Form Approved Through 09/30/2007 OMB No. 0925-0001

Department of Health and Human Services
Public Health Services

Grant Application

Do not exceed character length restrictions indicated.

LEAVE BLANK—FOR PHS USE ONLY.

Type	Activity	Number
Review Group		Formerly
Council/Board (Month, Year)		Date Received

1. TITLE OF PROJECT *(Do not exceed 81 characters, including spaces and punctuation.)*
DPBRN Study 5: Longitudinal study of dental restorations

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION ☒ NO ☐ YES
(If "Yes," state number and title)
Number: Title:

3. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR — **New Investigator** ☐ **No** ☐ **Yes**

3a. NAME (Last, first, middle)
DPBRN c/o , Ivar A. Mjör

3b. DEGREE(S)
BDS MSD Dr.odont.

3h. eRA Commons User Name

3c. POSITION TITLE
Professor/Eminent Scholar

3d. MAILING ADDRESS *(Street, city, state, zip code)*
College of Dentistry
1600 SW Archer Road
Gainesville, FL 32610

3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT
Operative

3f. MAJOR SUBDIVISION
Dentistry

3g. TELEPHONE AND FAX *(Area code, number and extension)*
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E-MAIL ADDRESS:
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4. HUMAN SUBJECTS RESEARCH
☐ No ☒ Yes

4b. Human Subjects Assurance No.

4c. Clinical Trial ☐ No ☒ Yes

4d. NIH-defined Phase III Clinical Trial ☒ No ☐ Yes

4a. Research Exempt ☐ No ☐ Yes

If "Yes," Exemption No.

5. VERTEBRATE ANIMALS ☒ No ☐ Yes

5a. If "Yes," IACUC approval Date

5b. Animal welfare assurance no.

6. DATES OF PROPOSED PERIOD OF SUPPORT *(month, day, year—MM/DD/YY)*		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT	
From	Through	7a. Direct Costs ($)	7b. Total Costs ($)	8a. Direct Costs ($)	8b. Total Costs ($)

9. APPLICANT ORGANIZATION
Name
Address

10. TYPE OF ORGANIZATION
Public: → ☐ Federal ☐ State ☐ Local
Private: → ☐ Private Nonprofit
For-profit: → ☐ General ☐ Small Business
☐ Woman-owned ☐ Socially and Economically Disadvantaged

11. ENTITY IDENTIFICATION NUMBER
DUNS NO. Cong. District

12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE
Name
Title
Address
Tel: FAX:
E-Mail:

13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Name
Title
Address
Tel: FAX:
E-Mail:

14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

SIGNATURE OF PI/PD NAMED IN 3a.
(In ink. "Per" signature not acceptable.)

DATE

DESCRIPTION: See instructions. State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project (i.e., relevance to the **mission of the agency**). Describe concisely the research design and methods for achieving these goals. Describe the rationale and techniques you will use to pursue these goals.

In addition, in two or three sentences, describe in plain, lay language the relevance of this research to **public** health. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. **DO NOT EXCEED THE SPACE PROVIDED.**

Longitudinal study of dental restorations

A number of factors affect the longevity of restorations, including the restoration quality at the time of insertion, the type and size of the restoration, the restorative material involved, patient factors like oral hygiene, patient age; dentition, and if the patient maintains regular recall appointments in the same dental practice. Most failures occur some time after the restoration was inserted and they are a result of gradual development of secondary caries, some physical defects like discoloration of the restoration, or some form of degradation like marginal breakdown or 'ditching'. Restorations inserted in DPBRN Studies 2 ('primary' restorations) and 3 ('replacement' restorations) provide a unique opportunity to follow-up on these restorations in a practice-based setting for up to three years to assess how defects that may lead to failure develop over time. This study will differ from those in randomized controlled clinical trials in that the restorations are consecutively placed by practitioners in general dental practice in the routine treatment of patients. No exclusion and inclusion criteria have been applied and the clinicians have not received any special training in restorative procedures. The specific aims include (1) to quantify the annual and three-year incidence of defects in DPBRN Studies 2 and 3, (2) test the hypothesis that composite restorations have a significantly higher replacement rate after three years than amalgam restoration, (3) test the hypothesis that there is no significant differences between repaired and replaced restorations in DPBRN Study 3, and (4) to test the hypothesis that the three-year replacement rate of restorations in adolescents is significantly higher than that of restorations in adults

The criteria used to evaluate the restorations over time will be the same as those employed in Study 3. The recall frequency will be according to the schedule used in the practice where the restoration was placed. The patients in Studies 2 and 3 will have been informed about the follow-up study as part of the informed consent procedure. If a patient seeks future treatment in a different practice, the informed consent will include permission to contact that practice for information related to the restoration(s) being part of Study 5.

Relevance to public health: Longitudinal studies of the development of defects will give information that may lead to increased longevity of restorations. Measurements of the longevity of restorations reflect all conditions that affect the restoration from the day of insertion until failure occurs. The longevity of restorations and the cost of placing/replacing restorations are two decisive factors determining the long-term cost of restorative therapy

PERFORMANCE SITE(S) (organization, city, state)

RESEARCH GRANT
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CONTEXT IN WHICH THE STUDY WILL BE CONDUCTED

Dental restorations are inserted to replace pathologically affected, lost and defective dental tissues to restore anatomy, function, and esthetics. Direct or indirect restorative techniques may be used. Direct restorations, the most frequently placed restorations, involve the use of a pliable material which sets hard after they have been inserted into the cavity preparation. Resin based composite materials; amalgam, glass ionomer cement, and gold foil are examples of materials which are inserted in a soft state. Indirect restorations are made from alloys, ceramics, or resin based materials and they include inlays, onlays, and crowns. The crowns are either fabricated in a dental laboratory on models made from impressions of the prepared teeth or they are manufactured from a computer image of the prepared teeth (CAD/CAM technique). All types of the indirect restorations are cemented in place as one unit. Therefore, undercuts must be removed in the prepared tooth, which usually requires the removal of more sound tooth structure than required for direct restorations, especially if the indirect restoration replaces restoration in a cavity with conventional retention features. Although indirect restorations cost more than similar direct restorations, by a factor of 5-10 times depending on the practice (Christensen, 1998) they last longer (Mjör, 1992b; Nieuwenhuysen et al., 2003).

The safety and efficacy of any treatment, including dental restorations, are of paramount interest to the subjects involved. Restorative materials contain a number of allergenic and toxic components, but the concentration of leachable components is low. The safety of dental restorations is well established and the risk of toxic side effects from restorative therapy is very low, although allergic reactions occasionally occur (Kallus and Mjör, 1991; Mjör, 1992a). The safety of luting cement is also important for the efficacy of indirect restorations.

