Unit 3, 44 McCauley Street
MATRAVILLE NSW 2036

PROC-011

PROCEDURE
RESEARCH & DEVELOPMENT

Prepared by:	**Date:**	**Position:** QA Manager
Checked:	**Date:**	**Position:**
Approved by:	**Date:**	**Position:** CEO

The following ATTACHMENTS form part of this document.

Clinical Data (Requirements obtained from TGA as part of CE submission information)

This revision supersedes all previous revisions.
Controlled copy only if stamped with Controlled Copy Stamp and issued with copy number

1. INTRODUCTION

1.1 Purpose of Document

To set out the procedure for dealing with research & development of a product or process for Portland Orthopaedics.

1.2 Purpose of Procedure

To structure the process of R & D including the generation of related documents and records. This includes:

- Compliance with Regulatory Affairs requirements;
- Verification that product meets requirements;
- Validation showing that product is of benefit to patient;
- Major project milestones;
- Risk Analysis showing that product has been made & designed to be as safe as possible; and
- Project management with documentation related to reviews per regulatory requirements (e.g. FDA, CE, TGA).

1.3 Scope

This procedure covers the major stages in research and development program. If a program is unusual, extra stages may be added or subtracted as needed.
Stages can be repeated as necessary and sub projects can be raised.
Every stage in the procedure does not need to be implemented but the stage has to be considered before it is not used to make sure it will not affect the final product or its records.
This procedure does not include project control although project control can be used to control tasks in a program, refer to PROC-015 Procedure Project Control.

1.4 References

Internal References:
PROC-002 - Procedure Document Change
PROC-005 - Procedure Purchasing, Receiving, Stock Control of Product & Disposition
PROC-009 - Procedure – Assessing Vendors and Subcontractors
PROC-010 - Procedure Document & Record Control
PROC-015 - Procedure Project Control
PROC-017 - Regulatory & Distribution Approvals
PROC-018 - Purchasing & Receiving/Verification
PROC-019 - Risk Management of Medical Devices

External References:

TGA DR4 Section 1.24 ACCESS TO UNAPPROVED THERAPEUTIC DEVICES: CLINICAL TRIALS & SPECIAL ACCESS SCHEMES (SAS)

Guidance on Quality System Regulation Information for Various PreMarket Submissions (For background information only, on FDA web site).

ISO 14971 Medical devices – Application of risk management to medical devices

1.5 Responsibility/Authority

The responsibility and authority for the procedure is with the Chief Executive Officer and the Chief Technology Officer who have the authority to delegate responsibility to other people to carry out the work. The major positions are:

Program Manager: Overall responsibility for the program including technical and financial areas. The program manager has the authority to delegate tasks.

Program Administrator: A person authorised by the Program Manager to administer a program. The Program Administrator can be the Program Manager. This person is responsible for:

- approving commencement & closing of projects;
- determining and informing management of the program status;
- maintaining program records.

The Program administrator does not make major decisions, especially technical; this is the Program Manager responsibility.

Work may be subcontracted to an organisation outside of Portland Orthopedics, however at each stage a Portland member will be responsible for the products and services of these outside organisations.

1.6 Subcontracting

If a task if subcontracted, then the subcontractor must be approved. Approval involves determining if the subcontractor can do an adequate service (e.g. designing or testing etc.) and documenting this analysis. Refer to PROC-009 Procedure – Assessing Vendors and Subcontractors for details and PROC-018 Procedure – Purchasing & Receiving/Subcontracting.

1.7 Program Documentation and Record Control

The documentation required for each stage of development is described for each stage.

Program History: A record is to be kept of the program history. This includes Requirements, Plans, Risk analyses (business & product), meeting minutes and projects. Detail history can be retained in the projects with its history.

Document security: Where documents are of different security level, they shall be handled per PROC-010 Procedure Document & Record control. Refer to Appendix B.

1.8 Definitions

DCN: Document Change Note controlled by PROC-002 Procedure – Document Change Note.

