



U.S. Department of Health & Human Services

Food and Drug Administration

SAVE REQUEST

USER: (smw)
FOLDER: K062386 - 112 pages
COMPANY: MEDIS MEDICAL IMAGING SYSTEMS, B.V. (MEDIMEDIIMAGSYST)
PRODUCT: SYSTEM, X-RAY, TOMOGRAPHY, COMPUTED (JAK)
SUMMARY: Product: QANGIO CT

DATE REQUESTED: Oct 19, 2015

DATE PRINTED: Oct 19, 2015

Note: Printed



12. SUMMARY OF SAFETY AND EFFECTIVENESS

Submission in accordance with the requirements of 21 CFR Part 807.87(h)

- **Submitter** : Medis medical imaging systems bv
- Address : Schuttersveld 9
- : 2316 XG Leiden, The Netherlands
- Telephone : +31 71 522 3244
- Fax : +31 71 521 5617
- Contact Person : J.I. Hollander, Quality Coordinator
- Prepared : August 10, 2006
- **Device Name** : Automatic quantitative analysis of CTA images
- Common Name : QAngio® CT
- Device Class. Name : Class II; PACS software
- Regulation Number : 21 CFR 892.1750 (90 JAK)
- **Predicate Device(s)** : MRA-CMS, K040746

OCT - 5 2006

- **Device Description and indications for Use**

QAngio CT is able to read DICOM CT images from all major CT scanner vendors. Vessel analysis data, generated by automated (and/or manual) segmentation, detected stenosis, and quantitative results, can be saved in separate files enabling the comparison of results from different users.

Radiologists, cardiologists and technicians use the QAngio CT analytical software package to obtain objective and reproducible results. The obtained results may be used to support the interpretation of CTA data, or they are used in the evaluation of follow-up studies and the effectiveness of treatment.

In clinical practice the QAngio CT software is used on workstations in review rooms or integrated in a PACS environment..

- **Intended use**

The QAngio CT software solution has been developed for the objective and reproducible analysis of vessels in CTA images. It enables the quantitative analysis of CT angiograms based on automated segmentation. More specifically, QAngio CT can be used to quantify a number of lesion characteristics.

QAngio CT is intended for use as an auxiliary tool in assessing CTA studies in clinical practice and in clinical trials. The analysis results obtained with QAngio CT are to be interpreted by cardiologists or radiologists.

- **Substantial equivalence Information**

QAngio CT is substantially equivalent to the Predicate Device of MRA-CMS, K040746, using the same technique for the same intended use; only CT- instead of MR images.

Conclusion

In Medis' opinion, QAngio CT is a safe medical device. During the development, potential hazards were controlled by a risk management plan, including hazard and risk analyses, verification and validation tests. Evaluations by hospitals and literature information support this statement. The software package QAngio CT itself will not have any adverse effects on health. The operator interprets the objective values of the analysis and chooses to accept or reject the results.

In current thinking, the level of concern for the standalone software in image post-processing is 'Minor' and the use of QAngio CT does not change the intended use of CT scanners in practice, nor does the use result in any new potential hazard.

Based on the information supplied in this 510(k), Medis concludes that the subject device is safe, effective and substantially equivalent to the predicate device.



Food and Drug Administration
9200 Corporate Blvd.
Rockville MD 20850

OCT - 5 2006

Mr. J. I. Hollander
Quality Coordinator
Medis Medical Imaging Systems bv
9 Schuttersveld
Leiden
The Netherlands 2316XG

Re: K062386
Trade/Device Name: QAngio CT
Regulation Number: 21 CFR 892.1750
Regulation Name: Computed tomography x-ray system
Regulatory Class: II
Dated: August 11, 2006
Received: August 16, 2006

Dear Mr. Hollander:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.



Protecting and Promoting Public Health

Page 2 –

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. ~~The~~ FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at one of the following numbers, based on the regulation number at the top of this letter:

21 CFR 876.xxx	(Gastroenterology/Renal/Urology)	240-276-0115
21 CFR 884.xxx	(Obstetrics/Gynecology)	240-276-0115
21 CFR 894.xxx	(Radiology)	240-276-0120
Other		240-276-0100

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address <http://www.fda.gov/cdrh/industry/support/index.html>.

Sincerely yours,



Nancy C. Brogdon
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K062386

Device Name: **QAngio CT**

Indications For Use:

QAngio CT software solution has been developed for the objective and reproducible analysis of vessels in CTA images. It enables the quantitative analysis of CT angiograms based on automated segmentation. More specifically, QAngio CT can be used to quantify a number of lesion characteristics.

