity dealings with directors have been entered into with terms and conditions no more favourable than those that the entity would have adopted if dealing at arm's length.

notes to and forming part of the financial statements continued

**21. SEGMENT INFORMATION**

The economic entity operates solely in the biotechnology industry. The economic entity operates predominantly in Australia.

**22. FINANCIAL INSTRUMENTS**

(a) Interest rate risk

The economic entity's exposure to interest rate risks and the effective interest rates of financial assets and financial liabilities, both recognised and unrecognised at the balance date, are as follows:

	Weighted Average Effective Interest Rate		Non-Interest Bearing		Balances Subject to a Floating Interest Rate			Total
	2003 %	2002 %	2003 \$	2002 \$	2003 \$	2002 \$	2003 \$	2002 \$
<i>(i) Financial Assets</i>								
Cash at bank	4.1	4.5	31	250	2,611,822	4,413,850	2,611,853	4,414,100
Receivables	N/A	N/A	30,832	29,602	-	-	30,832	29,602
Total			30,863	29,852	2,611,822	4,413,850	2,642,685	4,443,702
<i>(ii) Financial Liabilities</i>								
Payables	N/A	N/A	465,826	156,874	-	-	465,826	151,322
Total			465,826	156,874	-	-	465,826	151,322

(b) Net fair values

All financial assets and liabilities have been recognised at the balance date at their net fair values.

(c) Credit risk exposures

The economic entity's maximum exposure to credit risk at balance date in relation to each class of recognised financial assets is the carrying amount of those assets as indicated in the statement of financial position.

**23. EMPLOYEE BENEFITS**

	Consolidated		EpiTan Limited	
	2003 \$	2002 \$	2003 \$	2002 \$
(a) The aggregate employee benefit liability is comprised of :				
- Provisions	69,625	53,954	69,625	53,954
- Accrued wages, salaries and on costs	78,168	61,583	78,168	61,583
	147,793	115,537	147,793	115,537

(b) Employee option plan

An employee option plan has been established where directors, staff and consultants are issued with options over the ordinary shares of EpiTan Limited. The options, issued for nil consideration, are issued in accordance with performance guidelines established by the directors of EpiTan Limited. The options are issued for a term of 5 years, however this does vary for the various plan participants. The options cannot be transferred and will not be quoted on the ASX. There are currently three directors, five staff and three consultants eligible for this scheme.

notes to and forming part of the financial statements continued

**EMPLOYEE ENTITLEMENTS (CON'T)**

Information with respect to the number of options granted under the employee option scheme is as follows :

	2003		2002	
	Number of Options	Weighted average exercise price	Number of Options	Weighted average exercise price
Balance at beginning of year				
- granted	5,385,937	\$0.20	1,250,000	\$0.10
- forfeited	1,650,000	\$0.22	4,450,000	\$0.24
- exercised	(321,042)	\$0.30	(314,063)	\$0.30
	-	-	-	-
Balance at end of year	6,714,895	\$0.20	5,385,937	\$0.20
Exercisable at end of year	3,200,277	\$0.19	1,136,873	\$0.21

The following table summarises information about options outstanding and exercisable at 30 June 2003.

Exercise price	Expiry date	Number of options:	
		Outstanding	Exercisable
\$0.10	3 April 2006	1,250,000	1,250,000
\$0.10	22 October 2006	1,300,000	466,666
\$0.12	30 May 2007	300,000	50,000
\$0.30	30 September 2004	1,935,937	1,290,625
\$0.30	30 September 2005	428,958	142,986
\$0.30	31 March 2006	750,000	-
\$0.16	2 February 2008	750,000	-
		6,714,895	3,200,277

**directors' declaration**

In the opinion of the directors:

1. the financial statements and notes, of the company and of the consolidated entity, are in accordance with the Corporations Act 2001, including:
  - (a) giving a true and fair view of the company's and the consolidated entity's financial position as at 30 June 2003 and of their performance for the year ended on that date;
  - (b) complying with Accounting Standards and the Corporations Regulations 2001; and
2. there are reasonable grounds to believe that the company will be able to pay its debts as and when they become due and payable.

This declaration is made in accordance with a resolution of the board of directors.