The long term cost of restorative therapy is based on two major factors: the cost of the restorations at the time of its placement/replacement and the longevity of the restoration. In the permanent dentition the restorations should last for the life time of the individual, but it is well known that so-called permanent restorations have a limited longevity. Since the life expectancy approaches 80 years in most industrialized countries, the longevity of restorations should be viewed in a long term perspective. Permanent teeth often require restorations between the ages of 10 and 20. Thus, restoration should last for at least 60 years. Based on this goal and knowing that restorations have a limited lifespan, it is important to apply preventive therapy to postpone the placement of the first restoration. When restorations become inevitable, minimal intervention is important in order to save tooth tissue for future replacement of failed restorations. It is also generally accepted that small restorations have an enhanced longevity compared to larger ones (Maryniuk and Kaplan, 1986; Wilson and Mjör, 1996; Opdam et al., 2004) but that is not necessarily true for patients with regular recall appointments (Smales and Hawthorne, 1996).

The Dental PBRN Study 2 of restorations in previously un-restored tooth surfaces and Dental PBRN Study 3 with ‘replacement’ restorations provide a unique opportunity to conduct a longitudinal practice-based study by follow-up examination of the restorations using common clinical criteria, which were defined and described in DPBRN Study 3. These criteria will be rated as ‘acceptable’ or ‘repair or replace’ using the same criteria as those for failure of restorations in DPBRN Study 3.

Since the restorations placed in DPBRN Studies 2 and 3 will be followed and become the study restorations of the present DPBRN Study 5, makes this study protocol time sensitive, because DPBRN Studies are already enrolling patients.

A. SPECIFIC AIMS

Specific Aim 1: To quantify the annual and three-year incidence of defects and replacement rates on restorations inserted by DPBRN practitioner-investigators during DPBRN Study 2 (‘primary/first’ restorations) and DPBRN Study 3 (‘replacement’ restorations).

Rationale: Longitudinal studies of how defects on restorations develop in a practice-based setting will provide information that may lead to increased longevity of restorations. This aim will be achieved by using data based on annual clinical recall examination for up to three years. Restorations placed during DPBRN Study 2 and Study 3 will serve as the baseline for DPBRN Study 5.

Specific Aim 2: To test the hypothesis that directly placed resin-based composite restorations have a significantly higher three-year incidence of defects and significantly higher replacement rate after three years compared to amalgam restorations done by practitioner-investigator in DPBRN.

Rationale: Resin-based composite restorative materials are more technique sensitive than amalgam. Composite restorations have up until the present time show a shorter longevity in practice-based studies, but patients still request tooth colored composite restorations. Improvements in the longevity of composite are being reported and the present study will provide data to accept or dispute this notion.

Specific Aim 3: To test the hypothesis that there is no significant difference in three-year replacement rates between restorations inserted during DPBRN Study 3 that were partially replaced as compared to restorations that were completely replaced during DPBRN Study 3.

Rationale: Repair or partial replacement saves tooth structure. Total replacement is tooth tissue destructive in that it leads to gradually larger restorations.

Specific Aim 4: To test the hypothesis that the three-year replacement rate of restorations in permanent teeth of adolescents during DPBRN Study 2 and Study 3 is significantly higher than that of restorations in adults done during DPBRN Study 2 and Study 3.

Rationale: Studies have indicated that the adolescent age period is a particularly vulnerable period for replacement of restorations. Further data on restorations in this age group are needed as a basis for improvements.

B. BACKGRPOUND AND SIGNIFICANCE

B. 1. The most common types of restorations

Directly placed amalgam and resin based composite restorations represent the most common types of materials used in primary and replacement restorations, but the proportion of each type has changed dramatically over the last 30 years in favor of tooth colored materials, including in stress bearing areas of posterior teeth (Christensen, 1998a). Tooth colored materials have always predominated in anterior teeth, even in past times when the quality of the materials was substandard as during the times of silicate cements and unfilled resins. Now the use of various types of tooth colored composite resin has taken over as the routine restorative material in anterior teeth. Glass ionomer restorations were strongly recommended when they were introduced some 30 years ago because of their chemical bonding to the mineralized component of dental tissues and due to the leaching of fluorides from these materials. Both these properties were considered attractive because they might reduce the occurrence of secondary caries. However, practice-based studies did not support the anticipated reduction of secondary caries; in fact it turned out to be similar to other directly placed restorations and their longevity was short as recorded in practice-based studies (Mjör et al., 2000a; Mjör et al., 2000b). The physical properties of glass ionomer restorations restrict their use to small restorations (Mjör and Jokstad, 1993). However, the use of glass ionomer materials has varied markedly in different countries, being prominent in Australia and certain Scandinavian countries, especially Finland; a likely reason for this specific geographical distribution in the use of glass ionomer materials is linked to the enthusiastic support by two different individuals involved in continuing dental education in these countries; Dr. Mount in Australia and Dr. Forsten in Finland.

The change from amalgam to composite resin in stress bearing areas of posterior teeth occurred gradually in some practices, while in others it occurred quickly to include all types of posterior restorations. In other practices the use of posterior composites was restricted to small restorations in premolars. Marked local and geographic variations have been noted. The major change occurred about 15-20 years ago in Florida (Mjör and Moorhead, 1998) and Scandinavia (Mjör, 2001) and has in part been due to strong marketing of tooth colored restorative materials and the demand for tooth colored restorations by patients (Fig 1).

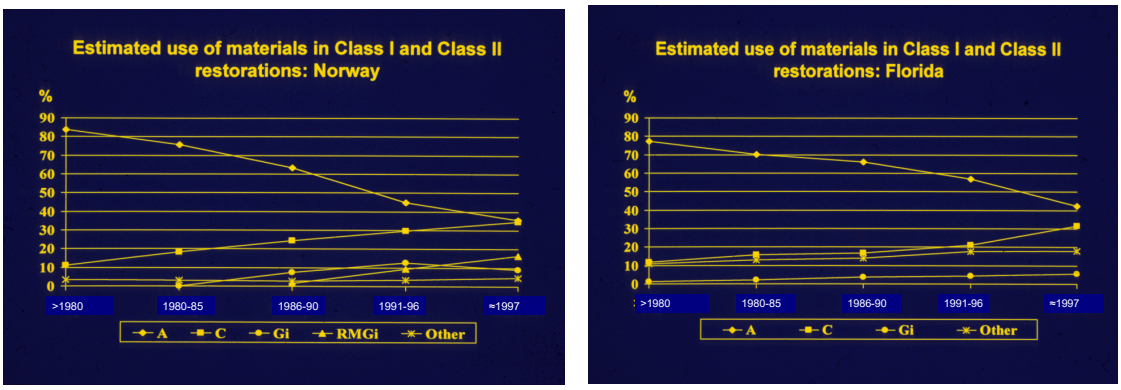

Figure 1. Estimated use of restorative materials in Norway and in Florida during the time from prior to 1980 and up to about 1997. A, amalgam; C, composite; GI, glass ionomer; RMGI, resin modified glass ionomer.