Design Changes: During design, latest versions documents are determined by date and later version number. At end of stages, documents are to be marked up as to their status. If a document is to be used in a later stage (e.g. making prototypes), it should be signed off by the project leader.

Design History File (DHF)

"a compilation of records which describes the design history of a finished device." (Source – US Code of Federal Regulations #21 Part 820.3(e))
The Design History File contains the design history of a product. Documentation required to go into the Design History File is set out in Documentation section for each stage of the procedure.

Device Master Record (DMR)

"a compilation of records containing the design, formulation, specification, complete manufacturing procedures, quality assurance requirements, and labelling of a finished device (Source – US Code of Federal Regulations #21 Part 820.3(j)) A file containing the documents or a listing with location of these documents that specifies the product & its manufacture. Refer to PROC-010 for more details.

Device History Record (DHR)

"a compilation of records containing the complete production history of a finished device". (Source – US Code of Federal Regulations #21 Part 820.3(i))

Verification: Confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.

Validation: The establishment of documented evidence that a system does what it purports to do.

Product Changes: These are design changes to existing product. These changes are controlled via PROC-002 Procedure – Document Change Note. The first release of a design is set out later in Design Approval and follow the process as Product changes.

Program: A defined method of developing & managing a product or range of products from conceptual beginnings until the end of the product's life cycle.

Project: A define method of carrying out & documenting a series of tasks that has a define start with a target & a finish.

Design Approval: The acceptance of a design by the company including the checking and signing off that all requirements have been met. The first release of a design or later design change is set out later in Design Approval and follows the same process as Product changes.

MDR: Medical Device Report. This is also known as Vigilance in Europe & IRIS in Australia. These can be found in Adverse Outcome reports PROC-001 or Customer Feedback Reports PROC-003

POR Purchase Order Record, see PROC-018

CEO: Chief Executive Officer

CTO: Chief Technical Officer

Idea Sponsor: Origin of request to undertake a change or creation of a product or process.

1.9 Flowchart Summary

In general, the stages in a Research & Development program are as below with flowchart following.
These stages can be modified depending on the program. These stages can be carried out in one project or as a series of projects. Refer to PROC-015 Procedure Project Control.

1. Research, Concept Design & Review
   - Document the original Idea
   - Research, Concept Design
   - Review

2. Initiating & Planning Project
   - Initiating Project
   - Determine Marketing, Regulatory and Technical Requirements
   - Planning Project

