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November 2018

Version: 181118XH



Sementis: Revolutionizing the Global Vaccine Industry



sementis™

Disclaimer



August 2018

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Executive Summary



Sementis has revolutionary vaccine “platform” technology that has the potential to create totally safe¹ and highly effective² vaccines to any number of diseases and conditions.

Sementis also has revolutionary manufacturing technology that allows for the rapid production of huge volumes of vaccines³.

Sementis is initially focusing on vaccines for allergies and mosquito borne diseases, namely:

- A cure for peanut allergy addressing a market estimated to be worth well over \$U.S.10 billion
- A world first combined vaccine for Zika and Chikungunya

Sementis’ revolutionary vaccine and manufacturing technology together make the world’s best⁴ and maybe only effective solution to pandemic and bio-terror threats.

Successful proof of concept work has been completed and published in peer reviewed journals that reports on the effectiveness and safety¹ of the platform technology and for the vaccines. The next step is to complete the manufacturing processes in order to proceed to human trials within the next year⁵.

After an extensive review process, the American National Institute of Allergies and Infectious Diseases (NIAID) will fund the first stage of preparation for the Sementis manufacturing process. Sementis is also working with the Australian CSIRO in bringing the manufacturing process to completion which is expected by the end of 2018.

Peered reviewed publications that describes our SCV platform technology and the proof-of-concept studies carried out with our single vectored chikungunya+Zika virus candidate vaccine:

- Eldi P *et al* (2017) Production of a Chikungunya Vaccine Using a CHO Cell and Attenuated Viral-Based Platform Technology. Mol. Ther.; 25 (10): 2332-2344 ([http://www.cell.com/molecular-therapy-family/molecular-therapy/abstract/S1525-0016\(17\)30280-0](http://www.cell.com/molecular-therapy-family/molecular-therapy/abstract/S1525-0016(17)30280-0))
- Prow NA *et al* (2018) A vaccinia-based single vector construct multi-pathogen vaccine protects against both Zika and chikungunya viruses. Nat Comms. DOI: 10.1038/s41467-018-03662-6 (<https://www.nature.com/articles/s41467-018-03662-6>)
- Prow NA, Jimenez Martinez R, Hayball JD, Howley PM, Suhrbier A.(2018) Poxvirus-based vector systems and the potential for multi-valent and multi-pathogen vaccines. Expert Rev Vaccines. Oct 9:1-10. doi: 10.1080/14760584.2018.1522255 (<https://www.tandfonline.com/doi/full/10.1080/14760584.2018.1522255?needAccess=true>)

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The Evolution of the Vaccine Market

Past, Present and Future Scourges



Past Scourges

- Smallpox epidemic with a kill rate of 1 in 3, Polio, Pandemic Flu



Present Scourges

- HIV been with us since 1980 and yet still no effective vaccine available
- Seasonal flu that is difficult to control with current vaccines
- No effective vaccines for food allergies, hepatitis C, and new emerging diseases such as Zika, chikungunya, and MERS



Present Scourges under control in the developed world but not eradicated

- Vaccines for measles, mumps, rubella, polio, Hepatitis A and B, etc.
- Many of these diseases are not under control in the underdeveloped world
- Many vaccines have limited effectiveness



Future Scourges

- The ever looming fear of Pandemic flu, Zika, Nipah, Ebola, Lassa, SARS, MERS, ??????

The Vaccine Market Today



Historically, the vaccine market was a small part of the Pharmaceutical Industry, however in the past decade, its growth has outstripped the rest of the industry.



The global vaccine market is expected to reach ***\$US48 billion*** by 2021 (from \$US 32 billion in 2016) – a CAGR of 8.3 % (a). Other studies expect double-digit growth (b).

(a) *Vaccines by Technology, Disease Indicator, End User and Type – Forecasts to 2021. Markets and Markets, August 2016*

(b) *Global Human Vaccine Market 2016-2020. Research and Markets, January 2016*

Growth Drivers in the Vaccine Market



Growth in the global vaccine market has been driven by:

01

The high prevalence of infectious diseases

02

Rising government funding for vaccine development and increased focus on immunization programs

03

Advances in technology, which are dramatically expanding the possibilities of vaccine treatments (e.g. cancer)

04

Advances in manufacturing technology, which will change the economics of vaccinations.



A Potted History of Vaccines



In the late 1700s, it was observed that milkmaids were immune from smallpox.

It was eventually discovered they had the cowpox virus, which gave them immunity to smallpox.



The smallpox vaccine was the first and is the only vaccine that has been used to eradicate a human disease!

The smallpox vaccine (the **vaccinia virus**) is a derivative of the cowpox virus and has been successfully used for over two hundred years.

The vaccine industry was born, with the Latin word 'vaccine' meaning "from Cows".