B. 2. The use of resin based restorative materials

The teaching of posterior composite restorations in dental schools lagged behind their use in general dental practice, and the clinical teaching of composite materials was limited to large restorations in posterior teeth (Mjör and Wilson, 1998; Wilson and Mjör, 2000). The restrictive use of composite materials in dental schools continued through the 1990's. This situation is a likely explanation for the short longevity of Class II composite restorations reported at that time (Mjör et al., 1990). In fact, the frequent replacement of large composite restorations resulted in the recording of similar ages for functioning and failed restorations (Jokstad et al., 1994) The 'learning curve' for the use of posterior composite restorations in general practice appeared to have been rather flat, i.e., it took some time before the use of these technique sensitive materials reached an optimal standard. In addition the resin based composite materials of the 1970's and 1980's were of inferior quality compared to the present day materials. As clinicians became familiar with the use of the materials, the quality of the restorations has improved considerably. Recent cross-sectional studies indicate that the longevity as well as the reasons for failure of the composite restorations now approaches that of amalgam restorations (Wilson and Mjör, 2000; Mjör et al., 2002). Thus, the time has come to investigate the longevity of composite restorations using recently developed products and compare it to that of similar amalgam restorations.

B. 3. Indirect restorations

Indirect restorations are less commonly used than directly placed restorations, possibly due to their higher cost, although their longevity is much greater; thus, the initial higher cost is reduced or eliminated when viewed in a long term perspective (Mjör, 1992a). The use of indirect restorations, usually cast alloy restorations including full crowns, differs quite markedly, being higher in Florida, comprising about 18% of all restorations placed, while in Scandinavia only 2-3% were indirect restorations in the 1990's (Fig. 1). No recent data are available to confirm if these different trends have continued. The present study will provide information on the use of direct and indirect restorations at the different sites included in the DPBRN. The early indirect resin restorations were prepared in situ and post-cured prior to cementation (van Dijken, 2000). Further development of CAD/CAM techniques has also made indirect resin based restorations more common than previously, but no data are available on the frequency of their use.

The advantages of the indirect restorations over directly placed composite restorations are the enhanced morphology of the restorations, including optimal proximal contacts with neighboring teeth, and the uniform consistency of the materials used to prepare the restorations. Bonding to dentin at the gingival cavosurface margin, which is quite common, is also enhanced by using the indirect technique (van Dijken, 2000; Pallesen and Qvist, 2003). Few clinical studies have compared the performance of direct and indirect composite restorations in long term studies and no significant differences between the two types could be shown in controlled clinical studies using a meticulous direct clinical technique (Pallesen and Qvist, 1998; van Dijken, 2000), which differ from techniques in routine clinical practice. Thus, the higher cost of these indirect restorations may not be outweighed by an increased longevity. Long term data on CAD/CAM ceramic restorations indicate that such restorations have an increased longevity compared to indirect resin restorations (Pallesen and van Dijken, 2000; Manhart et al., 2004)

B. 4. Longevity of restorations

Numerous factors affect the longevity of restorations, and these may be subdivided into operator factors, quality of the restorative material, and on patient factors (Manhart et al., 2004). The longevity of restorations is closely linked to their replacement rate and the diversity of opinions among clinicians of what constitutes a failed restoration is a major problem when reporting on the longevity of restorations. No generally accepted, objective criteria have been established for what degree of failure constitutes a condition that will cause future damage to the tooth or to the patient. Subjective decision-making prevail (Nuttall and Elderton, 1983) and marked variations between clinicians in diagnosing failures have been demonstrated in many studies (Merrett and Elderton, 1984); (Tveit and Espelid, 1986; Maryniuk, 1990; Tveit and Espelid, 1992; Bader and Shugars, 1992; Bader and Shugars, 1993; Setcos et al., 2004). The quality of restorations is also to a large extent dependent on the craftsmanship of the operator.

Longevity of restorations may be recorded in longitudinal prospective and retrospective studies and in cross sectional studies. The lack of uniform criteria for decisions to place and replace restorations, coupled with the variations between different clinicians complicate the studies (Elderton and Nuttall, 1983). Controlled longitudinal studies may seem to be the best way to study the longevity of restorations, but these studies are hampered by other problems such as selection of patients, limited number of restorations and few clinicians, often specially trained, are involved (Maryniuk, 1984; Mjör, 2001). The present practice-based design of a study will reflect 'real life' longevity studies without defined inclusion and exclusion criteria, with ordinary patients and with a large number of clinicians without special training.

Comprehensive reviews of the longevity of direct and indirect restorations in permanent teeth have recently been published (Manhart et al., 2004). It focused on studies published after 1990. The longevity of restorations was expressed as the annual failure rate, but the median longevity, i.e., the 'half life' of restorations or the time when 50% of the restorations in a sample has failed, is most commonly reported in cross sectional, practice-based studies. Marked variations between different types of restorations have been reported, including effects of patient age, factors such as access to fluorides and other caries preventive agents, patients' oral hygiene, difficult conditions during placement of the restorations, improper clinical technique, and material degradation. The longevity of restorations in permanent teeth of children and adolescents are generally lower than that in adults (Qvist et al., 1990a; Qvist et al., 1990b; Mjör et al., 2000a).

The longevity of restorations in the present prospective clinical studies will involve all types of restorations in permanent teeth in general dental practice; small and large, direct and indirect - including single crowns, using all types of restorative materials and techniques.

B. 5. The longevity of amalgam and composite restorations in posterior teeth

When resin based Class II composite restoration came into common use about 15-20 years ago, the difference in longevity between amalgam and composite restorations was quite marked (Mjör et al., 1990; Manhart et al., 2004). Recent long term data indicate that the longevity of composite restorations has increased and that it is approaching that of amalgam (Manhart et al., 2004). A number of factors affect this enhanced performance of tooth colored resin based materials; experience by the clinicians in using resin based composite materials in Class II restorations and improved material properties being two major reasons for the increased performance of composite restorations. It must also be kept in mind that the replacement of functional amalgam restorations without significant defects may also occur in order to obtain more esthetic restoration than the dark gray, metallic color of amalgam and the yellow color of gold alloys. Functional restorations may also be replaced due to potential adverse biological reactions. The frequency with which such replacements of functional amalgam restorations occurs is not known, but DPBRN Study 3 may provide these answers, and the effect on the overall longevity of amalgam restorations may be estimated. Since the longevity of restorations is a decisive factor for the long term cost of restorations, the factors that affect this parameter must be analyzed in detail. However, the cost factor is an inherent problem with composite restorations because it takes longer to place a composite restoration than a comparable amalgam restoration.