**S.R. MCLIESH** DIRECTOR  
Dated this 8th day of September, 2003.



**W.A. MILLEN** DIRECTOR

## independent audit report



### Independent audit report to members of EpiTan Limited

#### Scope

##### *The financial report and directors' responsibility*

The financial report comprises the statement of financial position, statement of financial performance, statement of cash flows, accompanying notes to the financial statements, and the directors' declaration for both EpiTan Limited (the company) and EpiTan Limited and controlled entities (the consolidated entity), for the year ended 30 June 2003. The consolidated entity comprises both the company and the entities it controlled during that year.

The directors of the company are responsible for the preparation and true and fair presentation of the financial report in accordance with the *Corporations Act 2001*. This includes responsibility for the maintenance of adequate accounting records and internal controls that are designed to prevent and detect fraud and error, and for the accounting policies and accounting estimates inherent in the financial report.

##### *Audit approach*

We conducted an independent audit in order to express an opinion to the members of the company. Our audit was conducted in accordance with Australian Auditing and Assurance Standards in order to provide reasonable assurance as to whether the financial report is free of material misstatement. The nature of an audit is influenced by factors such as the use of professional judgement, selective testing, the inherent limitations of internal control, and the availability of persuasive rather than conclusive evidence. Therefore, an audit cannot guarantee that all material misstatements have been detected.

We performed procedures to assess whether in all material respects the financial report presents fairly, in accordance with the *Corporations Act 2001*, Accounting Standards and other mandatory financial reporting requirements in Australia, a view which is consistent with our understanding of the company's and the consolidated entity's financial position, and of their performance as represented by the results of their operations and cash flows.

We formed our audit opinion on the basis of these procedures, which included:

- Examining, on a test basis, information to provide evidence supporting the amounts and disclosures in the financial report; and
- Assessing the appropriateness of the accounting policies and disclosures used and the reasonableness of significant accounting estimates made by the directors.

While we considered the effectiveness of management's internal controls over financial reporting when determining the nature and extent of our procedures, our audit was not designed to provide assurance on internal controls.

(1 of 2)



**Independence**

In conducting our audit, we followed applicable independence requirements of Australian accounting ethical pronouncements and the Corporations Act 2001.

**Audit opinion**

In our opinion, the financial report of EpiTan Limited is in accordance with:

- (a) the Corporations Act 2001, including:
  - (i) gives a true and fair view of EpiTan Limited's and the consolidated entity's financial position as at 30 June 2003 and of their performance for the year ended on that date; and
  - (ii) complying with Accounting Standards in Australia and the Corporations Regulations 2001; and
- (b) other mandatory financial reporting requirements in Australia.

William Buck  
Chartered Accountants

K W Glynn  
Partner

Dated this 8th day of September 2003.  
Melbourne, Australia.

(2 of 2)

**additional information required by the Australian stock exchange**

Additional information required by the Australian Stock Exchange and not shown elsewhere in this report is as follows. The information is current at 29 August 2003.

**1. SHAREHOLDING**

(a) Distribution of shareholders number

Category (size of Holding)	Ordinary shares
1 – 1,000	118
1,001 – 5,000	779
5,001 – 10,000	604
10,001 – 100,000	327
100,001 – and over	83
	<b>2,411</b>

(b) The number of shareholdings held in less than marketable parcels is 34 for ordinary shares.

(c) The names of the substantial shareholders listed in the holding company's register as at 30 June 2002 are:

Weighton Pty Ltd  
 MelanoTan Corporation USA  
 Chartport Financial Services Pty Ltd

(d) Voting rights

Ordinary shares entitle their holder to one vote, either in person or by proxy, at a meeting of the company.