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(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDHR, Office of Device Evaluation (ODE)

Prescription Use ✓

(Optional Format 3-10-98)

David A. Legro
(Division Sign-Off)
Division of Reproductive, Abdominal,
and Radiological Devices
510(k) Number K062386



Food and Drug Administration
9200 Corporate Blvd.
Rockville MD 20850

OCT - 5 2006

Mr. J. I. Hollander
Quality Coordinator
Medis Medical Imaging Systems bv
9 Schuttersveld
Leiden
The Netherlands 2316XG

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Regulation Number: 21 CFR 892.1750
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Protecting and Promoting Public Health

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21 CFR 894.xxx	(Radiology)	240-276-0120
Other		240-276-0100

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Sincerely yours,



Nancy C. Brogdon
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K062386

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(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDHR, Office of Device Evaluation (ODE)

Prescription Use _____ ✓

(Optional Format 3-10-98)

David G. Hegrov
(Division Sign-Off)
Division of Reproductive, Abdominal,
and Radiological Devices
510(k) Number K062386

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

August 17, 2006

MEDIS MEDICAL IMAGING SYSTEMS, B.V. 510(k) Number: K062386
9 SCHUTTERSVELD Received: 16-AUG-2006
LEIDEN, Product: QANGIO CT
NETHERLANDS 2316 XG
ATTN: J.I. HOLLANDER

The Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), has received the Premarket Notification, (510(k)), you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product and for the above referenced 510(k) submitter. Please note, if the 510(k) submitter is incorrect, please notify the 510(k) Staff immediately. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. We will notify you when the processing of your 510(k) has been completed or if any additional information is required. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (DMC) (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official 510(k) submission.

Please note the following documents as they relate to 510(k) review:
1) Guidance for Industry and FDA Staff entitled, "FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act (MDUFMA). Please review this document at www.fda.gov/cdrh/mdufma/guidance/1219.html.
2) Guidance for Industry and FDA Staff entitled, "Format for Traditional and Abbreviated 510(k)s". This guidance can be found at www.fda.gov/cdrh/ode/guidance/1567.html. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).
3) Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review". Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html.

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of an premarket submission (e.g., 510(k), IDE, PMA, HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at www.fda.gov/cdrh/electsub.html.

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Lastly, you should be familiar with the regulatory requirements for medical devices available at Device Advice www.fda.gov/cdrh/devadvice/. If you have questions on the status of your submission, please contact DSMICA at (240) 276-3150 or the toll-free number (800) 638-2041, or at their Internet address <http://www.fda.gov/cdrh/dsma/dsmastaf.html>. If you have policy or procedural questions, please contact anyone on the 510(k) Staff at (301)594-1190.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Office of Device Evaluation
Center for Devices and Radiological Health

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

August 16, 2006

MEDIS MEDICAL IMAGING SYSTEMS, B.V. 510(k) Number: K062386
9 SCHUTTERSVELD Received: 15-AUG-2006
LEIDEN, Product: QANGIO CT
NETHERLANDS 2316 XG User Fee ID Number: 6026959
ATTN: J.I. HOLLANDER

The Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

The Act, as amended by the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) (Public Law 107-250), specifies that a submission shall be considered incomplete and shall not be accepted for filing until fees have been paid (Section 738(f)). Our records indicate that you have not submitted the user fee payment information and therefore your 510(k) cannot be filed and has been placed on hold. Please send a check to one of the addresses listed below:

By Regular Mail	By Private Courier(e.g., Fed Ex, UPS, etc.)
-----	-----
Food and Drug Administration	U.S. Bank
P.O. Box 956733	956733
St. Louis, MO 63195-6733.	1005 Convention Plaza
	St. Louis, MO 63101
	(314) 418-4983

The check should be made out to the Food and Drug Administration referencing the payment identification number, and a copy of the User Fee Cover sheet should be included with the check. A copy of the Medical Device User Fee Cover Sheet should be faxed to CDRH at (301) 594-2977 referencing the 510(k) number if you have not already sent it in with your 510(k) submission. After the FDA has been notified of the receipt of your user fee payment, your 510(k) will be filed and the review will begin. If payment has not been received within 30 days, your 510(k) will be deleted from the system. Additional information on user fees and how to submit your user fee payment may be found at www.fda.gov/oc/mdufma.

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, or HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at www.fda.gov/cdrh/elecsb.html.