Evolution of Sementis' Vectored Vaccine Technology

- In the 1980s, gene for rabies surface antigen was inserted into the vaccinia virus (Copenhagen Version), then injected into fox bait and fed to animals in Northern Europe.
- The theory was that this new vaccine would not only give the animals immunity to smallpox but, importantly, also to rabies. It *worked*, and its effectiveness as a rabies vaccine has been proven in multiple studies over the past twenty years.
- However, because the vaccine replicates (multiplies) it can cause harm in a small proportion of recipients. This was acceptable during the smallpox era, as this disease had a kill rate of 1-in-3. However, now that smallpox has been eradicated it is no longer acceptable.



The question,
therefore, remained:

"If this version of the vaccinia virus could be made non-replicating, i.e. *totally safe*, why not use it as a platform for all sorts of diseases in humans?"



Enter Sementis: The Platform

Revolutionizing the Global Vaccine Industry



Sementis' revolutionary SCV vaccine platform technology and groundbreaking manufacturing technology are **both poised to revolutionize the vaccine industry and make a significant medical contribution to the world.**



A working vaccine for Peanut Allergy and the world's first dual vaccine for the Zika and Chikungunya mosquito borne diseases are just two of the multiple vaccine applications made possible by Sementis' SCV platform technology

The Revolutionary SCV Platform



The Sementis vaccine platform is called Sementis Copenhagen Vector (**SCV**).

The **SCV** platform is essentially the old smallpox vaccine (the original *vaccinia virus*), which was effectively used to eradicate rabies in Northern Europe and smallpox worldwide.

However, Sementis has genetically manipulated the vaccine that is expected to make it:



Totally safe¹

It does not replicate (multiply) to make it harmful¹.



Powerfully immunogenic

It is more visible to the immune system, thereby making it more active, resulting in a highly potent immune response⁶.

How the SCV Platform Works



Genes for antigens from particular diseases are inserted into the SCV platform.



This transforms the platform into a vaccine for whatever disease this inserted antigen originated from.




The body's immune system reacts to the transformed platform.



The body produces immunity to the disease the antigen originated from, as well as *immunity to smallpox (induced by the SCV platform) itself.*

Totally Safe, Effective and Versatile

A background image showing a person's hand holding a large, glowing white cross. The hand is positioned in the center, with the cross appearing to be held between the fingers. The background is a blurred image of a person in a white lab coat. Overlaid on the image are several white icons: a car on the left, a padlock on the right, and a network of dots connected by lines across the bottom and right side.

Every one of Sementis' extensive Proof of Concept Studies confirms the SCV platform's total safety¹ and potent immunogenic properties in animals and in experiments with human blood.

A peer-reviewed publication describes the properties of the non-replicating (non-harmful) platform.

In principle, the SCV platform will also:



Accommodate any number of genes for antigens from agents causing diseases and conditions



Improve the effectiveness and availability of current vaccines⁴

A Single Shot Vaccination Strategy



Where most vaccines require priming and boosting strategies, Sementis' Proof of Concept Studies have confirmed the SCV platform's powerful immunogenic properties, *which should only require a single shot vaccination strategy*⁷.

It is important to note that the potency of the SCV platform gives it superiority over many vaccines⁶, some of which have questionable consistency and efficacy.



SCV platform use in human clinical trials are the next step, however, as the vaccinia virus has been successfully used as a smallpox vaccine in humans for over 200 years, its effectiveness and properties are well understood.

With SCV platform technology, we have eliminated the safety issues associated with the original smallpox vaccine.

Hence, there are high expectations that human trials will simply confirm its previous success as a vaccine delivery vector when vaccinia virus was used as a rabies vaccine to eradicate rabies from Northern Europe.

A Vaccine to Cover Multiple Diseases



Because many genes for different antigens can be inserted into the SCV platform, it can handle a big payload.



Unlike other platforms, SCV can handle more complex antigen combinations and also target two (and possibly more) diseases in the one vaccine.



This is far superior to classical combination vaccines that consist of different vaccines that need to be manufactured *separately* before mixing into the same bottle.



SCV only requires one manufacturing process (a single batch run) to create a vaccine that covers multiple diseases, thereby reducing the cost of manufacturing.



Sementis Manufacturing

Game Changing Manufacturing Technology

At the Leading Edge of Technological Advances



Vaccine manufacture can be highly complex, with thousands of eggs often used in the production process. This is expensive and time consuming. It can also result in batch-to-batch variation and much can go wrong.



However, there have been a number of recent innovations and the respected Roots Analysis Report* on global vaccine contract manufacturing concludes that recent technological advances are “far superior” to traditional egg based methods.

Sementis is at the leading edge of every one of the technological advances noted in the Roots Analysis Report.

*Vaccine Contract Manufacturing Market, 2016-2026 by Roots Analysis Business Research and Consulting

Dramatically Improving the Time and Cost of Vaccine Production



The unique combination of the SCV proprietary platform and Sementis' game changing manufacturing technology has enabled multiple improvements in the efficiency of production – even over more recent advanced methods³.