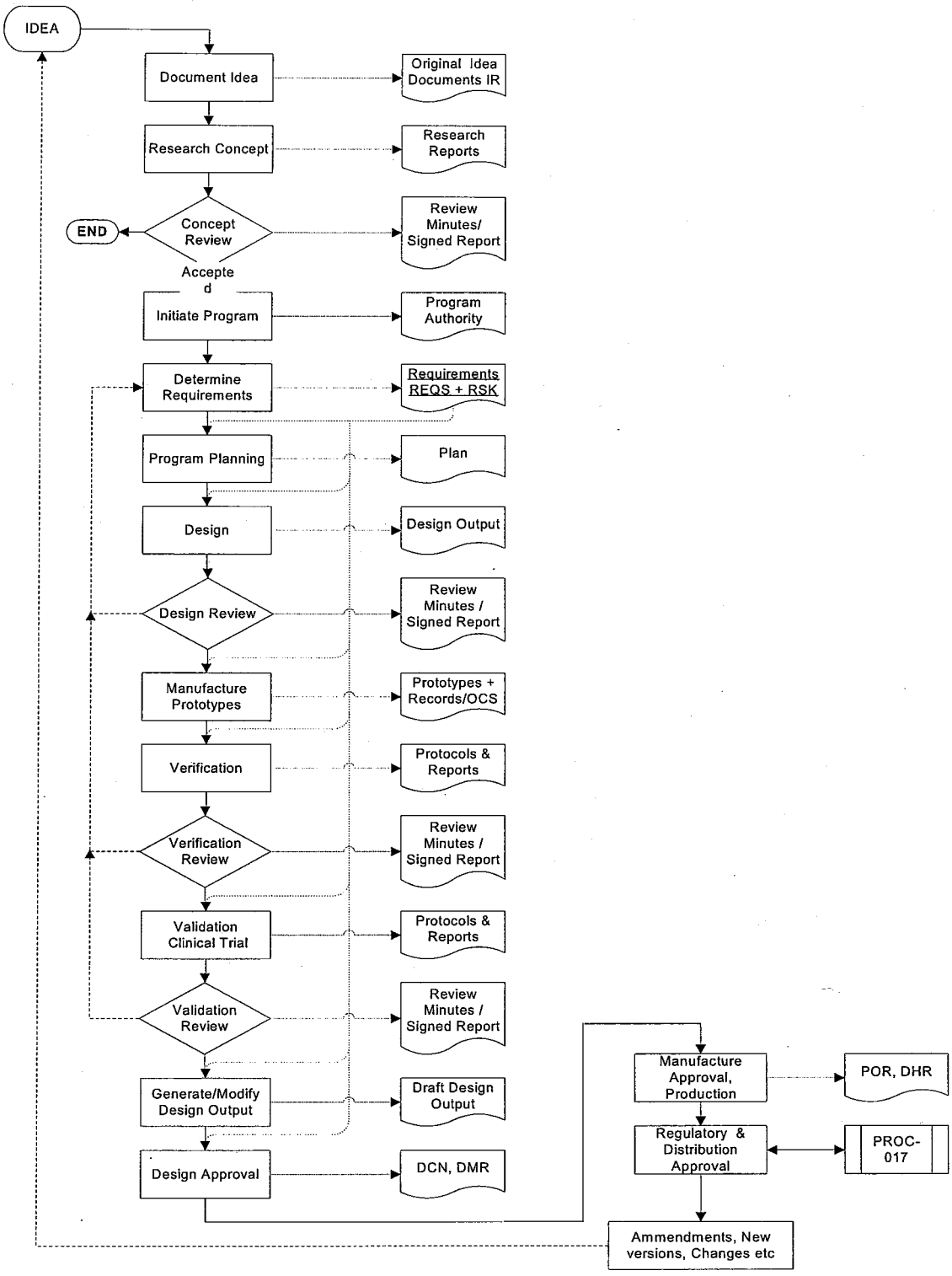
3. Development
   - Design
   - Design Review
   - Prototypes
   - Verification
   - Verification Review

4. Validation
   - Validation
   - Validation Review

5. Production
   - Generate or Modify Product Specification (Design Output)
   - Design Approval
   - Production Approval & Manufacture

6. Regulatory Approvals & Approval for Release to Distribute

7. Amendments / New Versions / Product & Process Changes


IDEA
Document Idea
Original Idea Documents IR
Research Concept
Research Reports
END
Concept Review
Review Minutes/ Signed Report
Accepte d
Initiate Program
Program Authority
Determine Requirements
Requirements REQS + RSK
Program Planning
Plan
Design
Design Output
Design Review
Review Minutes / Signed Report
Manufacture Prototypes
Prototypes + Records/OCS
Verification
Protocols & Reports
Verification Review
Review Minutes / Signed Report
Validation Clinical Trial
Protocols & Reports
Validation Review
Review Minutes / Signed Report
Generate/Modify Design Output
Draft Design Output
Design Approval
DCN, DMR
Manufacture Approval, Production
POR, DHR
Regulatory & Distribution Approval
PROC-017
Ammendments, New versions, Changes etc

2. PROCEDURE

2.1 Research, Concept Design & Review

This stage is only the idea stage and design controls do not apply. Documentation should be kept together by the idea sponsor until it is turned into a program and/or a project.

2.1.1 Documenting the Original Idea

Responsibility
Idea Sponsor.

