THERAMETRIC TECHNOLOGIES

ADA-QUALIFIED cGLP & cGCP TESTING FACILITY

Therametric Technologies develops and conducts a variety of test methods that evaluate oral care products and innovations. This includes bespoke testing or research and development services tailored to the client's specific needs.

QUICK LINKS: IN VIVO AND EX VIVO | IN SITU

IN VITRO TESTING

TEST METHOD	DESCRIPTION
Relative Dentin Abrasion (RDA) ISO 11609 Annex A / ADA Method	This is a test method to determine the relative abrasive level of oral care products (i.e. toothpastes, tooth gels, abrasive powders, etc.) to human dentin substrate. Applying a controlled brushing to radioactive teeth and then comparing the amount of radioactivity that comes off the tooth with the test dentifrice to the amount that comes off with a reference standard gives a relative abrasion level.
Relative Enamel Abrasion (REA) ISO 11609 Annex A / ADA Method	This is a test method to determine the relative abrasive level of oral care products (i.e. toothpastes, tooth gels, abrasive powders, etc.) to human enamel substrate. The methodology is the same as the RDA except enamel is the tested substrate.
Prophy Paste Abrasion (RDA/REA) ANSI/ADA No. 62 Method	This is a method to determine the relative abrasive level of professional use prophy pastes / abrasives to dentin and/or enamel substrates. The methodology is similar to the RDA and REA except the treatment procedure uses a prophy application rather than brushing.
Pellicle Cleaning Ratio (PCR) & Enamel Whitening Potential In Vitro Stain Removal and/or Whitening	This test method is used to determine the ability of oral care products (primarily dentifrices) to remove stained integuments from enamel using spectrophotometric assessments. The model, as normally performed, has significant correlation to clinical stain removal studies. Although not designed to measure changes in actual tooth color, the model has been used for whitening claims.
Enamel Polishing Potential Surface Gloss or Luster	This test method is used to determine the enamel polishing efficacy of oral care products (i.e. toothpastes, tooth gels, abrasive powders, etc.) using spectrophotometric surface gloss assessments. Dulled enamel surfaces are treated using the appropriate method and the post treatment gloss is compared to the pretreatment gloss. This can be done as a one-time treatment to find maximum polish or a series of treatments to establish a polish profile.

TEST METHOD	DESCRIPTION
Power Toothbrush RDA/REA/PCR Abrasion/Cleaning of Power Toothbrushes	This is a test method for determining the enamel/dentin abrasivity and/or cleaning and stain removal potential of power toothbrush devices. The measured variables are the same as outlined above for RDA, REA and PCR except the treatment of the specimens are performed using specialized equipment designed to hold and articulate power toothbrushes.
Floss Abrasion and Cleaning Abrasion/Cleaning of Dental Floss	This is a test method for determining the enamel/dentin abrasivity and/or cleaning and stain removal potential of dental floss or flossing devices. The measured variables are the same as outlined above for RDA, REA and PCR except the treatment of the specimens are performed using specialized equipment designed to hold and articulate floss or flossers.
Enamel Fluoride Uptake (EFU) FDA Monograph Method for Fluoride Dentifrices	This test method is used to determine the efficacy of oral care products in promoting fluoride uptake into sound or demineralized human enamel substrate (fluoride bioavailability) as per FDA Monograph requirements. Treatments are done by slurry immersion and assays are performed by acid etch enamel removal or microdrill biopsy and then fluoride analysis using ion selective electrodes.
Enamel Solubility Reduction (ESR) FDA Monograph Method for Fluoride Dentifrices	This is a method to determine the efficacy of oral care products in reducing the solubility of human enamel to lactic acid challenges (preventing enamel demineralization or erosion) as per FDA Monograph requirements. Treatments are done by slurry immersion and assays are performed by acid etch enamel removal and then phosphorus analysis using spectrophotometric methods.
Modified Enamel Fluoride Uptake (EFU) Flow Model for Fluoride Varnishes	This method of standard EFU testing modified for determining the efficacy of fluoride varnishes to promoting fluoride uptake into demineralized enamel substrate (fluoride bioavailability). This model employs a constant flow of artificial saliva over the varnish treated specimens to simulate the dilution that occurs over time in the mouth.
In Vitro pH Cycling (White Model) Enamel Remineralization & Fluoride Bioavailability *(Microhardness & Enamel Fluoride Concentration Assessments)*	This is a test method to determine the ability of oral care products to promote remineralization / hardening and fluoride uptake into artificially white spotted human enamel substrate following a dynamic, multi-week treatment regimen. The outcome metrics can include fluoride uptake, surface microhardness changes and profile (cross sectional) microhardness measurements of the internal structure of the lesion.
In Vitro pH Cycling (White Model) Enamel Remineralization *(Surface Microhardness ONLY)*	This is a test method for determining the ability of oral care products to promote remineralization / hardening of artificially white spotted human enamel substrate following a dynamic, multi-week treatment regimen. It has the same outcomes as above except no fluoride uptake analysis.