In addition, in the near future we expect to be able to produce tens of millions of vaccine doses in a compact 500-litre Bioreactor in the space of a few weeks³. We will achieve this by increasing vaccine yields from smaller batch production sizes, thus vastly improving the time to produce and the cost of production³.

This will dramatically change the economics of the vaccine manufacturing industry and, significantly, can be applied as a highly effective, rapid response global solution to Pandemics and Bio-Terror.

After an extensive review process, the American National Institute of Allergies and Infectious Diseases (NIAID) will fund the “*cell banking*” of Sementis’ cell line in order to prepare for the manufacturing process. Sementis is working with the CSIRO to bring the manufacturing of the vaccines to fruition.



Vaccines in Development



The proven versatility of the SCV platform^{3&6} will enable Sementis to develop vaccines for numerous diseases and conditions. However, our initial focus has been the successful development of totally safe¹ and highly effective vaccines for:



Allergies

Peanut and Cat



Mosquito borne diseases

Zika and Chikungunya



Sementis Allergies

Finally a True Vaccine for Peanut Allergy !

The Size of the Allergy Market

1

It is estimated that, in the U.S. alone, **\$US25 billion per year** is being spent on food allergies.

2

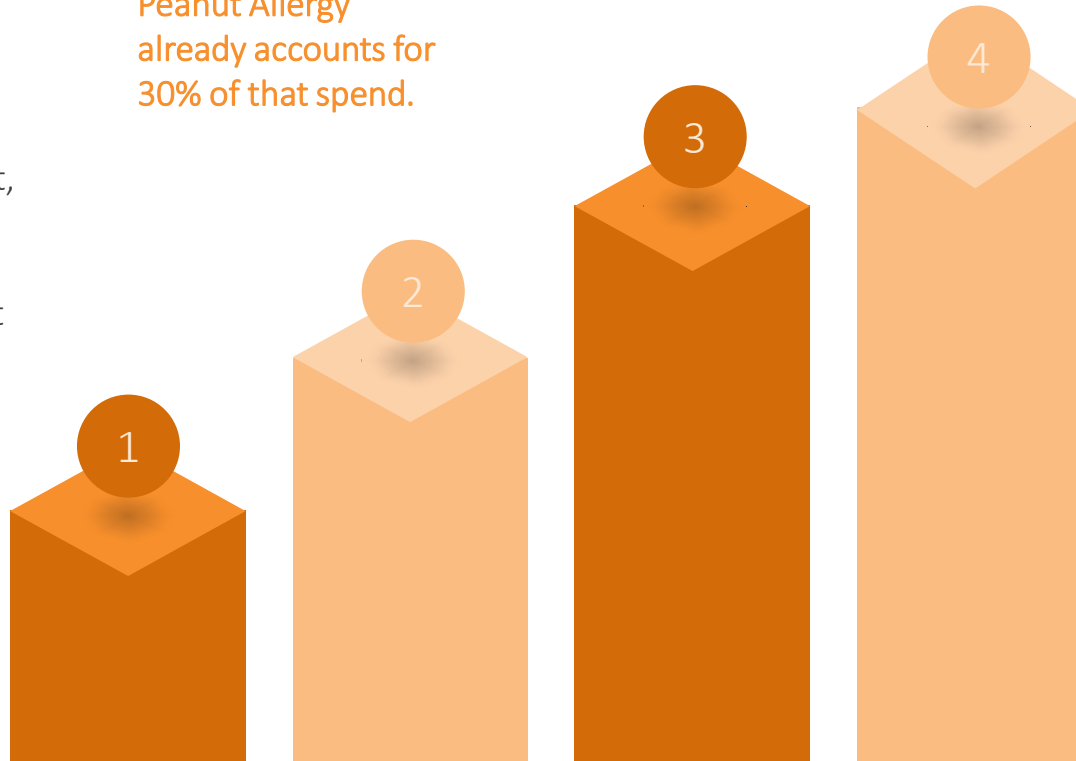
Peanut Allergy already accounts for 30% of that spend.

3

The stakes are high, with Sementis estimating that revenue from a solution to Peanut Allergy would be well in excess of **\$U.S.10 billion**.