B. 6. Systematic review vs. less structured reviews

Formal systematic reviews adhere to strict scientific designs to ensure that only comprehensive, unbiased, and reliable studies are included in the review. Inclusion criteria for publication are defined at the start and are

based on study design and outcome measures. Randomized controlled clinical trials give the most reliable estimates for longevity of restorations, however, as pointed out in a recent extensive and comprehensive review of the longevity of dental restorations, reports have limitations because they do not reflect 'real life' dental care (Chadwick et al., 2001). Most studies included in the review were dental school based, i.e., they differed from reports where no standardization of criteria for failure was done. However, the longevity of restorations did not vary much from less well defined studies such as cross sectional practice-based studies, possibly because teachers at dental schools also vary much in their assessment of what constitutes a failed restoration(Rytömaa et al., 1979) It has been suggested that standardization of the criteria for what constitutes a failure of restorations may improve the diagnosis in both teaching environments (Mileman et al., 1982) and in clinical practices (Pitts, 1983). The large number of restorations in cross sectional studies may possibly even out the differences in diagnostic level and in that way mask the effect of standardization of criteria for failures. In fact, the longevity from the large systematic review by Chadwick et al. (2001) do not differ from that reported in cross-sectional studies involving thousands of restorations (Mjör et al., 2000a; Mjör et al., 2002).

It is claimed that if criteria for failure are defined, it is more likely that clinicians are determining failure of a restoration more consistently than if the criteria are based on the clinicians experience (Chadwick et al., 2001). The present study will use the same definitions and descriptions of criteria as those in DPBRN study 3 where reasons for replacement of restorations were recorded.

It is important to differentiate between the age of restorations at replacement and the longevity of restorations. Most cross sectional studies report on the age at replacement of restorations. Longevity studies should ideally be carried out until restorations became defective to the stage at which they caused damage to the teeth in question. However, the rate of replacement is so high for many types of restorations that the difference in age of functioning restorations is minimally different from that of replaced restorations (Jokstad et. al., 1994). It is unlikely that the present study with the limitation of three years observation period will provide information on the overall longevity of restorations, but it will provide information on variations in short term longevity of different types of restorations. It may also provide a basis for extension of the studies provided the patient drop-out does not become a prohibiting factor.

B.7. Longevity as a function of reason for replacement of restorations

The present list of reasons for replacement of restorations include 10 diagnoses plus 'other reasons' so that any unforeseen/unexpected reason for failure could be recorded. Previous studies of restorations in permanent teeth have shown that 'other reasons' vary depending on the time the study was done and the type of restorative material evaluated. The longevity of restorations in permanent teeth of adolescents is shorter than in adults (Qvist et al., 1990a; Qvist et al., 1990b; Mjör et al., 2000c). The reasons for replacement of restorations vary markedly and include continued disease/caries development at the restoration margin, physical failures such as restoration fractures, discoloration of tooth colored materials, pain sensitivity and possible iatrogenic defects.

Few studies have associated the reasons for replacement of restorations to the longevity or age at replacement of restorations. Three studies have brought attention to the age at replacement for the different reasons for replacement (Qvist et al., 1990a; Qvist et al., 1990b; Mjör et al., 2000a). The median age of the restoration at the time of diagnosis of a failure depended on the restorative material, being more marked for composite than for amalgam restorations. The most recent data (Mjör et al., 2000a) showed minor differences in median age of different reasons for replacements of amalgam restorations in adults; most restorations were replaced at a median age of 10-12 years, except 'marginal fracture' (14 years) and 'change of material' (15 years). Much greater variation in median age for the different reasons for failure were recorded for composite restorations; the range being from 5–12 years with 'pain/sensitivity' having the shortest median longevity, and 'bulk discoloration' and 'change of material' the longest. Detailed information on the age of a diagnosed failure may provide information that may useful in the analysis of the failures.

C. PRELIMINARY STUDIES

C.1. Status of restorations as a function of time

Two of the investigators in the present group of dentists (Mjör and Qvist) have been involved in practice-based studies over the last 20-30 years which have provided a knowledge base which will benefit the

present study in the same way as preliminary data would. The types of failures recorded will be differentiated on the bases of: 1. Primary/replacement restorations, 2. Clinicians' experience expressed as years since graduation, 3. The type of restorative material, and 4. The size of the restoration.

C.2. Composite vs. amalgam restoration

Data on reasons for replacement of restorations from the group involved in the design of the DPBRN Study 5 will provide a basis for comparison of the status of the present-day restorations being placed. No up-to-date study has been conducted comparing restorations made by these two types of restoration. Looking back it is clear that the reason for replacement of amalgam restorations have changed little, and their longevity has remained fairly stable. Although some increase occurred about 30 years ago when 'non-gamma–2 was introduced and gradually took over as the amalgam of choice, the increased trend in replacement of functional, non-failed amalgam restorations in favor of tooth colored restorations, may be part of the explanation for the slight difference in age at replacement noted during the last 25-30 years.

While the reasons for replacement of amalgam restorations have remained fairly constant, the reasons for failure of resin based composite restorations and their longevity have changed markedly during the last 25-30 years. The reason for this change is manifold, including improved material quality and clinical experience in handling the materials. No recent practice based studies have been conducted to compare the status of present day primary and replacement restorations.

C.3. Repaired/partially replaced restorations

Repair of defective restorations rather than replacement of the entire restoration is a somewhat controversial treatment. Some dental schools do not teach repair of restorations while others do. The advantage of repair/partial replacement is that it saves tooth structure and chair time. It also places minimal stress on the pulp of the tooth. The approach is therefore in conformity with the concept of minimally invasive dentistry.

Two investigators in the present group (Gordan and Mjör) have ongoing studies on repair of localized defects on restorations as an alternative treatment to replacement of the entire restorations (Gordan et al., 2004; Shen et al., 2004; Moncada et al., 2006;Gordan et al., 2006a; Gordan et al., 2006b). These will provide a basis for comparison to the outcome of repaired/partly replaced restorations in the present study. Our preliminary studies are encouraging and we expect to prove that a simple repair of a localized defect may significantly enhance the longevity of restorations.

C.4. Longevity of restorations in adolescents

The DPBRN Study 5 group has researchers (Qvist and Mjör) who have data showing that the longevity of restorations in permanent teeth of adolescents is significantly shorter than restorations in adults. These have been referred to in the introductory text (Qvist et al., 1990a; Qvist et al., 1990b; Mjör et al., 2000c). The median age at replacement of composite restorations was about three times higher in adults than in adolescents; 2 vs. 6 years. The comparative numbers for amalgam restorations were 4 vs. 8 years. No data are available to show if this finding applies to primary restorations as well as replacement restorations in adolescents using the restoration materials in present use. Little attention has been paid to these findings and they may indicate a need for special preventive approaches in the adolescent age group. This may be a difficult age group to work with, but if the present studies verify the results from previous studies, the adolescent group may be targeted for intensified preventive measures.

D. RESEARCH PLAN

D.1. Inclusion criteria

Restorations placed in DPBRN Studies 2 and 3 are eligible be included in this study. Each of these studies comprises approximately 10,000 restorations. The two sets of data will be from restorations placed in previously un-restored teeth (DPBRN Study 2) and from restorations that replace or repair existing restorations for any reason (DPBRN Study 3).

D.2. Recruitment process

The 200 clinicians involved in DPBRN Studies 2 and 3 will be informed at the start of the studies that there will be a longitudinal follow-up of the restorations. We anticipate the restorations placed will be recalled at least annually and characterized then for defects developing according to defined criteria, but allowing for adjustments in the timing to accommodate the routines in the practice.