(e) 20 Largest shareholders – ordinary shares

Name	Number of ordinary fully paid shares held	% Held of issued ordinary capital
1 Weighton Pty Ltd	19,531,380	21.10
2 MelanoTan Corporation USA	15,165,415	15.61
3 Merrill Lynch (Australia) Nominees Pty Ltd	2,902,123	2.99
4 Chartport Financial Services Pty Ltd	2,256,188	2.32
5 Citicorp Nominees Pty Limited	1,886,002	1.94
6 National Nominees Limited	1,841,252	1.89
7 ANZ Nominees Limited	1,299,716	1.34
8 Mr Stephen Charles O'Halloran	961,950	0.99
9 Grunwald Design International Pty Ltd	854,332	0.88
10 Westpac Custodian Nominees Limited	852,404	0.88
11 JFR Investments Pty Ltd	713,228	0.73
12 Mr Cheng Han	531,690	0.55
13 Mr Doug McLachlan & Mrs Wendy McLachlan	530,000	0.55
14 Lippo Securities Nominees Ltd	465,000	0.48
15 Seawise Nominees Pty Ltd	434,503	0.45
16 Mr Michisuke Asami	425,000	0.44
17 Dynamic Press Investments Pty Ltd	400,000	0.41
18 Mr Alan Douglas Parker & Mrs Jannette Rachel Parker	400,000	0.41
19 Edward St Consulting Pty Ltd	392,382	0.40
20 Mr David John Lewis	347,198	0.36
	<b>52,189,763</b>	<b>53.72</b>

**2. COMPANY SECRETARY**

The name of the company secretary is Mr Iain Kirkwood.

**3. REGISTERED OFFICE**

The address of the principal registered office in Australia is Level 10, 52 Collins Street, Melbourne, Victoria, 3000, Telephone (03) 9662 4688.

**4. REGISTER OF SECURITIES**

Computershare Investor Services Pty Ltd  
Level 12, 565 Bourke Street  
Melbourne Victoria 3000

**5. STOCK EXCHANGE LISTING**

Quotation has been granted for all the ordinary shares of the company on all Member Exchanges of the Australian Stock Exchange Limited (ASX code: EPT).

**6. RESTRICTED SECURITIES**

Restricted securities on issue at 30 June 2003: Nil

## glossary

**Armamentarium** Drugs, treatments or resources available.

**Bolus** A large dose given intravenously so that the desired therapeutic concentration in the blood is reached rapidly.

**CDER** Centre for Drug Evaluation & Research. A division of the FDA.

**cGMP** Current good manufacturer practices. These practices are more fine tuned and up to date methodologies and procedures, mandated by regulatory authorities, which are to be followed in testing and manufacturer of pharmaceuticals to ensure manufacture of safe clinical supplies.

**DNA** The molecule that carries genetic information in all living things; the chemical basis of heredity. Damaged DNA can lead to uncontrolled growth of cells which is commonly known as cancer.

**ELISA** Enzyme-Linked Immunosorbent Assay. A method of analyzing Melanotan in the blood of clinical trial subjects.

**EMA** European Medicines Evaluation Agency. London based agency in Europe began in 1995. Co-ordinates drug licensing and safety through Europe.

**Eumelanin** The UV-protective dark pigment produced by melanocytes.

**FDA** United States' Food & Drug Administration.

**Fitzpatrick Skin Type** Classification system based on a person's sensitivity to sunlight. People with skin types I and II are at the highest risk for photoaging effects including wrinkles and skin cancer.

**IND** Investigational New Drug. Companies seeking to begin clinical studies of a new pharmaceutical drug are required to lodge this application with the FDA.

**Keratinocytes** Skin cells that receive melanin from the melanocytes.

**LC/MS/MS** Liquid Chromatography/Mass spectrophotometry. A sophisticated method of analyzing Melanotan in the blood of clinical trial subjects.

**MCA** Medicines Control Agencies - in concert with Communication Safety in Medicines regulates the approval safe pharmaceutical products in UK.

**Melanin** Produced by melanocytes, the amount of which produces skin pigmentation.

**Melanocytes** The cells in the skin that produce melanin.

**Melanogenesis** A unique biochemical process whereby melanin is produced in the body.

**Melanotan** A more potent synthetic copy of the naturally occurring hormone,  $\alpha$ -MSH. Induces a natural tanning of skin, via melanogenesis, without the harmful effects of UV radiation.

**MRA** Mutual Recognition Agreement.

$\alpha$ -MSH alpha-Melanocyte Stimulating Hormone.

**NCE** New Clinical Entity.

**NDA** New Drug Application.

**Phaeomelanin** The red-yellow non UV-protective pigment produced by melanocytes.

**PK** Pharmacokinetics - deals with what happens to a substance that is introduced into a living system e.g. how quickly broken down and pathway etc. Branch of pharmacology dealing with the reaction between drugs or synthetic food ingredients and living structures.