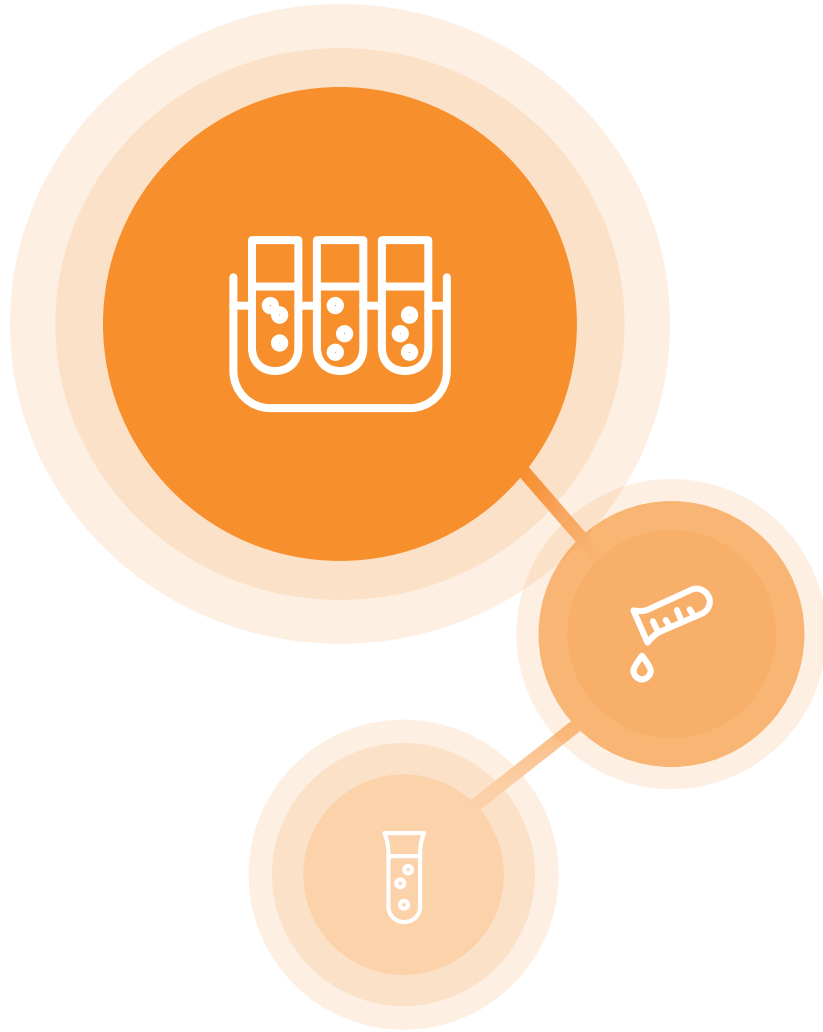
4

A working vaccine for Peanut Allergy will also pave the way for Sementis to develop vaccines for countless other food allergies, as the science is identical.



For detailed information on the Peanut Allergy market, please see Appendix 1.

A Unique Strategy for Peanut Allergy



Sementis' initial focus on allergies led to the development of a Peanut Allergy vaccine.

Sementis' approach is a unique strategy in an array of possible treatments being explored by companies worldwide.

Unlike 'toleration' (or desensitising) approaches to peanut allergens, Sementis' vaccine solution is expected to be far superior

As it results in a cure and not simply a toleration⁶.

Why the Vaccine Works



Sementis Peanut Allergy Vaccine does *not* work by promoting toleration to peanut allergens by 'taming' the peanut-specific “Th2” allergic immune response. That is, it is the immune system responding in this “Th2” way that causes the allergic response.

Sementis peanut vaccine is designed to *permanently* switch the Peanut-specific allergy causing “Th2” immune response to a peanut-specific *non harmful*, non-allergic “Th1” immune response.

Being a *true vaccine*, the switching will have long lasting memory to stop switching back to the ‘Th2’ allergic immune response⁶.



For detailed information on Sementis Peanut Allergy theory and results, see Appendix 1.

A Faster More Effective Solution



The 'toleration' approach to peanut allergy is a very long and involved process (often exposing the patient to some danger), requiring frequent desensitisation treatments over an 18-month period or longer.

In a large percentage of individuals the solution is not long lasting.

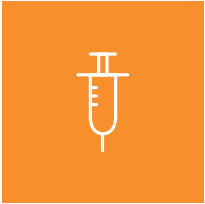
However, in an *expected vast majority of sufferers* Sementis Peanut Allergy Vaccine should provide:

01

A much shorter,
more efficient
treatment
regime⁶

02

Long lasting
(potentially lifelong) cure
i.e. total desensitisation
in just 1-2 months⁸.



The results of extensive Proof of Concept Studies in both peanut-sensitized mice and immune cells isolated from peanut allergic individuals, are extremely encouraging and strongly suggest the vaccine will work.

Proof of Concept Studies have been completed, with human trials expected to begin in late 2019.



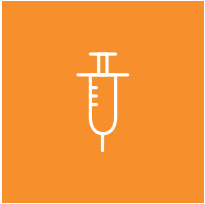
For detailed information on Sementis Peanut Allergy theory and results, see Appendix 1.



Sementis Infectious Diseases

A dual Vaccine for Mosquito Borne Diseases

A Dual Chikungunya & Zika Virus Vaccine – a World First



Sementis proprietary SCV platform is ideally suited to providing vaccines for many infectious diseases and we have already developed a dual vaccine to prevent both the Zika and Chikungunya mosquito borne diseases in one vaccination.

This dual vaccine is a world first, where two (and potentially more) vaccines in the SCV platform only require one manufacturing process, as opposed to a multiple manufacturing process, which is required for conventional combination vaccines.



For detailed information on mosquito borne diseases, see Appendix 2.