D.3. Discussion of this protocol with practices

Before any data collection begins a DPBRN Project Coordinating staff member will review all of the materials with the p-i and available office staff. This training may be by telephone conference or a face-to-face meeting, at the discretion of the Research Coordinator, to explain the protocol for the study. All offices will have had in-office training for Study 2 and/or 3 prior to enrolling for Study 5. Our previous experience suggests that, if an in-office meeting is recommended, having this meeting during lunch (provided by the DPBRN) with all the practice's dentists and staff is the preferred method. Other possibilities occur if the practice has a pre-arranged time for meetings or when no patients are being treated. This mechanism provides an opportunity to address all questions that staff members might have about the protocol. Human subjects/informed consent issues will be reviewed, as well as procedures specific to this study. It is important that the clinicians and their staff familiarize themselves with the Data Collection Form, including the definitions, terms and criteria for data to be entered. Proper completion of the Data Collection Form will be reviewed with all practitioners and staff in the practice.

D.4. Rating of defects

Upon recall examination of the restoration, each restoration should be rated according to the following two criteria:

A*cceptable:* The restoration is of satisfactory quality and is expected to protect the tooth and the surrounding structures or has one or more features that deviate from ideal conditions, but it does not need to be replaced or repaired.

Replace or repair: Not acceptable because future damage to the tooth and/or surrounding tissues is likely to occur or is occurring. Not acceptable to the patient who has asked for repair or replacement.

D.5. Criteria for why a restoration is failing

The restorations will be examined according to the usual procedure employed in the practice on recall patients. The severity of any defect(s) is rated according to the criteria outlined in D.5.

'Secondary/recurrent caries' is a lesion detected at the margin of an existing restoration. The lesion should have the same characteristics as primary caries lesions. At the pre-cavitation stage it may appear as a "white spot lesion" if the cavosurface margin is in enamel. More advanced lesions will show variable discoloration from white to dark and the margin may have crumbling leading to frank cavitation. If the lesion may be visually inspected and reaches into dentin, it will, in its active stage, be soft, have a yellow/light brown discoloration, and present a wet appearance. Inactive/arrested dentin lesions are hard, discolored brown/dark brown and appear dry. Secondary caries must be differentiated from caries left behind during the previous restorative procedure. This "remaining caries" is usually diagnosed after the restoration is removed and, it may appear as a bluish-gray hue through the transparent enamel. It may also be seen radiographically as a demineralized zone under a restoration. If it is located at the margin it may be misdiagnosed as a secondary caries lesion even though it may have been left behind during a cavity preparation.

'*Entire restoration was discolored'* includes any mismatch between the color of the body of a tooth-colored restoration and the tooth that leads to replacement of the restoration.

'*Restoration margins were discolored'* leading to replacement of a restoration is found at the tooth/restoration interface. Stained margins must be differentiated from carious margins by not having the characteristics listed for active caries.

'*Bulk fracture'* of a restoration includes isthmus fracture or any fracture through the body of the restoration or the marginal ridge, but with the restoration still in place.

'*Restoration margins were degraded or ditched'* is often referred to as "ditching" of restorations. Only those restorations with marginal fractures or degraded margins, but without caries, should be recorded in this category of failure.

'*Restoration was missing'* is recorded when either all of the restoration or a major part is missing due to lack of retention.

"*Tooth was fractured'* is any kind of tooth fracture adjacent to a restoration, for example the fracture of a cusp or of an enamel margin. This classification allows tooth fractures to be distinguished from restoration fractures.

'*Pain/sensitivity'* of any kind requiring replacement of a restoration is listed under this category. It may be the sole reason for replacement or it may occur in addition to other reasons, such as secondary caries lesions or fractured tooth or restoration, in which case both reasons should be recorded.

'Patient request' includes any reason for replacement of a restoration deemed acceptable by the practitioner.

'*Other reason*" includes any other reason for replacement/repair of restorations than those listed above.

If a serviceable or intact restoration is replaced because it is incorporated into a larger restoration, this is not recorded as a failure. An example would be the removal of an intact occlusal Class I restoration so that it can become part of a Class II restoration.

D.6. Data collection process

Each p-i will examine the primary and/or replaced/repaired restorations they placed in Study 2and/or Study 3. Most p-is will be examining up to 50 restorations placed per study, however some may be examining as many as 100 as described in the protocols for Studies 2 and 3. Some clinicians may participate in both DPBRN Study 2 and Study 3. The examinations will likely be done on less 100 patients, per study for Studies 2 and 3, as we expect some patients will have had multiple restorations and some patients may drop out of the studies. It is essential that as many restorations as possible that were placed, or replaced/repaired from small one-surface restorations to single crowns, including temporary restorations be examined. The data on each participating patient should be entered on a separate Data Collection Form and all examinations be reported on separately. Completed Data Collection Forms will be sent to the DPBRN Regional Coordinator monthly. For patients who have not had an examination within the specified time intervals the Regional Coordinator will contact the practice and attempt to identify the reason(s). The office, according to its established procedures, or the Regional Coordinator will try to locate patients who have not had a recall appointment since yearly examinations are considered standard of care. For those patients who have not had any examinations by approximately 2.5 years from the placement of the restoration, the RC may initiate contact with the patient to encourage the patient to have an examination The Regional Coordinator may attempt to determine if a patient has moved to a new dentist and if follow-up is possible.

The Data Collection Form is designed so that a dental assistant may do the actual data recording by asking the clinician questions. However, it is essential that the clinician examining or working on the restoration check the information entered. It is important that the data be entered at the time the restoration is examined and with the patient still in the dental chair.

The data will be sent to the CC via two methods. Dentists in the Kaiser Permanente Dental Associates group and in the HealthPartners group will enter the data in a secure web-based portal. Dentists in the Alabama and Florida Regions and Scandinavia will mail the completed forms to the Regional Coordinator who will process the forms and forward them to the CC.

The signed informed Consent Form, any Patient Contact Information updates, and a copy of the Data Collection Form will be maintained in a secure manner by the regional offices.

P-is will be remunerated on a predetermined schedule, when the forms for all qualified restorations have been submitted, or at the termination of data collection for the study. DPBRN p-is will be remunerated $10 for the year one examination, $15 for the year two examination, and $25 for the year three examination appointment for each patient irregardless of the number of forms per patient for any one visit. Queries from the CC regarding illegible or unclear responses must be addressed before any payments will be made. We expect that payments will take up to 4 weeks from the date processing is initiated. P-is in the PDA and HP

organizations will not receive payment directly. Instead, a single lump sum payment will be paid to their organizations and this payment will indirectly contribute to remuneration.