TEST METHOD	DESCRIPTION
In Vitro pH Cycling (Featherstone Model) Enamel Demineralization/Caries Prevention	This test method is designed for determining the ability of oral care products to prevent enamel demineralization (caries initiation and progression) following a dynamic, multi-week treatment regimen. The outcome metric is lesion progression based on cross-sectional (profile) microhardness.
In Vitro Erosion Potential / Safety ISO 28399 Annex B Method Surface Hardness & Profilometry	This is a test method for determining the erosive potential of oral care products (i.e. oral rinses and whitening/bleaching agents) on enamel and/or dentin substrate following a dynamic treatment regimen.
In Vitro Erosion Prevention Model Surface Hardness & Profilometry	This model is used for determination of the ability of oral care products to prevent enamel and/or dentin erosion form dietary acids (i.e. citric acid).
ISO 28888 Erosion Potential Screening Chemical Method for Oral Rinses pH monitoring	This is a screening test method for oral rinses to determine their potential to cause erosion of enamel and/or dentin using a pH monitoring procedure. This is an ISO Standard method.
In Vitro Dentin Tubule Occlusion Model SEM Surface Imaging Analysis and/or Hydraulic Conductance Assessment	This test method is used for determining the ability of oral care products to occlude dentin tubules and provide anti-hypersensitivity effects.

ANALYTICAL FLUORIDE ASSAYS	
TEST METHOD	DESCRIPTION
Direct Ion Selective Electrode Assays Total Fluoride Soluble/Available Fluoride	An analytical method for determination of total and/or soluble available fluoride using direct ion selective electrode (ISE) analysis. (NaF and SnF2 based formulations).
Diffusion Method Assays (ISO 11609) Total Fluoride Soluble/Available Fluoride	An analytical method for determination of total and/or soluble available fluoride using an acid hydrolysis diffusion-based technique. (Sodium Monofluorophospate formulations).
ADA Seal Fluoride Profile Assays Soluble Available & 1-Minute *(Fresh & Aged Samples)*	An analytical method for determination of soluble, available fluoride and 1-minute fluoride release on fresh & aged samples for ADA Seal Submission requirements.
Varnish Total Fluoride Assays	An analytical method for determination of total fluoride in a fluoride varnish formulation.
Varnish Aqueous Fluoride Release ISO 17730	An analytical method for determining the rate/magnitude of fluoride ion released in aqueous solution from fluoride varnish formulations.

Customized test method development and/or modifications to any of the above tests are available. For additional information, questions or clarifications regarding in-vitro studies, please contact Heath C. McClure

OTHER ACTIVE INGREDIENT ANALYTICAL TESTING METHODS	
TEST METHOD	**DESCRIPTION**
Hydrogen or Carbamide Peroxide Content USP/ISO Methods	Using titrimetry, determination of either hydrogen or carbamide peroxide content in dental bleaching systems, including gels, mouthwash, pens, and other topically applied dental systems are made. Useful for quality control purposes especially, the peroxide content can be determined for both over- the-counter and professional-strength peroxide topical systems.
Potassium Nitrate (KNO_3) Analysis	A colorimetric, spectrophotometric quantification method is utilized to determine the total KNO_3 concentration is oral care products marketed for anti-hypersensitivity.

MICROBIOLOGY TESTING METHODS

TEST METHOD	DESCRIPTION
Plaque Glycolysis and Regrowth	This model can be adapted to be conducted in vivo, ex vivo, or in vitro. It is useful for screening potential antiplaque/antigingivitis agents, and is recommended by the FDA and ADA for antiplaque claims. Participants' plaque is sampled at baseline and at timed events following administration of a test product in the clinic and/or at home. The plaque is then analyzed for glycolytic action and regrowth. Such models are recommended by the FDA and ADA for antiplaque claims. Additional endpoints may be added to quantify products' ability to influence specific virulence factors such as acid production and/or microbial species such as S. mutans or P. gingivalis.
Minimum Inhibitory Concentration (MIC)	MIC is the lowest concentration of an agent that inhibits the visible growth of a microorganism overnight. MIC is evaluated utilizing a microtiter plate method. Different concentrations of treatments of interest are prepared and analyzed for their potential to inhibit visible bacterial growth, and compared to the growth of untreated biofilm through measuring absorbance (Optical Density).
Critical Kill-Time Determination	This in vitro assay allows identifying the percent of bacteria remaining viable after exposure to an antimicrobial agent for a stated period of time. Fresh, pooled saliva is exposed to different agents for a predetermined treatment time (e.g. 30-seconds). Samples are neutralized chemically, plated and incubated. Then viable microorganisms are counted in each sample. Such model is recommended by FDA for antimicrobial claims.
Bacterial Viability Testing	Using Spread Plating Method, Bacterial Viability (Colony Forming Units [CFU/mL]) can be conducted through automatic or manual colony counting. It can be conducted on whole biofilm samples on differential agar plates, or isolated species using selective agar plates.