Proof-of-Concept Studies



Extensive Proof of Concept Studies in mice have proven the effectiveness of the dual vaccine in protecting against both Zika and Chikungunya *with one vaccination shot*.

Prow NA, *et al* (2018) A vaccinia-based single vector construct multi-pathogen vaccine protects against both Zika and chikungunya viruses. Nat Comms. DOI: 10.1038/s41467-018-03662-6

<https://www.nature.com/articles/s41467-018-03662-6>

In a Zika virus proof of concept study in Non-Human-Primates the dual vaccine protected all monkeys against Zika virus infection *with just one vaccination shot*.

Results soon to be submitted to a peer reviewed journal

Peered review proof-of-concept studies published in Nature Communications



Successful Proof of Concept Studies are complete, with human trials expected in late 2019⁵.



This should give Sementis a firm foothold in the infectious diseases space, which is a major part of the vaccine market.



For detailed information on mosquito borne diseases, see Appendix 2.



Sementis Tactical Response

Solutions for Pandemics and Bioterrorism



The World Bank report on Pandemic Preparedness has found that:

“The world’s investment in Pandemic Preparedness and response remains woefully inadequate...The result is the world remains scarily vulnerable...It is inevitable the world will see another pandemic in the not too distant future”. (a)



Bio-Terror is also a real threat. Experts have warned we are in the midst of a bio scientific revolution, which makes building and using biological weapons more deadly and increasingly easy.

*(a) Panic and neglect to investing in Health Security” Financing Pandemic Preparedness at a National Level (2017).
By international working group on financing preparedness. Supported by World Bank and Wellcome Trust*

Pandemics and Bioterrorism – a Clear and Present Danger



The Sementis SCV platform can make a vaccine to protect for most, if not all, pandemic and bio-terror threats and, when combined with Sementis' manufacturing technology, can potentially make tens of millions of vaccines in weeks^{3&6}.

We believe we may have world's only effective solution.

It is important to note here that the SCV platform is expected to be a *totally safe and vastly more efficient* version of the original *proven* smallpox vaccine⁶.



Sementis

Looking Ahead



With Animal Proof of Concept Studies complete for efficacy and one shot vaccination strategy, Sementis will now actively:



01

Explore potential partnerships and alliances for the various divisions of Infectious Diseases and Allergies within the group.

02

Pursue a working relationship with CSIRO to develop the SCV vaccine manufacturing process that amenable to up-scaling.

03

Explore strategies for the development of vaccines for cancer treatment

04

Explore strategies for the development of a dual vaccine for Hepatitis A and B, together with the development of a 'one shot' vaccination strategy for multiple diseases.

It is also anticipated that a liquidity event and possible listing may occur within the next eighteen months.



Sementis People

Board, Collaborators & Advisors

Paul Howley PhD

*CEO, Chief Scientist, Board Director, Co-Founder
and Inventor*

Paul's scientific background is in the field of molecular virology, specialising in viral vector systems and vaccinology. Paul is the inventor of the Sementis SCV platform vaccine delivery technology and the vaccines in development. He directs and manages the vaccine development programs for Sementis, utilising his extensive knowledge, experience and networks in the areas of antigen design and discovery, proof of concept studies in animal models, GLP preclinical and toxicology studies, process development and cGMP manufacturing, regulatory affairs and first in man studies concerning live viral vectored vaccines.

Maurice O'Shannassy

Non-Executive Chairman

Maurice spent 25 years in the financial services industry in Australia and overseas. He held a number of CEO and CIO roles around the world for BlackRock and its antecedents prior to becoming CEO of BlackRock Australia. He currently holds a number of directorships in a variety of industries and not for profit organisations.

Peter Wulff MSc

*Retired European Patent Attorney
Non-Executive Director*

Peter has over 30 years experience in the biotech and pharma industry, especially vaccines and patents. Peter co-founded Bavarian Nordic, a biotechnology company listed on the Copenhagen Stock Exchange, developing vaccines for infectious diseases and cancer. He served as president and CEO from 1994 until the company had secured a large supply contract with the U.S. government for its MVA smallpox vaccine, Immvamune, in 2007. Peter has participated in several private placements, two IPOs, and a number of follow-on offerings. He also has extensive experience with investor relations and government relations in Europe, Asia, and North America. He is currently an Independent Consultant to the Biotech industry.

Dr Glen Burgess MB BS FRACS

Non-Executive Chairman

Glen is an Otolaryngologist , Head and Neck surgeon. He is based in Melbourne Victoria where he is principal of Southern ENT, and Director of Monash Health, Snoring and Sleep Apnoea Clinic. He is a lecturer (adj) at Monash University Dpt of Surgery. He graduated from Monash University in 1988 and completed his FRACS - ENT Head and Neck surgery in 2000. He worked at Stanford University medical school before completing consecutive fellowships in Head and Neck Surgery at St Georges Hospital, London and Queens University Hospital Nottingham. He has been a medical consultant for the medical industry including time with Arthrocare , Smith and Nephew and Phonak. He is currently a director of Victorian Hearing. He has published papers on airway management, sleep apnoea and hearing loss. He is currently engaged in research in assessment and treatment of sleep apnoea.