Purpose
To document the idea(s) so other people can understand the concepts necessary to work on the idea(s) and to be able to generate initial program or project documentation if it progresses past this stage.

Task
Documentation of ideas.

Documentation
Ideas documented in Lab Book for preference, refer to PROC-010 Procedure Document & Record Control.

2.1.2 Research / Concept Design

Responsibility
The CEO or Idea Sponsor who can assign a preliminary Administrator who can delegate/subcontract this work.

Purpose
This stage is often done to find out as much information as possible, especially establishing basic requirements, at a low cost to determine if the program should go into costly stages.

Task
The amount of work carried out depends on the idea but will at least include a literature review of relevant technologies and establishing basic design requirements. This could also include:

- market research (highly confidential);
- feasibility studies (highly confidential);
- business finance & risk analysis (highly confidential);
- preliminary product risk analysis; and
- take concept to paper designs etc.

Note – Business documents (market research, business risk analysis) should be kept separate from the technical documentation, as technical documents are auditable by external authorities.

Documentation

The work should be documented depending on the likelihood that the data will be required later for review.

2.1.3 Review

Responsibility

The CEO and Idea Sponsor.

Purpose

A review is to be conducted of collected documents, reports and records to:

a) Evaluate the ability to fulfill requirements;
b) Review preliminary risk analysis (product & business)
c) Assess feasibility and viability;
d) Identify problems and propose follow-up actions (including patenting idea).

Task

The documents are to be reviewed. The participants shall include representatives of functions concerned with the stage being reviewed.

The results of the review and subsequent follow-up actions shall be recorded. At this stage the project will be initiated, closed as considered not feasible, or redesigned and resubmitted in a new form.
If moving to next stage, then detailed requirements will be required.

Documentation

Record results of the review (e.g. review meeting minutes) that are to be signed & dated.

2.2 Initiating & Planning a Program

NOTE: From the authorisation of a program and then from this stage on, design controls apply.

2.2.1 Initiating a Program (Document Project Idea or Purpose of Design Change)

Responsibility

CEO, CTO. The work can be delegated but responsibility is Portland's.

Purpose

To control a program.

Task

Include reasons for the program so priorities can be determined.
On acceptance, sign as approved as a project by CEO (Budget information may be required).
Determine Program Manager.
Determine Program Administrator

Documents

Initiating documents (these could be confidential, possibly at board level).

2.2.2 Determine Marketing, Regulatory and Technical Requirements

Responsibility
Program Manager, Program Administrator.

Purpose
The purpose of this section is to reduce design and/or development costs to a minimum by supplying requirements as early as possible, to keep the number of iterations to a minimum. The program can start without all requirements known and specifications can be modified later, but this must be balanced against possible extra costs (e.g. from extra iterations).

Task
Determine product requirements (Inputs) and document. These shall include:
a) Functional, performance and safety requirements according to the intended use (can refer to other documents, standards etc);
b) Applicable regulatory and legal requirements;
c) Applicable information derived from previous similar deigns, and
d) Any other requirements essential for design and/or development e.g. any contract review activities, and
e) Output(s) of risk management.

For Medical devices, the following aspects should be addressed:
a) Intended use
b) User/patient/clinical interfaces and inputs (e.g. intended conditions of use)
c) Performance characteristics
d) Safety characteristics
e) Limits and tolerances for safety and performance parameters
f) Risk analysis (see attachment)
g) Toxicity and bio-compatibility (of materials)
h) Electromagnetic compatibility (EMC)
i) Compatibility with accessories/auxiliary devices
j) Compatibility with the environment of intended use
k) Human factors
l) Physical/chemical characteristics
m) Labeling/packaging (including marking and Instructions for Use)
n) Reliability (including wear and its effects)
o) Statutory and regulatory requirements
p) Voluntary standards
q) Manufacturing processes
r) Sterility
s) MDRs/complaints/failures and other historical data
t) Past design history files (DHFs)

This task will include determining which standards apply.