**Phase I** The first in a series of human tests of new pharmaceuticals. The primary purpose of the Phase I clinical test is to detect if the new pharmaceutical is toxic or otherwise harmful to normal, healthy humans. The conclusion of Phase I testing leads to Phase II and Phase III testing

**Phase II** The second in a series of human tests of new pharmaceuticals. The primary purpose of the Phase II clinical tests is to determine the pharmaceutical's efficacy (i.e., does it work?). Successful conclusion of Phase II tests allows Phase III clinical tests to begin.

**Phase III** The third in a series of human tests of new pharmaceuticals. The primary purpose of Phase III clinical tests is to increase the number of people exposed to a new pharmaceutical and verify proper dosage.

**PMLE/PLE** Polymorphic light eruption (PLE), otherwise termed polymorphous light eruption (PMLE), is a skin disorder caused by sunlight. A delayed-onset, spotty, itchy eruption appears on the skin, and may take between 5 to 10 days to clear. The rash usually consists of small red spots or blisters and can appear on any part of the body that has been exposed to sunshine, although commonly the face and the backs of the hands will be spared. It tends to heal without scarring.

**PUVA** Treatment involving exposing patients to ultraviolet radiation after they have taken a drug called methoxsalen (8-MOP). The UV light activates the drug, which then binds to DNA and causes cell death.

**Restoraderm™** A technology invented by Mr Thomas Sköld to transport molecules through the skin.

**Sustained-release** A process whereby the drug is released from a formulation over a long period time with only one injection.

**Tan** The body's natural response to protect itself from further skin damage caused by UV radiation.

**TGA** Therapeutic Goods Administration.

**Topical lotion** A cream or gel applied to the skin.

**UV light / UV radiation** Ultraviolet light / Ultraviolet radiation.

**Vitiligo** Vitiligo (also called "leukoderma") is a skin condition in which there is loss of pigment from areas of the skin resulting in irregular white spots or patches, even though the skin has normal texture. Vitiligo may appear at any age. Although it is a progressive condition, many people experience years or decades without developing new spots. The cause of vitiligo is not greatly understood, and there may be many causes that result in the condition.

# corporate directory

## **Registered Office**

Level 10, 52 Collins Street  
Melbourne Australia 3000  
Telephone: +61 3 9662 4688  
Facsimile: +61 3 9662 4788  
Email: mail@epitan.com.au  
Website: www.epitan.com.au

## **Directors & Executives**

### *Non Executive Directors*

Dr Helmer Agersborg (Deputy Chairman)  
Dr Terry Winters  
Mr Stanley McLeish

*Executive Chairman & Managing Director*  
Dr Wayne Millen

*Chief Administrative Officer & Company Secretary*  
Mr Iain Kirkwood

*Clinical Development Manager*  
Dr Stuart Humphrey

*Pharmaceutical Development Manager/New Business Development*  
Mr Michael Kleinig

*Pharmaceutical Products Manager*  
Mr Chris Rossidis

## **Australian Stock Exchange**

The company's shares are quoted on the official list of the Australian Stock Exchange.

ASX Code: EPT

## **Auditor & Independent Accountants**

William Buck  
Level 2, 215 Spring Street  
Melbourne Victoria 3000

## **Bankers**

National Australia Bank

## **Lawyers**

Minter Ellison  
Rialto Towers, 525 Collins Street  
Melbourne Victoria 3000

## **Share Registry**

Computershare Investor Services Pty Ltd  
Level 12, 565 Bourke Street  
Melbourne Victoria 3000  
or  
GPO Box 2975EE  
Melbourne Victoria 3000



**Media Announcement****Increasing melanin levels could aid protection against malignant melanoma, says leading Australian dermatologist following UK research into ineffective sunscreens**

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For more information contact:

Mr Iain Kirkwood, Chief Administrative Officer, EpiTan Limited, Tel: 03 9662 4688

Mr Richard Allen, Monsoon Communications, Tel: 03 9620 3333

Royal Prince Alfred Hospital, Tel: 02 9515 6111

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Melbourne, Australia

A drug that increases melanin levels in the skin could be a significant addition to traditional skin cancer protection, a leading Sydney dermatologist has said in the wake of British studies that show sunscreens are not protecting people enough against malignant melanoma, the worst form of skin cancer.