D.7. Data management and quality assurance procedures

Completed Data Forms may be mailed to Regional Coordinators or Faxed on a secure and dedicated fax line. Forms sent both as hard copies or faxes, to the Regional Coordinator, will be scanned into electronic images and sent to the CC either as scanned images or hard copies. If scanned images are processed, staff at the CC will take the electronic images and professional data entry staff will use a dual monitor system to view the electronic image on one monitor and enter data into a second. Forms will be organized into identifiable batches for data entry and two 10% samples of forms will be selected. The first will be re-entered by the original data entry technician to determine intra-rater reliability and the second by a different technician for inter-rater reliability. If the discrepancy rate for either re-entry sample is above 0.5%, then the full batch will be re-entered. Re-training may be necessary if unacceptable error rates continue to occur.

All electronic data stored for the study will be located on a secure network drive with severely restricted access. All personnel at the CC are required to have current IRB and HIPAA training certification and all must sign confidentiality forms. All paper copies will be stored in a secured location.

The data will be stored using the current version of ACCESS or SQL database software packages. The database programming staff will work with the CC investigators and Network Chair to make sure that the required systems are available on time and function efficiently.

The final dataset and documentation will be prepared by members of the CC statistical consulting unit (SCU). Data analysis will be performed by one member of the SCU and subsequently verified by another, using the SAS® statistical software system.

D.8. Monitoring recruitment and data collection during the field phase

A DPBRN Regional Coordinator will be assigned responsibility for the practice. Telephone contact may be initiated with each practice during the first few weeks of their participation in the study with subsequent contact at least quarterly thereafter. The Regional Coordinator will assess progress in that practice to that date and answer any questions the practice has. This monitoring may also involve asking the practice to FAX or email to the DPBRN Regional Coordinator or staff assigned to the practice a small number of initially completed forms. This will allow the DPBRN Regional Coordinator or staff member to review them for completeness and legibility. Following this review and any necessary discussion with the practice, these Faxed or emailed forms will be immediately destroyed. Face-to-face meetings will be held with the practice staff at the discretion of the Regional Coordinator assigned to the practice.

D.9. Study design and statistical analysis

The study will be conducted as a longitudinal cohort study with measurements made at dental exams at up to four times: baseline, and up to three annual follow-up exams or at restoration failure. The primary analytic method will be a logistic regression model, implemented with generalized estimating equations (GEE) in order to account for correlated observations due to multiple subjects being observed within dental practices and examinations at multiple time points being observed for each subject, and for incomplete data due to interval censoring or loss to follow-up. The status of restorations will be evaluated on a four-point ordinal scale, as described in Section D.4, as well as using a dichotomous failed / did not fail, rating. The primary outcome variable for each of the Specific Aims will be the dichotomous rating of “failed” vs. “did not fail” for each restoration. Secondary analyses will be conducted using the four-category rating of restoration condition as an ordinal multinomial outcome variable in separate GEE models. Additional dichotomous secondary dependent variables will be constructed using different cutpoints on the four-point ordinal scale in order to evaluate the sensitivity of the results to decisions regarding the cutpoint that is chosen.

Terms representing subject and dentist will be included as blocks in each analysis in order to account for correlation among measurements within these units. This analysis approach will allow the inclusion of all available information for each restoration in the model, as missing values for some observation times do not cause loss of non-missing information on a particular restoration. With appropriate coding of the dependent variable, this approach also allows the Least-Squares means (LS Means) for each group to serve as estimates

of the failure rates, adjusted for covariates and missing observations. 95% confidence intervals for these adjusted estimates will also be calculated, based on the LS Means.

This approach will also be used to address the survival analysis hypothesis; time intervals will be categorized corresponding to three annual follow-up examinations. Thus, the survival outcomes are interval censored to a relatively extreme degree. The logistic regression model will account for censoring due to loss to follow-up, as the GEE approach will allow all available observations for each subject to be included in the analysis.

If few restoration failures occur in the study data, regressions incorporating Poisson, zero-inflated Poisson, and negative binomial distributions for the dependent variable may be evaluated for potentially better fit to the data than that provided by the binomial model that is implicit in logistic regression.

Analysis plans are presented separately for each Specific Aim in the following paragraphs.

Specific Aim 1: To quantify the annual and three-year incidence of defects and replacement rates on restorations inserted by DPBRN practitioner-investigators during DPBRN Study 2 ('primary/first' restorations) and DPBRN Study 3 ('replacement' restorations) based on annual clinical recall examination for up to three years.

The frequency distribution of the ordinal scores for the restorations, and for the dichotomous "failed / did not fail" rating, will be tabulated for each of the following groups: subject age group at baseline (adolescent or adult), type of restoration (initial, partial replacement, full replacement), and restoration material (resin, glass ionomer, amalgam, ceramic or porcelain, cast gold or other cast metal, combined metal/ceramic, or temporary restorative material).

Adjusted percentages and the associated 95% confidence intervals will be based on LS Means, calculated from a GEE logistic regression model. The model will adjust for correlation due to clustering of subjects within dentists.

Specific Aim 2: To test the hypothesis that directly placed resin-based composite restorations have a significantly higher three-year incidence of defects and significantly higher replacement rate after three years compared to amalgam restorations done by practitioner-investigators in the DPBRN.

A GEE logistic regression model will be implemented using restoration failure as the dichotomous outcome variable. The model will include terms representing the individual subject, dentist, exam (baseline, 1, 2, 3 years), subject age group at baseline (adolescent or adult), type of restoration (initial, partial replacement, full replacement), and resin or amalgam restorations. The statistical test that will be of primary interest in addressing this Specific Aim will be the test for the main effect of restoration material.

Specific Aim 3: To test the hypothesis that there is no significant difference in three-year replacement rates between restorations inserted during DPBRN Study 3 that were partially replaced as compared to restorations that were completely replaced during DPBRN Study 3.

The analytic model for this aim will be a GEE logistic regression model, constructed as described for Specific Aim 2, with the exception that initial restorations will not be eligible for this analysis. Thus, the observations that will be included in the analysis to address this Specific Aim will be those originating in DPBRN Study 3. The statistical test that will be of primary interest for this Specific Aim will be the test for the main effect of type of restoration. The two-factor interaction term for restoration material by restoration type will be tested to evaluate whether the performance of the different restoration types differs between restorative materials.

Specific Aim 4: To test the hypothesis that the three-year replacement rate of restorations in permanent teeth of adolescents is significantly higher than that of restorations placed in adults during DPBRN Studies 2 and 3.

This Specific Aim will be addressed using a GEE logistic regression model to evaluate whether the proportions of restorations surviving differ between adolescents and adults. The statistical test that will be of primary interest will be the test for the time by age group interaction term, which would reflect a difference in

the time course of restorations between adolescents and adults.