These inputs shall be reviewed for adequacy. Incomplete, ambiguous or conflicting requirements shall be resolved by contacting relevant people involved. Where conflicts remain unresolved, the CTO shall decide. The CTO is to sign off as approved.

Documents
For a program, an approved product Requirements Specification (REQS-XXX) listing the requirements, refer to PROC-010 Procedure Document & Record Control.

2.2.3 Program Planning

Responsibility
Program Manager.

Purpose
Again the purpose of this section is to reduce design and/or development costs to a minimum by keeping the number of iterations to a minimum by outlining all the work that is to be done.
The program can start without being fully planned and modified later when more information is available but this must be balanced against possible extra costs (e.g. from extra iterations).

Task
Develop a plan to control the design and/or development of the product, with reference to the requirements.
The Plan will determine:
a) Stages of design and/or development processes (see rest of document);
b) Review, verification, validation and design transfer activities appropriate to each stage;
c) Responsibilities and authorities for activities (including only assigning these to qualified personnel equipped with adequate resources);
d) Approximate costing;
e) Time expectations; and
f) Major project milestones.

Interfaces between different groups involved in design and/or development shall be managed to ensure effective communication and clarity of responsibilities (including necessary information documented, transmitted and regularly reviewed).
The planning should include risk analysis (see PROC-019) and the following:

- Determining the effect on business & marketing as timing & method of introduction of new or modified product, can greatly affect business results e.g. will old product be sold easily or will it be left on shelf as surgeons want latest version;
- Determine effects on other parts or processes e.g. new labels required for revisions, new instruction leaflets required as old leaflets have unchanged sizes, will old & new items need to be clearly identified other than sizes on labels (for stock control);
- Does a change affect instruments or cause confusion in operating theatre;
- Determining if a modification to regulatory specification is required as this will impact on time expectations;
- Analysis of resources required and determined if available
- Ensuring design outputs are verified as suitable for manufacturing before becoming final production specifications.

This plan should have provisions for reviewing, updating and approving of the plan as project progresses.
The plan should make reference to various projects for managing the tasks. Refer to PROC-0015 Procedure Project Control.

Documents
The plan can be a separate document (e.g.: a project plan using MS project). It should include what is to be done, who will be responsible and timing (can be an estimate). This includes information on:

- chronology of development strategy (e.g. Gantt Chart);
- outline of timing strategy i.e. initiation, completion & analysis for all testing, with specification & justification of data needed prior to subsequent studies contained or referenced in the plan;
- identification of critical milestones that must be completed before initiation of subsequent tasks;
- specific deliverables of each stage & criteria for initiation & completion; and
- cash flow & budgets (highly confidential).

Any relevant information from the previous Research, Concept Design & Review stage should be transferred, copied or referenced into a project file.

2.3 Development

2.3.1 Design

Responsibility
Program Manager. The task can be done by Portland or subcontracted. The results are to be documented at Portland with pointers to other documents.

Purpose
Design or develop product.

Task
Work to be done depends on requirements and planning.
At this stage, we need to do risk analysis and risk management on the product e.g. how does new design affect strength of product or interface with other parts, surgical processes or surgical instrumentation. See PROC-019 on risk analysis.
The output shall be in a form that enables verification against the requirements.

Documents
All work should be documented depending on the likelihood that the data will be required later for review.
Examples of documentation:

- Draft product specification, e.g SPEC-XXX, drawings etc;
- Risk Management Report (RSK-XXX) see PROC-019;
- Results of any analysis, e.g. stress analysis, FEA.

Refer to PROC-010 Procedure Document & Record Control for general documentation.

2.3.2 Design Review

Responsibility
Program Manager. The review is to be done by Portland. Even if a subcontract did the above task, the results need to be reviewed by Portland.

Purpose
A review is to be conducted to:
a) Evaluate the ability to fulfil requirements as per Project Authority;
b) Identify problems and propose follow-up actions;
c) Review status and planning effectiveness.