Professor Ross Barnetson, from Sydney's Royal Prince Alfred Hospital, said the studies in Britain – which found that sunscreens fail to stop harmful ultraviolet A (UVA) rays from penetrating the skin – were especially worrying for Australians, who have among the highest rates of skin cancer in the world.

Professor Barnetson said he had high hopes for a new drug, Melanotan®, which he is currently taking through Phase II "sunburn" trials in Sydney. Melanotan increases melanin levels in the skin, which increases protection against harmful UVA rays.

"The British research shows that our traditional methods of protection against the worst form of skin cancer malignant melanoma, are not working," said Professor Barnetson. "If Melanotan is shown to be effective, then it could be another key bullet to fire in the fight against malignant melanoma."

In Britain this week Professor Roy Sanders, a consultant plastic surgeon with the Restoration of Appearance and Function Trust (RAFT), said sunscreens were much less effective at blocking UVA light, which can cause the skin cancer melanoma, than UVB.

The RAFT study examined skin samples that had been exposed to UVA light at intensities similar to that of sunlight. The skin had been treated with three popular high-factor sunscreens, all of which said they contained some UVA protection. The results showed that, while the creams prevented the sun from burning the skin they did not stop UVA rays from penetrating it.

"When ultraviolet A impinges on the skin, it triggers the release of highly reactive chemicals called free radicals, which we believe can induce a malignant change," Professor Sanders told BBC Radio. "Since ambient sunlight is principally ultraviolet A and since sunscreens protect mostly against ultraviolet B, if we use the sunscreens, it may increase the risk of us developing malignant melanoma."

In Britain, cases of malignant melanoma have doubled every 10 years since the 1950s and the cancer now kills around 1,500 British people every year. RAFT predicts that by the year 2010, the lifetime risk of the disease will approach one in 50 of the British population.

Professor Sanders said the concern was that people were using the creams believing that they offered protection against cancer and, comforted by that, might be putting themselves at risk. "We're lulled into a sense of false security ... and so people are inclined to take a much greater dose of the sun," he said.

Melanotan, developed by Melbourne based biotechnology company EpiTan Limited, is currently completing Phase IIb "sunburn" trials at both the Royal Prince Alfred Hospital in Sydney and the Royal Adelaide Hospital, where it was tested on 80 healthy volunteers. Results of the trial are expected by early November 2003

**ABOUT THE COMPANY:** EpiTan Limited (ASX: EPT) is an emerging biotechnology company with a pre-eminent position on the prevention of DNA and skin damage from ultra-violet (UV) radiation exposure. Based in Melbourne, Australia, EpiTan holds a unique technology platform centred on its leading drug candidate Melanotan®. The company has the exclusive worldwide rights to develop Melanotan which, like sunlight, stimulates the production of melanin in the skin or "melanogenesis" – a unique biochemical process. A resulting natural tan develops without exposure to harmful levels of UV light.

Melanotan has concluded its Phase IIb clinical trials at two sites – the Royal Prince Alfred Hospital in Sydney and the Royal Adelaide Hospital. These trials are designed to demonstrate that Melanotan can reduce the incidence of skin damage resulting from harmful exposure to UV light. The last of 80 volunteers completed their participation in the trial in mid-September and preliminary results are anticipated early November 2003.

EpiTan has now successfully developed a more user-friendly drug delivery formulation of Melanotan in the form of a slow release implant. This will be used in the remaining clinical programme and the commercialised product.

EpiTan is also investigating Melanotan as a therapeutic agent for other indications such as vitiligo, albinism and psoriasis and UV induced skin allergies such as polymorphous light eruption ("PMLE") and solar urticaria. PMLE is a significant UV induced skin allergy in northern latitudes.

Potential markets worldwide for Melanotan for dermatology purposes are estimated at US\$2.5 billion. An even greater market (more than US\$5 billion) exists for Melanotan as a new safe (sunless) tanning drug.

**-End-**