Please note that since your 510(k) has not been reviewed, additional information may be required during the review process and the file may be placed on hold once again. If you are unsure as to whether or not you need to file a 510k Submission with FDA or what type of submission to submit, you should first telephone the Division of Small Manufacturers, International and Consumer Assistance (DSMICA), for guidance at (240) 276-3150 or its toll-free number (800)638-2041, or contact them at their Internet address www.fda.gov/cdrh/dsma/dsmastaf.html, or you may submit a 513(g) request for information regarding classification to the Document Mail Center at the address above. If you have any questions concerning receipt of your payment, please contact Christina Zeender at 301-827-2860. If you have questions regarding the status of your 510(k) Submission, please contact DSMICA at the numbers or address above.

Sincerely yours,

Marjorie Shulman
Consumer Safety Officer
Office of Device Evaluation
Center for Devices and
Radiological Health

excellence in medical imaging



K062386

Document Mail Center (HFZ-401)
Attn. Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland
United States of America.

Leiden, August 11, 2006

Our ref. : HH/06M0107
Subject : 510(k) Notification QAngio CT

Dear Sir / Madam,

Enclosed you will find 2 submissions with product documentation for the 510 (k) notification of the QAngio CT analytical software package of Medis medical imaging systems B.V.

With this information regarding 510(k) notification, I hope to have sufficiently informed your office. We look forward to the FDA market-clearance letter.

Sincerely yours,

J. I. Hollander
Quality Coordinator
Medis medical imaging systems, B.V.

Handwritten vertical text: 19 15 14:42

Handwritten notes: 19, K43, RA, TI, and an ISO 9001 certification logo.

Form Approved: OMB No. 0910-511 Expiration Date August 31, 2005. See Instructions for OMB States

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE USER FEE COVER SHEET**

PAYMENT IDENTIFICATION NUMBER: MD6026959-956733
Write the Payment Identification number on your check.

A completed Cover Sheet must accompany each original application or supplement subject to fees. The following actions must be taken to properly submit your application and fee payment:

1. Electronically submits the completed Cover Sheet to the Food and Drug Administration (FDA) before payment is sent.
2. Include printed copy of this completed Cover Sheet with a check made payable to the Food and Drug Administration. Remember the Payment Identification Number must be written on the check.
3. Mail Check and Cover Sheet to the US Bank Lock Box, FDA Account, P.O. Box 956733, St. Louis, MO 63195-6733. (Note: In no case should payment be submitted with the application.)
4. If you prefer to send a check by a courier, the courier may deliver the check and Cover Sheet to: US Bank, Attn: Government Lockbox 956733, 1005 Convention Plaza, St. Louis, MO 63101. (Note: This address is for courier delivery only. Contact the US Bank at 314-418-4821 if you have any questions concerning courier delivery.)
5. For Wire Transfer Payment Procedures, please refer to the MDUFMA Fee Payment Instructions at the following URL: <http://www.fda.gov/cdrh/mdufma/faqs.html#3a>. You are responsible for paying all fees associated with wire transfer.
6. Include a copy of the complete Cover Sheet in volume one of the application when submitting to the FDA at either the CBER or CDRH Document Mail Center.

1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code)

MEDIS MEDICAL IMAGING SYSTEMS
Schuttersveld 9
Leiden NO DATA 2316 XG
NL

1.1 EMPLOYER IDENTIFICATION NUMBER (EIN)
NO DATA

2. CONTACT NAME
Hans Hollander

2.1 E-MAIL ADDRESS
hhollander@medis.nl

2.2 TELEPHONE NUMBER (include Area code)
31 71 5225241

2.3 FACSIMILE (FAX) NUMBER (Include Area code)
+31 71 5215617

3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: <http://www.fda.gov/dc/mdufma>)

Select an application type:

- Premarket notification(510(k)); except for third party
- Biologics License Application (BLA)
- Premarket Approval Application (PMA)
- Modular PMA
- Product Development Protocol (PDP)
- Premarket Report (PMR)

3.1 Select one of the types below

- Original Application
- Supplement Types:
- Efficacy (BLA)
- Panel Track (PMA, PMR, PDP)
- Real-Time (PMA, PMR, PDP)
- 180-day (PMA, PMR, PDP)

4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status)

- YES, I meet the small business criteria and have submitted the required qualifying documents to FDA
- NO, I am not a small business

4.1 If Yes, please enter your Small Business Decision Number:

5. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.