Michael Hickinbotham BEc LLB

Non-Executive Chairman

Michael is the Managing Director of the Hickinbotham Group which is the largest and longest established building and development group in South Australia and has been awarded a Centenary Medal for service to the Australian Building industry and community. He has a strong interest in entrepreneurial ventures that create value as well as innovation, education, and community building having established Australia's, and one of the world's, first joint ecumenical Anglican Catholic Schools at Andrews Farm in the north of Adelaide. He also funds educational scholarships for children from high needs families, and supports many cultural, sporting and community groups and charities. Prior to joining the Hickinbotham Group, Michael was a solicitor at the Melbourne office of national law firm Black Dawson (now Ashurst) and he holds a degree in Economics from the university of Adelaide and an Honours degree in Law From University College London.

University South Australia (UniSA)



Sementis has a long standing relationship with UniSA where it uses the labs and pays for a number of scientists to undertake research and animal trials under the guidance of our Chief Scientific Officer, Paul Howley.



ARC-Linkage: for a 3 year period; Post-Doc salary and consumable costs



Science and Industry Endowment Fund STEM+ Business Industrial Research Fellowship Award: for a 3 year period; Post-Doc salary and consumable costs

QIMR Berghofer Medical Research Institute



Advance Queensland Research Fellowship Award; for a 3 year period Post-Doc salary and consumable costs commencing 2017

CSIRO-Manufacturing (Victoria)



CSIRO Manufacturing headed by Prof. George Lovrecz has been commissioned by Sementis to develop a commercial scale cGMP SCV manufacturing process and to produce vaccines for clinical trials

Jim Ackland

Sementis' Regulatory Affairs Consultant

Jim Ackland of Global BioSolutions has over 30 years' experience in the manufacture, quality control, development and international regulatory requirements for biopharmaceutical products. He has provided regulatory and product development advice and assistance to large and small companies. Prior to establishing Global Bioscience Solutions, Jim was employed at CSL Limited as Head of Regulatory Affairs.

Zarifah Hussain-Reed

Sementis' Clinical Development Director Consultant.

Masters in Public Health, John Hopkins University School of Public Health. 20 Years of experience in clinical sciences and as Medical Officer and Clinical Investigator, US Naval Medical Research Unit-2, Jakarta, Indonesia; Scientific Officer, WHO Initiative for Vaccine Research (IVR), Geneva, Switzerland; Assistant Director, Clinical Research and Training, The US HHS sponsored Regional Emerging Diseases Intervention (REDI) Center, Singapore; and Medical Director, Sentinext Therapeutics, Penang, Malaysia.

Dr Larry Ward

Sementis' Product Development and Clinical Consultant

Dr Larry Ward of Medicines Development for Global Health is a highly experienced biotechnology executive with broad R&D, product development, operational and general management experience, including manufacturing, pre-clinical and clinical development and regulatory affairs. He has direct experience in the development of therapeutic vaccines for HIV, HBV and cancer targets. He has more than 20 years' experience in the biotechnology industry at companies including AMRAD, Virax and Medicines Development for Global Health.

Prof. John Hayball

Immunologist at University of South Australia, South Australia, Australia
Heads the Experimental Therapeutics Laboratory (ETL) at the University of South Australia. Professor Hayball has an interest in understanding the fundamental mechanisms involved in controlling the mammalian immune response, particularly those involved in the development of an early innate immune response. He is using this information in rational approaches to develop new therapeutics for the prevention and treatment of diseases such as cancer, infection and wound healing. Sementis (with Prof. Hayball's oversight) conducts all preclinical immunological research and testing the efficacy of its new vaccines at ETL.

Prof. Andreas Suhrbier

NHMRC Principal Research Fellow and head of the Inflammation Biology laboratory at QIMR Berghofer Medical Research Institute, Queensland, Australia. Prof Suhrbier's group has developed mouse models for chikungunya and Zika virus infection and disease that are used in collaboration with several biotech/industry partners to assess new interventions. Using these models, he is currently testing our multi-pathogen chikungunya/Zika vaccine. He has >150 peer reviewed publications and is an inventor on 17 patents. He is/was a consultant for a number of international and local biopharmaceutical companies.

Jim Ackland

Regulatory Affairs Consultant
Jim has over 30 years experience in the manufacture, quality control, development and international regulatory requirements for biopharmaceutical products. He has provided regulatory and product development advice and assistance to large and small companies. Prior to establishing Global Bioscience Solutions, Jim was employed at CSL Limited as Head of Regulatory Affairs.