Task

The review shall included representatives of functions concerned with the design stage being reviewed, as well as other specialist personnel.

The results of the review and subsequent follow-up actions shall be recorded.

At this stage, the project could be:
- closed if it is not feasible or;
- returned to design stage (with updated plan) or;
- moved to the next stage.

If moving to the next stage, then requirements specification may require modification and plan changed (replacing plan if more information is available).

Documents
This has to be documented for regulatory authorities (TGA, CE & FDA) e.g. retain a file copy of drawing/fax from subcontractor in the design history file and signed off & dated by Portland and the results with any modifications noted.

2.3.3 Prototypes

Responsibility
Program Manager. This work can be subcontracted but results are to be documented at Portland with pointers to other documents.

Purpose
In most circumstances, prototypes may be required before final approval. These could be used for clinical trials before regulatory approval or for customer to approve samples before full commitment.

Task
Work to be done depends on requirements, the plan and documents from previous stage. Verification of prototypes to prototype drawings etc is part of this stage.

Documents
Requirements documents would include a full description and specification for each prototype to be manufactured.

Depending on the purpose of the prototypes, up to full production documentation may be required. Documents used to be signed off from previous stage.

2.3.4 Verification (Test)

Responsibility
Program manager. This work can be subcontracted but results to be documented at Portland with pointers to other documents.

Purpose
Verification is to be performed to ensure product (i.e. design outputs) meets requirements e.g. specification (REQS-XXX).

Task
Verification could be computer analysis, mechanical testing or any other work done to ensure the design is good and safe. The testing to be done is usually developed during the planning stage but can be modified by later experience.

Verification could include;
- Performing alternative calculations;
- Comparing the new design with a similar proven design, if available;
- Undertaking tests and demonstrations, and
- Reviewing the design stage documents before release.

Documents
Document the results including identification of the design, methods, date and individuals performing the verification. These need to be kept as required by Regulatory Authorities (TGA, CE & FDA etc). Refer to Appendix A for FDA requirements for a complete test report. These will become part of Design History Record if product is released.

2.3.5 Verification Review

Responsibility
Program Manager. The review is to be done by Portland even if above work is being done by subcontractors; the results need to be reviewed by Portland.

Purpose
A review is to be conducted to:
a) Evaluate the ability of the verification report to fulfils its purpose (i.e. the document is complete);
b) Evaluate that the verification shows that the product fulfils its requirements (specifications);
c) Identify problems and propose follow-up actions.

Task
The review shall include representatives of functions concerned with the stage being reviewed. The results of the review and subsequent follow-up actions shall be recorded.

At this stage, the project is likely require another iteration of design (with update of plan showing Design Development etc again) or move to next stage
Record results and update documents.

Documentation
Record results and update documents.

The results of subsequent follow-up actions shall be recorded.

2.4 Validation

2.4.1 Validation

Responsibility
Program Manager. This can be subcontracted but results to be documented at Portland with pointers to other documents.

Purpose
Validation is performed to confirm that the product is capable of meeting the requirements for the specified application or intended use. This also checks if the requirement specification is correct as well as the product. Validation shall be completed prior to the delivery. This does not include post marketing follow up trials.

Task

Clinical evaluation may include a compilation of relevant scientific literature, historical evidence that similar designs and/or materials are clinically safe, or a clinical investigation or trial, to ensure that the device performs as intended.

Any clinical trials are to meet regulatory requirements. Clinical trials in Australia are subject to either the CTN (Clinical Trial Notification) or CTE (Clinical Trial Exemption) schemes of TGA. Both schemes require Institutional Ethics Committee (IEC) approval and the IEC determines which scheme is selected. Refer to TGA DR4 Section 1.24 ACCESS TO UNAPPROVED THERAPEUTIC DEVICES: CLINICAL TRIALS & SPECIAL ACCESS SCHEMES (SAS).