- This application is the first PMA submitted by a qualified small business, including any affiliates, parents, and partner firms
- The sole purpose of the application is to support conditions of use for a pediatric population
- This biologics application is submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only
- The application is submitted by a state or federal government entity for a device that is not to be distributed commercially

6. IS THIS A SUPPLEMENT TO A PREMARKET APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA).)

- YES
- NO

7. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION (FOR FISCAL YEAR 2005)

\$3,833.00

07-Aug-2006

Form FDA 3601 (08/2003)

(Close Window)

(Print Cover sheet)



excellence in medical imaging

QAngio® CT: FDA 510(k) PRE-MARKET NOTIFICATION

Date: August 10, 2006
Document Mail center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850 USA

Attention: Document Control Clerk
Re: 510(k) Submission for 'QAngio CT' analytical software

Dear Sir / Madam:

Pursuant to HHS Publication FDA 95-4158 and 21 CFR 807 Subpart E herewith enclosed is Medis medical imaging systems bv the 510(k) pre-market notification for the "Automatic quantitative analysis of CT Angiography (CTA) images". This is an analytical software package, which Medis intends to market under trade name 'QAngio® CT'.

It is Medis' opinion that this device is substantially equivalent to other devices available on the market. The comparison matrices, from which this opinion was derived, is included as part of this 510(k) traditional submission.

This submission is believed to include all of the information required to enable your office to allow the commercial distribution of the above referenced device with the following identification data:

- Date of Application : August 10 2006
- Applicant : J.I. Hollander
: Medis medical imaging systems bv,
: Schuttersveld 9,
: 2316 XG Leiden,
: The Netherlands
: Tel: +31 71 522 3244
: Fax: +31 71 521 5617
- Manufacturer : Medis medical imaging systems bv,
: Schuttersveld 9,
: 2316 XG Leiden,
: The Netherlands.

FBI
AUG 15 2006
1:43
FBI/DOJ/DOH/MDH

If there are further data required, please contact me at the address above.

Sincerely,

J.I. Hollander
Quality Coordinator

Medis medical imaging systems bv
Schuttersveld 9 2316 XG Leiden - P.O.Box 384 2300 AJ Leiden The Netherlands
Tel. +31 (0)71 522 32 44 - Fax +31 (0)71 521 56 17 - www.medis.nl - info@medis.nl

Questions or Contact FDA/CDRH/OCE/DID at CDRH-FOI@STATUS@fda.hhs.gov or 301-796-8118



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2. Reason for 510(k)

The reason for this submission is that Medis considers the QAngio CT analytical software package ready for the market. This software is a state-of-the-art product for the objective and reproducible assessment of CTA images.

QAngio CT is a analytical software package for image post-processing that runs on Microsoft Windows XP. QAngio CT can be installed on working stations or integrated in a PACS environment. QAngio CT is able to read DICOM CT images from all major CT scanner vendors. Furthermore, QAngio CT has an open architecture, facilitating the exportation of results into DICOM SR files or to an xml general database file for further statistical analysis of the study results.

3. Truthful and Accurate Statement

I certify that, in my capacity as Quality Coordinator of Medis medical imaging systems bv, I believe to the best of my knowledge, all data and information in this pre-market notification are truthful and accurate and that no material fact has been omitted.

Signed :
Name : J.I. Hollander
Dated : August 10 2006

4. Device Name : Automatic quantitative analysis of CTA images
Common name : **QAngio® CT**
Classification name : System, Computed Tomography, Angiography

5. Registration Number : Establishment 9614587

6. Classification : Class II
Panel : Radiology
Product code : 90 JAK (21 CFR 892.1750)

7. Performance standards

- NEMA PS3; DICOM, Digital Imaging and Communications in Medicine
- ISO/IEC 12207:1995; Information Technology – Software Life Cycle Processes
- IEC 60601-1-1-4: Medical electrical equipment – General requirements for safety; 4 Collateral Standard: Programmable Electrical Medical Systems
- ISO 14971:2000; Medical Devices – Application of Risk Management to Medical Devices
- ISO 9001:2000; Quality management systems – Requirements
- ISO 13485:2003; Medical devices – Quality management systems – requirements for regulatory purposes

QAngio CT 510(k) Pre-market Notification

8. Labeling

QAngio CT is a computer program that can be provided to the user via electronic data communication systems or on physical media, including such industry standard storage media as CD-ROM. The standard to provide software is as follows:

Medis delivers the software on a CD-ROM, labeled with:

- The Medis logo
- The complete address of Medis, being the manufacturer
- The CE marking label, with 0120 identifying the Notified Body
- The software product name and version number
- The S/N number

The CD-ROM cassette contains also a printout with the same labeling information and instructions for initiating the installation of the product. The installation instruction leads the user to the electronic manual.