D.10. Power considerations

Power estimates were based on the numbers of expected observations to be recruited into DPBRN Studies 2 and 3. Each of these studies is planned to include 200 dentists, each to enroll 50 restorations. Thus, the expected pool of restorations observed at baseline is 20,000. It is inevitable that there will be loss to follow-up both due to refusal to participate in the longitudinal study, which would lead to the subject contributing no information to this study, and to drop-out, which would lead to the subject potentially contributing partial information. Drop-out of a dentist participant would lead to loss to follow-up of a cluster of observations. Since these studies have not yet been conducted, much of the information that is necessary to the calculation of power has been based on hypothetical scenarios. These include the numbers of dentists and subjects or surfaces at baseline, the numbers of subjects in each of the age-group, material type and restoration type groups, the magnitude of intraclass correlation (ICC) among subjects within dentist, and the loss to follow-up. These assumptions are not intended to anticipate the specific conditions that are likely to actually occur in the study, but are intended to make it possible to provide estimates of power and precision that account for the known effects of clustering and loss-to follow-up using values that are within what may be considered typical values for longitudinal studies. If the actual study yields data that departs substantially from these assumptions, the actual precision of the study may differ considerably from these estimates.

Power calculations were made using the nQuery Advisor, version 6.0, software package. All power estimates were based on two-sided testing at the 95% confidence level. Since there is no basis for estimation of the proportion of the total possible information that is likely to be obtained, these power analyses assume a loss of 20% of potential baseline observations across all four observation times to represent the effect of losses from both causes. No loss of dentists is assumed, so that the total number of clusters is unchanged. This results in a total sample size of 16,000 observations for the purposes of power calculation. This calculation assumes one restoration per patient or, equivalently, that restorations are independent.

To account for correlation among restorations within dentists, a variance inflation factor of 1.5 was incorporated into the estimation of precision. This corresponds to the variance inflation that would result from an intraclass correlation of between 0.01 and 0.02 for the entire study sample, with 40 observations per dentist. For comparisons involving smaller subgroups, this adjustment is likely conservative, leading to some underestimation of precision.

In order to provide conservative estimates of power and precision, confidence intervals were based on a “true” proportion of 0.50 and comparisons between proportions were calculated for proportions centered on 0.50.

The study design defines 12 subgroups. These are presented in the table presented below, along with expected percentages of observations occurring in each group. The sample sizes, N(i), are based on the expected percentages, multiplied by the expected number of observations from Studies 2 and 3, reduced by 20% loss to follow-up and non-participation.

Specific Aim 1: To quantify the annual and three-year incidence of defects and replacement rates on restorations inserted by DPBRN practitioner-investigators during DPBRN Study 2 (‘primary/first’ restorations) and DPBRN Study 3 (‘replacement’ restorations) based on annual clinical recall examination for up to three years.

Since Specific Aim 1 is descriptive only, precision of estimation was based on expected widths of 95% confidence intervals within the study subgroups. To provide conservative estimates of precision, the confidence interval widths were calculated assuming the true proportion to be 0.50. To account for correlation among restorations within dentists, a variance inflation factor of 1.5 was incorporated into the estimation of precision, as described above.

The expected numbers of observations in each subgroup, after 20% loss to follow-up, are presented in Table 1. Thus, for the largest subgroup in the study, the expected sample size would provide sufficient precision to estimate the true percentage within ±3.8%, and in the smallest subgroup, within ±19%.

Subgroup	Agegroup	Material	Type	Expected percentage of observations	N per group, w/ 20% loss	Expected width of 95% CI
1	adult	resin		24%	3900	0.038
2	adult	amalg		8%	1300	0.066
3	adolescent	resin		16%	2520	0.048
4	adolescent	amalg		2%	280	0.144
5	adult	resin	full	3%	400	0.12
6	adult	resin	partial	15%	2400	0.048
7	adult	amalg	full	3%	400	0.12
8	adult	amalg	partial	18%	2800	0.046
9	adolescent	resin	full	5%	800	0.084
10	adolescent	resin	partial	1%	160	0.19
11	adolescent	amalg	full	2%	240	0.154
12	adolescent	amalg	partial	5%	800	0.084
				100%	16000	

Specific Aim 2: To test the hypothesis that directly placed resin-based composite restorations have a significantly higher three-year incidence of defects and significantly higher replacement rate after three years compared to amalgam restorations done by practitioner-investigator in DPBRN.

Power of the logistic regression model was approximated using a chi-square test for the difference between two proportions, adjusted for variance inflation as described previously. The expected numbers of resin and amalgam restorations, after losses, are 10,180 and 5,820, respectively, based on Table 1. Adjusting for clustering yields effective sample sizes of 6787 and 3880 for the power calculation. These sample sizes would provide at least 80% power to detect a difference of 0.029 between the proportions failing in the two material groups.

Specific Aim 3: To test the hypothesis that there is no significant difference in three-year replacement rates between restorations inserted during DPBRN Study 3 that were partially replaced as compared to restorations that were completely replaced during DPBRN Study 3.

Power of the logistic regression model was approximated using a chi-square test for the difference between two proportions, adjusted for variance inflation as described previously. The expected numbers of full and partial restorations, after losses, are 1,840 and 6,161, respectively, based on Table 1. Adjusting for clustering yields effective sample sizes of 1227 and 4107 for the power calculation. These sample sizes would provide at least 80% power to detect a difference of 0.046 between the proportions failing in the two restorative groups.

Specific Aim 4: To test the hypothesis that the three-year replacement rate of restorations in permanent teeth of adolescents is significantly higher than that of restorations placed in adults during DPBRN Studies 2 and 3.

Power of the logistic regression model was approximated using a chi-square test for the difference between two proportions, adjusted for variance inflation as described previously. The expected numbers of restorations among adolescent and adult subjects, after losses, are 4,800 and 11,200, respectively, based on Table 1. Adjusting for clustering yields effective sample sizes of 3,200 and 7,467 for the power calculation. These sample sizes would provide at least 80% power to detect a difference of 0.03 between the proportions failing in the two age groups.

E. HUMAN SUBJECTS RESEARCH

E.1. Risks to the patients and health care providers

Human subjects' involvement and characteristics. This protocol involves human subjects. The human subjects directly involved in this study are the patients who have sought dental treatment in the p-is' practices. The p-is will be recruited from the clinicians enrolled in the Dental PBRN and they need to meet the eligibility criteria specific to this protocol. The p-is will record the examination observations or possible restorative treatment they provide to patients with qualified restorations, at recall or operative appointments, for a 3 year period. These patients will have provided informed consent. Because restoration data will be linked to characteristics of the p-s and their practices and comparisons will be made across practices and by practice characteristics practitioners will sign informed consent forms prior to participation in this study. Practitioners will

Source of materials. Data will be obtained from up to 50 Data Collection Forms per study, for studies 2 and 3, in which a practitioner participated. These forms represent 50 consecutive primary restorations and 50 consecutive replaced/repaired restorations, which may or may not derive from 50 consecutive patients per original study. Data on the primary and replaced/repaired restorations will also be linked to responses that practitioners provided in the Study 1 questionnaire, as well as data that practitioners completed for the DPBRN enrollment questionnaire.