The requirements for CE Approval are set out in “Clinical Data” which is included as an attachment to this procedure. The results of validation and subsequent follow-up actions shall be recorded.

Clinical trials may require production units before final sign off. A partial sign off should be done to produce these first units with the manufacture of those units under production control (see Production Approval process below). Provision of these medical devices is not considered to be delivery. If validation was performed on non-production devices, a report of the scientific method used to prove equivalence of these devices to production devices is required.

The validation process should include a risk management program to ensure the design does not have an adverse effect on the patients. The results of the risk management process will be documented and updated.

Documents
Any clinical trial reports need to be kept. If none are done, then a short report should be made explaining why none were required e.g. product is similar to another product where we already have positive results and any differences would not affect results.
Again the documentation including the written protocol, identification of the design, methods, dates and individuals performing the validation need to be kept as required by TGA, CE & FDA. These will become part of Device Master Record if product is released.
Results to be documented at Portland with pointers to other documents.
Requirements are in the notes from TGA.

2.4.2 Validation Review

Responsibility
Program Manager. The review has to be done by Portland even if above work is being done by subcontractors

Purpose
A review is to be conducted to:

a) Evaluate the ability of the validation report to fulfill its purpose (i.e. the document is complete);
b) Evaluate the ability of the design to fulfill purpose of the product (this could indicate that requirements specification is incorrect);
c) Identify problems and propose follow-up actions.

Task
The results need to be reviewed by Portland. It is to determine from the above results that the validation process has truly validated the product and its design.
If design does not meet requirements then the original design specification may require changing with the procedure repeated for the changes.

Documents
This review has to be documented for CE.

2.5 Production

2.5.1 Generate or Modify Product Specifications (Design Output)

Responsibility
Program Manager. This can be subcontracted but results to be documented at Portland with pointers to other documents.

Purpose
To document in a clear manner the design and production requirements of the product and where it will affect the product, the production methodology

Task

Design and/or development output shall:
a) Meet the design specification;
b) Provide appropriate information for purchasing, production and service operations;
c) Contain or reference product acceptance criteria;
d) Contain or make reference to the process or mechanism used to identify the design outputs considered essential for the proper functioning of the product;
e) Define the characteristics of the product that are essential to its safe and proper use (e.g. operating, storage, handling, maintenance and disposal requirements).

Documents
The outputs of design and/or development process shall be documented in a manner that enables verification against the specification. This is normally done during the entire process. These documents will form the Device Master Record and includes specifications, drawings etc.

2.5.2 Design Approval

Responsibility
CTO.

Purpose
To review design output documentation to make sure it is correct, update Device Master Record (DMR) and inform the appropriate people.

Task
Portland approves changes, change specifications and change Device Master Record (per Portland procedure PROC-002).

Documents
Document Change Note (DCN) as per PROC-002. This document can contain pointers to other documents stored elsewhere or documents can be attached to the DCN and stored with it.
The Device Master Record is generated or changes are compiled to the Device Master Record.
The output documents shall be approved by the Chief Technology Officer prior to release.

2.5.3 Production Approval & Manufacture

Responsibility
CEO. This can be subcontracted but results to be documented at Portland with pointers to other documents.

Purpose
To obtain product that meets specifications (Device Master Record).

Task
Production approval depends on the agreement between Portland and the subcontractors. The company has to confirm the product can be made correctly to a minimum standard before Production Approval. Approved subcontractors are to be

used and where necessary GMP Agreements are to be signed, refer to PROC-009 Procedure – Assessing Vendors and Subcontractors.

Purchase orders are placed and changed specifications/drawings distributed per PROC-005 & PROC-018. The product is also received per PROC-005 & PROC-018.

Where Vimek is doing the manufacturing, Vimek will carry out manufacturing planning as per its procedures [P0202]. This can be done during the previous development stages. This includes writing & verifying Operation Control Sheets, work instructions, CNC programs etc.

Documents
Purchase order
Certificate of conformance
Accounting documentation (Delivery Notes, Invoices etc.)