Paul Howley

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Allergen – A substance that causes an allergic reaction

Antigen - A foreign protein substance that induces an immune response in the body

Attenuation – Reduced or weakened virulence

Bioreactor – A vessel that grows cells as a suspension in a liquid volume

Desensitization – A process that makes the body less sensitive to an allergen

Genes – DNA that codes for the production of proteins such as antigens and allergens

Immunity – resistances to infection mediated by the immune system

Immunogenic - relating to or denoting substances able to produce an immune response

Pathogen – A bacteria, virus or other microorganism that can cause disease

Platform - A live virus (sometimes called a vector) that acts as a carrying vehicle for antigens (proteins) from diseases

Replicating (or multiplying) – Replication causes safety issues with vaccines, i.e. sickness

SCV - The Sementis platform, Sementis Copenhagen Vector

TH1 Response – TH1 cells are the body's immune cells, responsible for defense against viruses and bacteria

TH2 Response – TH2 cells are responsible for defense against parasite infections

Tolerization – Be capable of a continued subjection to an allergen without adverse reaction

Vaccine –Antigenic material used to stimulate an individual's immune system to develop an adaptive immunity to a pathogen

Virus - An extremely small piece of organic material that causes disease

Vaccinia Virus - The smallpox vaccine, which originated from the cowpox virus

Vector – an entity for delivering antigens to the immune system with the aim to stimulate an immune response to said antigens



Live attenuated vaccine (e.g., smallpox, measles, rubella)

These vaccines are made by weakening and crippling the disease causing virus that it no longer causes the disease but is still recognized by the immune system to stimulate life long immunity. Drawback is the possibility of reverse to virulence!



Inactivated (polio, flu, etc.)

To overcome the drawback to reversion to virulence, the original disease causing virus is inactivated (killed) but still recognized by the immune system. The disadvantages of these vaccines are lack of ability to stimulate potent immunity responses. There is also a risk the inactivation step has not killed all the virus in the batch of vaccine!



Subunits (HBV, etc.)

To maintain the safety of the inactivated vaccines and reduce the risk of incomplete inactivation, only parts of the disease causing virus is used in the vaccines, e.g., viral coat proteins that by themselves are non-infectious and non-virulent. However, they are unable to stimulate a potent immune response and need multiple vaccinations and regular boosting vaccination every 5 to 10 years.



VLPs (HPV)

Overcomes the drawback of subunit vaccine by increasing the potency of immunity but still require multiple vaccinations and regular boosting. The manufacturing process is more complicated than with attenuated, inactivated and subunit vaccines.



DNA vaccines (none)

New novel approach of addressing safety and long term immunity. However, to date, this technology developed in the 1980s has not proven effective in humans.



Vectored (Adv and MVA under advance development)

New technology that combines the advances of attenuated vaccine in terms of long lasting potent immune response to the safety of inactivated and subunit vaccines.



Appendices

Appendix 1 – Peanut Allergy theory and results

Peanut and other allergies result from the immune system reacting to the peanut allergens as if it was a parasitic invader. The immune system releases an attack on the invader in the form of chemicals (histamines etc.). This is known as a TH2 response. It is these chemicals that cause the allergic reaction.

Sementis' approach is to re-adjust the immune response to a non harmful Th1 response. In fact all of us have a Th1 reaction to all foods. Sementis approach is therefore simply reverting the allergic individual to respond to peanuts in the way that they and us respond to all food.

Genes for peanut allergens are inserted into the SCV and, because it is a live virus and not a parasite, the immune system undergoes what is termed a peanut-specific non-allergic TH1 response, which is *non harmful*. It is well founded that the immune system responds in a TH1 way to a live virus. Also, it is well established that TH1 response dominates the TH2 response - effectively telling it to 'stand down'. This has been *proven* multiple times in peer-reviewed studies and experiments over many years.



Sementis peanut vaccine induced response will switch off the harmful peanut-specific allergic TH2 response⁹. Hence, the Sementis solution should lead to a cure⁶. This is opposed to 'toleration treatments,' which is the current approach for allergies. Even when a toleration approach works, a fully blown allergy usually returns within a 5 to 10 year time frame.

Sementis has undertaken Proof of Concept experiments with its peanut vaccine in immune cells (outside the body) taken from blood of peanut allergic individuals and in peanut sensitized mice. As expected, in ALL cases the 'switch' has taken place. Furthermore, immune memory is induced so the solution should be permanent.

The Proof of Concept experiments and results are extraordinarily positive, in that practice is meeting the theory. Sementis is currently completing further experiments before publishing our results in peer-reviewed publications in the next few months. We expect to run human trials in the latter part of 2019 or during 2020⁵.



Appendix 1 – Peanut Allergy competing approaches

With revenues of potentially many billions of dollars to be generated in the Peanut Allergy market, competition for a solution is intense.

However, Sementis is one of two companies developing a true vaccine that will result in a cure for peanut allergy¹⁰.

Many companies are developing 'toleration' methods for the treatment of peanut allergy. However, the Sementis approach is different in that our vaccine will re-educate the immune system NOT to react to peanut proteins as allergens, thereby preventing an anaphylactic response upon ingesting a peanut.