A printed user manual (**See Appendix A**) is delivered as part of the product, and an extra copy is also provided on the CD-ROM help desk.

The manual contains the following information:

- An introduction with warnings, standards, CE-marking,
- A notification of the intended use,
- A short description of QAngio CT,
- The directions and instructions for use,

Medis has developed a product data sheet (**See Appendix B**) that also describes the characteristics and the features in using the product at review rooms.

9. Device Description and Indications for Use

QAngio CT is able to read DICOM CT images from all major CT vendors. Vessel analysis data, automatic (or manual) contour segmentation, detected stenosis, and quantitative results can be saved in separate files enabling the comparison of results from different users.

Radiologists, cardiologists and technicians use the QAngio CT standalone analytical software package to obtain objective and reproducible results. The obtained results may be used to support the interpretation of CTA data or are used in the evaluation of follow-up studies and the effectiveness of treatment.

In clinical practice the QAngio CT software is used in review rooms on workstations or integrated in a PACS environment.

10. Intended use

The QAngio CT software solution has been developed for the objective and reproducible analysis of vessels in CTA images. It enables the quantitative analysis of CT angiograms based on automated segmentation. More specifically, QAngio CT can be used to quantify a number of lesion characteristics.

QAngio CT is intended for use as an auxiliary tool in assessing CTA studies in clinical practice and in clinical trials. The analysis results obtained with QAngio CT are to be interpreted by cardiologists or radiologists.

11. Substantial Equivalence Comparison

QAngio CT can be compared (see Table below) with the **Predicate Device** under 510(k) **K040746** "MRA-CMS" software package of Medis at Leiden the Netherlands.

Comparison table for Substantial Equivalence

Vendor	Medis medical imaging systems bv	Medis
Name	MRA-CMS (new name: 'QAngio [®] MR')	QAngio CT
510(k)	K040746	Requested

Feature	Segmentation & quantification on 3D MRA data sets	Segmentation & quantification on 3D CTA data sets
	Automatic detection of 3D vessel contours	√
	CSA values over the entire segment	√
	Percentage of diameter and area of stenosis	√
	Volumes of stenosis, <u>plaque</u> , vessel and segment	Volumes of stenosis, vessel and segment
	Automatic calculation of 3D reference contour	√
	Images from major vendors are accepted	√
Intended use	Quantification of MR Angiography images	Quantification of CT Angiography images
Data Source	DICOM formatted images	√
Physical Characteristics	Software Package	√
	Operates on off the shelf hardware	√
	NT operating system	Windows XP
	DICOM Compatible	√
Safety	Clinical interactive review and editing of data is integral to the use of the software	√

12. SUMMARY OF SAFETY AND EFFECTIVENESS

Submission in accordance with the requirements of 21 CFR Part 807.87(h)

- **Submitter** : Medis medical imaging systems bv
- Address : Schuttersveld 9
- : 2316 XG Leiden, The Netherlands
- Telephone : +31 71 522 3244
- Fax : +31 71 521 5617
- Contact Person : J.I. Hollander, Quality Coordinator
- Prepared : August 10, 2006
- **Device Name** : Automatic quantitative analysis of CTA images
- Common Name : QAngio® CT
- Device Class. Name : Class II; PACS software
- Regulation Number : 21 CFR 892.1750 (90 JAK)
- **Predicate Device(s)** : MRA-CMS, K040746

• Device Description and indications for Use

QAngio CT is able to read DICOM CT images from all major CT scanner vendors. Vessel analysis data, generated by automated (and/or manual) segmentation, detected stenosis, and quantitative results, can be saved in separate files enabling the comparison of results from different users.

Radiologists, cardiologists and technicians use the QAngio CT analytical software package to obtain objective and reproducible results. The obtained results may be used to support the interpretation of CTA data, or they are used in the evaluation of follow-up studies and the effectiveness of treatment.

In clinical practice the QAngio CT software is used on workstations in review rooms or integrated in a PACS environment..

• Intended use

The QAngio CT software solution has been developed for the objective and reproducible analysis of vessels in CTA images. It enables the quantitative analysis of CT angiograms based on automated segmentation. More specifically, QAngio CT can be used to quantify a number of lesion characteristics.