Potential Risks. The only risk to the p-is and their patients will be the highly unlikely accidental disclosure of health care provider and patient's dental restorative information. However, every precaution will be taken to prevent such disclosures and the DPBRN has an unblemished track record in this regard. No experimental techniques or materials will be used and the burden on the patients, clinicians and dental office staff, will be the same as that experienced as part of regular dental treatment, except that an Informed Consent Form and Data Collection Form will be completed for each patient/subject in the study. Information on the restorations examination or replacement/repair will be entered on a Data Collection Form specially designed for this study. The treatment sessions will, therefore, be slightly longer in order to record the treatment that was provided.

The Data Collection Forms will be coded, kept confidential, and will be stored in a secure place. The Dental PBRN Executive Committee has closely reviewed the research protocol at each state of its development, has closely reviewed and pre-tested the data collection forms, and has provided its unanimous endorsement of the study, the protocol text, and the data collection forms. The Dental PBRN Executive Committee voting members comprise six representative dentists in full-time private practice from across the DPBRN, the NIDCR representative (Dr. Bruce Pihlstrom), the Network Chair (Dr. Gregg Gilbert), and the Coordinating Center PI (Dr. Dale Williams).

E.2. Adequacy of protection against risk

Recruitment and informed consent. We will provide the p-is and their patients information that explains the nature of the study, time commitment involved, any risks involved, and compensation information. We will also answer any questions they may have in a telephone conversation or face-to-face discussion with them. A specially designed Informed Consent Form will be explained to the patient by the p-I or staff trained in Human Subjects Protection. After assurance that the information provided is understood by the patient, he/she will sign the form, which then becomes part of the patient's research record.

Protection against risks. Records will be kept confidential to the extent permitted by law. Only authorized personnel will have access to the data, and all information, whether electronic or in paper form, will be stored in a secure manner. All personnel with access to this information have been certified in human subjects' research and HIPAA regulations. This information will not be sold or used for any reason other than research. Results will be published for scientific purposes, but participant identities will not be revealed.

E.3. Potential benefits of the proposed research to the subjects and practitioner investigators

P-is will benefit from the opportunity to reflect their views on the current diagnosis of restoration defects used in their practices and gain information on the practice methods of their peers. The p-is will also benefit from a better understanding of how the diagnosis of restoration defects may influence patients' treatment. The indirect benefit to the patients may be the ultimate improvement in dental restorative treatment in daily clinical

practice. The potential benefits to the p-is and indirectly to their patients will far exceed the risk involved with the participation. The p-is will charge their normal fees for the treatment provided.

Subjects will not be paid for their participation. DPBRN p-is will be remunerated $10 for the year one examination, $15 for the year two examination, and $25 for the year three examination appointment for each patient. Remuneration will be made at predetermined intervals after forms completed in that time period for all participating patients have been sent to the Regional Coordinator and clarification has been made on any queries from the RC or CC to verify illegible or unclear responses. P-is in the PDA and HP organizations will not receive payment directly. Instead, a single lump sum payment will be paid to their organizations and this payment will indirectly contribute to remuneration.

E.4. Importance of the knowledge to be gained

The knowledge to be gained from the current study will identify and quantify the various diagnoses of defects on restorations and the alternative treatments provided. When the results of this study become available, comparison can be made with responses provided for DPBRN Studies 1, 2, and 3.

E.5. Inclusion of women practitioner investigators and subjects

Practitioners of both genders will be included. The percentage of practicing dentists in 2003 by gender was 18% female and 82% male (ADA 2003). In Scandinavia the ratio of female: male clinicians is about 50:50 and the female component is steadily increasing. Based on the enrollment questionnaires completed by US DPBRN dentists, 14% are females. We anticipate that the responding group during recruitment will yield a sample of 20% female dentists for this study and anticipate that approximately 55% of the patients enrolled will be female.

E.6. Inclusion of minority practitioner investigators and subjects

Practitioners of racial and ethnic minorities will be included in the study at least proportional to their composition in the dental community. The racial and ethnic distribution of dental practitioners expected to participate in the study is shown in Target/Planned Enrollment table on a later page of this application. Because minority practitioners and practices that serve high percentages of minority patients will be targeted in Alabama and Florida, we anticipate that approximately 20% of the subjects in this study will be of a racial/ethnic minority group. Subjects will be enrolled without respect to racial or ethnic minority status.

E.7. Information to be provided for all clinical research studies

The p-is who participate in this study will be dental practitioners who participate in DPBRN Studies 2 and/or 3 and meet the other eligibility criteria. The patients will be informed of what the study entails and their questions will be answered before they sign an informed consent to participate. No gender or racial/ethnic group will be targeted or excluded. Our anticipated enrollment is shown in the Targeted/Planned Enrollment table on a later page of this application.

E.8. Inclusion of children

This study is designed to follow-up on the development of restoration defects diagnosed by DPBRN p-is that have placed, replaced or repaired restorations in permanent teeth in DPBRN Studies 2 and/or 3. The age of the patients will depend on the dental practice; some p-is may have restricted their practices to the treatment of adults only, some have ‘family type’ practices and some practices treat children and adolescents only. Patients will need to have participated in DPBRN Study 2 and/or 3 in which at least one permanent tooth had a restoration placed/replaced/repaired to be eligible to participate in this study. This means that subjects will be at least 6 years old because that is when the permanent first molar typically erupts. Parents/guardians of child subjects will provide the informed consent, although study participation also requires the child’s assent.

Targeted/Planned Enrollment Table (for the dentist participants)

This report format should NOT be used for data collection from study participants.

Study Title: Reasons for replacement and repair of dental restorations

TotalPlannedEnrollment: 200 DPBRN dentists who treat approximately 6,000 patients

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	2	3	5
Not Hispanic or Latino	18	77	95
Ethnic Category: Total of All Subjects *	20	80	100
Racial Categories			
American Indian/Alaska Native	1	1	2
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	8	10
White	17	69	86
Racial Categories: Total of All Subjects *	21	79	100

†We project that the 10,000 restorations (100 dentists each doing 100 restorations) will comprise 100 dentists performing treatment on 6,000 different patients.

The gender and racial and ethnic distribution of dental practitioners expected to participate in the study reflects the proportional distribution shown in the Targeted/Planned Enrollment for DPBRN Study 1 and the result of planned Study 3 targeting of dentists who are female and/or racial/ethnic minority.

Targeted/Planned Enrollment Table (for the patients participants)

This report format should NOT be used for data collection from study participants.

Study Title: Reasons for replacement and repair of dental restorations

Total Planned Enrollment: 200 DPBRN dentists who treat approximately 6,000 patients

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	2	3	5
Not Hispanic or Latino	18	77	95
Ethnic Category: Total of All Subjects *	20	80	100
Racial Categories			
American Indian/Alaska Native	1	1	3
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	8	10
White	17	69	86
Racial Categories: Total of All Subjects *	20	80	100

†We project that the 10,000 restorations (100 dentists each doing 100 restorations) will comprise 100 dentists performing treatment on 6,000 different patients.

Because minority practitioners and practices that serve high percentages of minority patients will be targeted in Alabama and Florida, we anticipate that approximately 20% of the subject in this study will be of a racial/ethnic minority group.

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