Appendix 1 – Peanut Allergy competing approaches conti

Current treatments for peanut allergy involve a method of inducing tolerance to small amounts of allergens. These methods involve a long process and can sometimes inadvertently set off an unwanted allergic response. These approaches suffer from some or all of the following problems:



They are intense and costly to administer



Require high maintenance – a missed treatment step can render the treatment up to that stage useless (e.g. 1 year of treatment maybe lost if the subsequent ongoing treatment is interrupted!)



The treatments have safety concerns, with exposure to the small tolerating doses, inadvertently setting off an allergic reaction



Because of lengthy processes (i.e. around 18 months) compliance is low, with occasional treatment interruptions and dropouts



In the early stages of the treatment most patients will feel ill, i.e., nauseous and sometimes vomiting, hence high rate of early drop outs from the treatment course are often observed



Appendix 1 – the Peanut Allergy market



An academic paper produced by JAMA Pediatrics in the U.S. has estimated that caregivers would be willing to **pay \$20.8 billion annually (\$3504 per year per child) for food allergy treatment. Peanut was the most common food allergy (28.7%).**

JAMA Pediatrics concluded, “Research to develop an effective food allergy treatment and cure is critically needed”. (a)

Peanut Allergy is on the increase, occurring in about 1 in 50 children and 1 in 200 adults. Peanut is the most likely food to cause anaphylaxis and death. It had been estimated that there is one death for every 200 episodes of anaphylaxis. (b)

Children who are allergic to peanuts and other nuts are at increased risk of anaphylaxis compared with those who are allergic to other foods such as eggs and milk. One in five children with a food allergy will have a severe reaction requiring emergency medical attention, and this is most often triggered by peanut. (b)

(a) JAMA Pediatr 2013;167(11):1026-1031.doic:10.1001/jamapediatrics.2013.2376

(b) <http://www.slhd.nsw.gov.au/rpa/allergy/resources/allergy/peanutallergy.pdf>

Appendix 2 – Mosquito borne diseases



- Over the past decade, there has been an increasing prevalence of the emergence of mosquito borne diseases.
- This has focused world governments' and world health authorities' attention to seeking a solution.
- Zika has been a particular concern, given the impact on unborn babies and the fact it can be sexually transmitted.
- Chikungunya, whilst less well known, has also raised serious concerns about its spread to many regions in the world. Chikungunya infection can lead to debilitating arthritic symptoms that can persist beyond 6 months and often require hospitalization
- The Zika and Chikungunya viruses are carried by the same mosquito and hence, tend to appear in the same regions at around the same time where a person can be infected by both viruses from a single mosquito bite.
- Sementis has developed a world first dual Zika/Chikungunya vaccine¹¹ to prevent both diseases in one vaccination. We aim to enlist an NGO to fund a clinical trial to test our Zika/Chikungunya vaccine.



SCV Cell Substrate for manufacturing:

- Viral Vector Manufacturing.
Inventor: Paul Howley and Liang Liu. International Application Number: PCT/AU2014/050330 (International publication number: WO 2015/061858)
- **Granted:** EPO, Russia, Singapore, South Africa



SCV Peanut Allergy Vaccine:

- Immune Modulation, Inventor: Paul Howley. International Application Number: PCT/AU2014/000286 (International Publication Number: WO 2014/138824A1)
- **Granted:** Australia, Israel(allowed), New Zealand, Russia (allowed), Singapore



SCV dual Zika/Chikungunya vaccine:

- Viral Vaccines, Inventor: Paul Howley. International Application Number: PCT/AU2017/050879
- PCT Preliminary Examination acknowledges inventive step
- Application pending in countries additional to PCT

1	So far only tested in animals with no antiviral immune response but the expectations are that it will be completely safe in humans with an uncompromised immune response and should be safe in humans with deficient immune responses.
2	So far only tested in animals but the expectations are that in humans with a fully functional immune response our SCV based vaccines will be effective at stimulating immune responses, however, this will need to be demonstrated in clinical trials.
3	Assumption based of theoretical upscaling using data from our of laboratory production process. This will be confirmed once the manufacturing scale process development has been completed.
4	Based on predictive data and outcomes but yet to be confirmed in practice.
5	Overall objective but influenced by availability of sufficient funds before starting, the bureaucracy of the regulatory process for getting approval to do clinical trial and timely progress of patient recruitment.
6	Based on preclinical proof-of-concept studies. Yet to be confirmed in human clinical trials. Due to the nature of the proof-of-concept studies, the expectation is, there will be a high degree of confidence that the proof-of-concept will translate to humans.
7	Will need to be proven in a human clinical trial.
8	As this is a true vaccination approach, where the function of vaccines are to stimulate immunological memory, this should also be true when vaccinating against allergies.
9	Based on preclinical proof-of-concept studies.
10	As far as we know. The other approach is a DNA vaccine strategy.
11	As far as we know.