2.6 Regulatory Approvals & Approval for Release to Distribute

Responsibility
CEO and Quality Management Representative.

Purpose
To make sure product is only deliver to countries where the product is approved for use.

Task
Generate documentation for each markets regulatory requirements and obtain necessary approvals per PROC-017 Regulatory & Distribution Approvals.
This is not a release of individual product but a written release that a type of product can be sold in a country (or groups of countries). This is because different countries require different notifications and it can take different amount of time.

Documents
Regulatory approval documents.
A signed document saying that release is approved for various countries.

2.7 Amendments / New Versions / Product & Process Changes

Responsibility
Idea sponsor

Purpose
To make new versions or changes to product.

Task

The new versions or changes are developed using similar process to this procedure. If it requires a project or series of projects, then follow the stages in this procedure. If the change is simple, then use PROC-002 Document Change Note with all documentation attached to the DCN.

This includes an evaluation of the effect of the changes on constituent parts and product already delivered.

If validation is not considered necessary, then the reasons must be supplied e.g. the changes do not affect the validation results and the old validation is still applicable.

Documents
All documents are stored in project file or attached to DCN as per relevant procedure.

APPENDIX A TEST REPORTS

A complete test report consists of the following:

1. The name and address of facility performing the test.
2. The name of the study director, investigators, and supervisors involved in the study.
3. The dates that testing was initiated and completed and the date the final report was completed.
4. The objectives, methods, materials, deviations from referenced protocols and standards, results and conclusions of the test. These sections must include:
    a. a description of the test system used and a schematic or clear photograph of the test set-up;
    b. a description of the samples tested including the differences, if any, in the composition, material structure and processing methods between the test samples and the device to be marketed (if multiple device sizes or configurations are under review, then select and justify the worst case device(s) to be tested);
    c. the assumptions of the test, including assumed physiological loading values and environmental conditions;
    d. the load directions and magnitudes;
    e. the full experimental data, complete to the extent that an independent conclusion and analysis can be made;
    f. results (mean ± standard error, standard deviation, etc., if applicable) from the testing of an adequate number of identical samples (e.g., 5) for each type of test and control specimens or statistical justification for the number of each;
    g. statistical evaluation of the differences between the test results where appropriate;
    h. the clinical implications of the results; and
    i. a post-test failure analysis of the specimens for identification of cracks, plastic deformation and any other signs of failure, including the location of the point of failure initiation.
5. A bibliography of all references pertinent to the report.

APPENDIX B

Record Filing Structure

A suggested format for the filing of records (and documents while program is still open) could be in the following order.

Program Files – Highly Confidential
market research (highly confidential);
feasibility studies (highly confidential);
business finance & risk analysis (highly confidential);
preliminary product risk analysis;
meeting minutes; and
cash flow etc.

Project Files - General

Projects are controlled in PROC-015 Procedure – Project Control.

APPENDIX C

RECORD OF CHANGES

Issue No.	RECORDED AMENDMENT	DATE	DCN #
1	Release	8/8/02	0049
2	Moved attachments to front page so it can be seen on issuing. Section 1.6 Added on subcontracting Introduced the concept of programs, Program Manager and Program Administrator.(multiple sections). Deleted items related to projects. Added references to PROC-015 Project Control. Section 2.3.1 Added sentence from ISO 9001:1994 4.4.5 Section 2.4.1 Added Note from 4.4.8 of BS ISO 13485:2000 Section 2.7 & reference to project forms deleted as applicable to a project, not a program. New section 2.7 Added sentence from ISO 9001:2000 7.3.7. Added reference to TGA caused by new regulations Added references to ISO 14971	3/6/03	0076
3	Change to Group Procedure Section 1.8 Added DHR & sources Included references to PROC-017, PROC-018, PROC-019 Included flowchart Included extra requirements from ISO13485:2003 Included a position for responsibility per Audit.160 Combined with Vimek P0401 for group procedure		