

# University Researchers, Private Industry Work Together To Fight Tooth Decay

University of Melbourne



RECALDENT (CPP-ACP) works to strengthen teeth by delivering calcium and phosphate, the building blocks of teeth, to re-mineralize the enamel. Used as an ingredient in sugar-free chewing gum and other products, RECALDENT™ (CPP-ACP) is marketed internationally by Cadbury Schweppes.

The collaboration to develop the RECALDENT (CPP-ACP) technology was led by professor Eric Reynolds, head of the School of Dental Science at the University of Melbourne, Victoria, Australia, and included contributions from other areas of the university as well as from government and private industry.

## **Nature Provides the Solution**

The project began in the 1980s, when even though levels of tooth decay in Australia had started to fall due to the introduction of fluoride, the disease was still a major public health problem. So Reynolds and his research team began

researching ways to repair teeth by replacing calcium and phosphate ions in the enamel.

The first major obstacle was to find a way to deliver calcium and phosphate to the teeth. “Calcium and phosphate are insoluble,” says Reynolds. “Our challenge was to deliver it in a practical way.”

For a solution, Reynolds turned to nature. Dairy products were well established as having dental health benefits, so Reynolds focused his attention on casein, the protein that carries calcium phosphate and is responsible for milk’s white color. “We researched what part of casein is responsible for this ability to carry and stabilize calcium phosphate,” he explains.

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Working with his research team, Reynolds was able to easily and inexpensively isolate the active sequences in casein to form a new complex called CPP-ACP. This complex, which would eventually become RECALDENT™ (CPP-ACP), was found in laboratory and clinical trials to bind to the teeth and provide a reservoir of calcium and phosphate on the surface. Simply, it repaired teeth and reversed tooth decay.

To confirm these results, the team embarked on a two-year population based study. In the study, 3,000 children were asked to chew sugar-free gum, which had been shown to reduce tooth decay on its own, for 12-24 months. In the double-blind study, some of the children received gum with CPP-ACP and others did not. The study showed that sugar-free gum with CPP-ACP produced 50 percent greater reversals of early signs of decay than did regular sugar-free gum. “It is the only technology apart from fluoride shown to slow development of decay,” says Reynolds, “and it could actually repair teeth.”

The study was used to build a case for regulatory approval to manufacture and market RECALDENT (CPP-ACP).

Working with Unimelb Pty. Ltd., which was the University of Melbourne’s technology transfer office at that time, Reynolds applied for a patent for RECALDENT (CPP-ACP) and set about looking for a partner to manufacture it on a commercial scale.

### **Assembling the Team**

The role of Melbourne Ventures, which now continues the work of Unimelb, is to build commercial value on the foundations of intellectual property developed at the university. “The major benefit we bring is bridging the divide between research and commercial enterprise,” says Charles Day, Ph.D., general manager of Melbourne Ventures. “We tackle the intricacies of licensing, finance, intellectual property, and so forth.”

Another role is bringing together a diverse set of skills, from outside the university and from within, to get technology into the marketplace.

A collaboration of a diverse set of skills was exactly what was required to manufacture RECALDENT (CPPACP), according to Reynolds. The project brought together Reynolds’ group from the university’s dental school, the chemical engineering department, and Bonlac Foods Ltd., an Australian dairy company.

Assembling an interdisciplinary team like the one assembled for the RECALDENT™ (CPP-ACP) project required funding. Reynolds and the team secured an Industry R&D grant through the Australian government to develop a commercial scale manufacturing process. Reynolds also attracted funding to clinically evaluate the CPP-ACP technology from the National Health and Medical Research Council.

But getting funding for tooth decay research was not easy, according to Reynolds. “The attitude was that fluoride eliminates tooth decay, and the funds go to cancer research and other areas,” he recalls. They were able to secure the grants, however, and the project continued.

“For the government to see the quality of the science showed a lot of foresight,” Reynolds says.

Above all, Reynolds points out that the interdisciplinary team effort was critical to the success of the project.

“Manufacturing on a commercial scale was a completely new thing to us,” he notes, adding that “Bonlac had no expertise in biotechnology.”

Brought together by the government grant, the dental school and chemical engineering researchers created a form of the RECALDENT™ (CPP-ACP) material that could be produced relatively easily. Bonlac, meanwhile, built a pilot plant and provided guidance to the researchers regarding their needs for production. “It was frontier science,” recalled Reynolds. “It was very exciting.”

### **Impact on Health, Economics**

Though RECALDENT (CPP-ACP) was developed several years ago, collaborative efforts are still ongoing to further develop the technology and find new applications for the product. Reynolds is working with dental academics in the United States, Japan and Europe on clinical trials.

These and other efforts have led to the further development of the technology and of several products featuring RECALDENT™ (CPPACP), including toothpastes, gum, mouthwash and professional products used by dentists. Global sales of products containing RECALDENT™ (CPP-ACP) have exceeded US\$200 million. The most popular

RECALDENT-enhanced product is Trident White gum, which has generated annual sales of over \$50 million in the United States. Other brands of gum with RECALDENT (CPP-ACP) have been successfully marketed in Mexico, Australia and Japan.

The development of RECALDENT (CPP-ACP) has enhanced the research reputation of University of Melbourne.

Currently, the university is teaming up with Harvard University in Cambridge, Mass., and the Toronto Dental School on an international benchmarking exercise. Other research efforts to progress the technology are also ongoing. According to Day, it has been “an incredible magnet” to attract other researchers and opportunities to the university.

Reynolds believes the benefits of RECALDENT (CPP-ACP) are only beginning to be known. “Clinical data is showing that people who use RECALDENT™ (CPP-ACP) are having fewer cavities,” he says.

This not only affects people’s health, but also the economics associated with treating decay. RECALDENT (CPP-ACP) also has a positive cosmetic effect on the teeth, which can improve people’s quality of life.

Reynolds notes, “With people living longer and having significant problems with their teeth, this can have a huge impact on society.”

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