All tests can be conducted either against whole biofilm samples (from pooled plaque, or pooled saliva samples), or against specific species associated with certain conditions such as gingivitis-associated species or oral malodor-associated species. Customized test method development and/or modifications to any of the above tests are available. For additional information, questions or clarifications regarding microbiology studies, please contact Hadeel M. Ayoub

TEST METHOD	DESCRIPTION
pH Buffering	This in vivo test method is designed to determine the ability of an oral care product to buffer/neutralize the pH within the oral cavity when exposed to challenges. Typically saliva is analyzed but this can also be applied to plaque sampled from specific sites.
Salivary Flow *(ADA Seal Model)*	This in vivo test method determines the ability of a chewing gum or mint to stimulate salivary flow compared to a clinically tested, ADA approved chewing gum. Increased salivary flow is one method to increase remineralization and prevent demineralization thus reducing a cariogenic challenge.
Salivary Peroxide Concentration in Saliva	This is an ex vivo model using colorimetric analysis to determine the concentration of peroxide released into saliva at multiple timepoints during and after tooth bleaching/whitening using a peroxide-containing oral care product; required by Health Canada for peroxide-containing products ≥ 3.0% Hydrogen Peroxide (or equivalent).
Dentinal Hypersensitivity	This is an in vivo clinical test method to determine the ability of an oral care product to reduce tooth sensitivity over a four week test period . Using a Visual Analog Scale (VAS), the outcome measures are subject reported perceptions to the severity of various pain provoking stimuli (i.e. exposures to an air blast, tactile force, and/or a thermal or hypertonic sucrose solution). Efficacy of the product is determined by comparing baseline sensitivity levels to post-treatment VAS scores, relative to a control.
Whitening	This in vivo test method determines the ability of an oral care product to bleach/whiten extrinsic stain and intrinsic tooth color. Efficacy is determined by using the VITA Bleachedguide 3D-MASTER and/or a handheld spectrophotometric device, comparing baseline tooth shade level to post-treatment scores relative to a placebo control.
Supragingival Plaque Removal	Studies are designed to assess plaque removal/reduction, and corresponding change in gingivitis levels, of a variety of dental products such as toothbrush, floss, oral irrigator, toothpaste and mouthrinse. Plaque and gingivitis levels are evaluated by a trained and calibrated dental examiner. Efficacy is determined by the reduction of plaque levels of the test product compared to the control.
Oral Safety	This in vivo model is used to assess the oral irritation potential of a formulated product under exaggerated use conditions over 5 days followed by an 18-day rest period, then a 48-hour product exposure period for sensitization assessment. A dental clinician evaluates the presence of oral soft issue responses based on a 0 to 3 irritation score over the 5-day test period and following the 48-hour challenge period. The outcome variable is the mean irritation score of the test group compared to the control group.

IN SITU CLINICAL TESTING METHODS

TEST METHOD	DESCRIPTION
Caries Prevention, Enamel Remineralization and/or Fluoride Bioavailability	This in situ model utilizes an intra oral appliance (IOA) to evaluate the ability of an oral care product formulated to prevent dental caries progression, promote enamel remineralization and/or promote fluoride uptake. The IOA houses sound or demineralized enamel substrates that are then evaluated for fluoride uptake, surface hardness, and/or cross-sectional (subsurface) hardness.
Erosion	This in situ model utilizes an intra oral appliance (IOA) to evaluate the ability of an oral care product formulated to prevent enamel erosion from dietary acids (i.e. citric acid). The outcome measure is surface microhardness with a non-contact 3D optical profilometry procedure.
Stain Removal	This is a partial denture in situ model useful for determining the ability of an oral care product to remove/reduce extrinsic tooth stain. Tooth pontics in the partial denture house stained enamel substrates used to evaluate the stain removal ability of the test product. Efficacy is measured ex-vivo using spectrophotometric evaluation.

Customized test method requests, protocol development, and/or modifications to any of the above tests are available. We can assist you with research design strategies to support your product claims and adhere to professional and regulatory standards.

Our seasoned clinical research professionals conduct industry-sponsored clinical research trials that investigate the safety and/or efficacy of dental products seeking to improve oral health, whether through detection, prevention or treatment of oral health diseases, or evaluation for cosmetic benefits.

We plan, coordinate, execute and manage the full lifecycle of each clinical research trial safely and efficiently, in accordance with current International Conference of Harmonization (ICH) Good Clinical Practice standards (cGCP) and in compliance with the United States Code of Federal Regulations. All clinical research trials are overseen by an independent Institutional Review Board to protect the rights and welfare of our research volunteers.

For additional information regarding clinical research studies, please contact Sylvia Santos or Heath C. McClure.

CONTACT INFORMATION

Heath McClure
Managing Director
(317) 565-8070
HMcclure@therametric.com

Hadeel M. Ayoub, PhD
Research Scientist
(317) 565-8065
HAyoub@therametric.com

Sylvia Santos, MS
Head of Clinical Research
(201) 572-9223
SSantos@therametric.com

Corporate Office: **(317) 565-8065 | 9880 Douglas Floyd Parkway, Noblesville, Indiana 46060-7900**