QAngio CT is intended for use as an auxiliary tool in assessing CTA studies in clinical practice and in clinical trials. The analysis results obtained with QAngio CT are to be interpreted by cardiologists or radiologists.

• Substantial equivalence Information

QAngio CT is substantially equivalent to the Predicate Device of MRA-CMS, K040746, using the same technique for the same intended use; only CT- instead of MR images.

Conclusion

In Medis' opinion, QAngio CT is a safe medical device. During the development, potential hazards were controlled by a risk management plan, including hazard and risk analyses, verification and validation tests. Evaluations by hospitals and literature information support this statement. The software package QAngio CT itself will not have any adverse effects on health. The operator interprets the objective values of the analysis and chooses to accept or reject the results.

In current thinking, the level of concern for the standalone software in image post-processing is 'Minor' and the use of QAngio CT does not change the intended use of CT scanners in practice, nor does the use result in any new potential hazard.

Based on the information supplied in this 510(k), Medis concludes that the subject device is safe, effective and substantially equivalent to the predicate device.

510(k) Number (if known):

Device Name: **QAngio CT**

Indications For Use:

QAngio CT software solution has been developed for the objective and reproducible analysis of vessels in CTA images. It enables the quantitative analysis of CT angiograms based on automated segmentation. More specifically, QAngio CT can be used to quantify a number of lesion characteristics.

QAngio CT is intended for use as an auxiliary tool in assessing CTA studies in clinical practice and in clinical trials. The analysis results obtained with QAngio CT are to be interpreted by cardiologists and radiologists.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

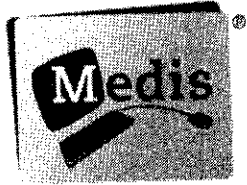
Concurrence of CDHR, Office of Device Evaluation (ODE)

(Optional Format 3-10-98)

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Appendix A

User Manual



QAngio[®] CT 1.0

Quick Start Manual

Legal Notices

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Trademark Acknowledgments

QAngio is a registered trademark of Medis medical imaging systems bv in the Benelux. All other brand, product, and company names mentioned herein are trademarks or registered trademarks of their respective owners.

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Conventions Used

The following conventions are used throughout this manual to indicate mouse and keyboard actions and to refer to elements in the user interface.

Mouse

Click	Press and release the primary mouse button. If you are left-handed, you may have set the right mouse button as your primary mouse button.
Right-click	Press and release the secondary mouse button. If you are left-handed, you may have set the left mouse button as your secondary mouse button.
Middle-click	Press and release the wheel button or the middle mouse button. If you have a two-button mouse, press and release the left and the right mouse button simultaneously.
Double-click	Press and release the primary mouse button twice.

Keyboard

CTRL+click	Press and hold down the CTRL key on your keyboard while you click a button or object.
CTRL+X	Press and hold down the CTRL key on your keyboard while you press X, then release both keys. This example closes QAngio CT.

Typographical Conventions

On the tab Report , select Generate .	Names of buttons, fields, menus, menu options and tab names are capitalized and in bold.
File > Open	A sequence of menu options that you select to perform a specific task, is indicated by angular brackets.
QAngioCT.xml	Text that you type or that appears on the screen, such as file names and file locations, is displayed in Courier New.

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Introduction

1 About QAngio CT

Welcome to QAngio CT, the software solution that is geared toward the quantitative analysis of vascular CT studies.

QAngio CT enables you to

- review CTA studies
- automatically detect vessel contours
- accurately quantify vessel parameters such as, length of stenosis, percentual degree of diameter and area stenosis, area and diameter values of cross-sectional contours
- create 2D and 3D representations of analysis results
- easily exchange results and reports

1.1 Intended Use

The QAngio CT software solution has been developed for the objective and reproducible analysis of vessels in CTA images. It enables the quantitative analysis of CT angiograms based on automated segmentation. More specifically, QAngio CT can be used to quantify a number of lesion characteristics.

QAngio CT is intended for use as an auxiliary tool in assessing CTA studies in clinical practice and in clinical trials. The analysis results obtained with QAngio CT are to be interpreted by cardiologists or radiologists.

WARNING

The automated stenosis detection in QAngio CT is **not validated** for the analysis of **coronary** angiographic CT studies.

Getting Started

2 Quick Tour

In this quick tour, you will become familiar with QAngio CT's key features and basic workflow. In the following sections, you will open a study in QAngio CT, review data, detect stenoses, view analysis results, and create reports.

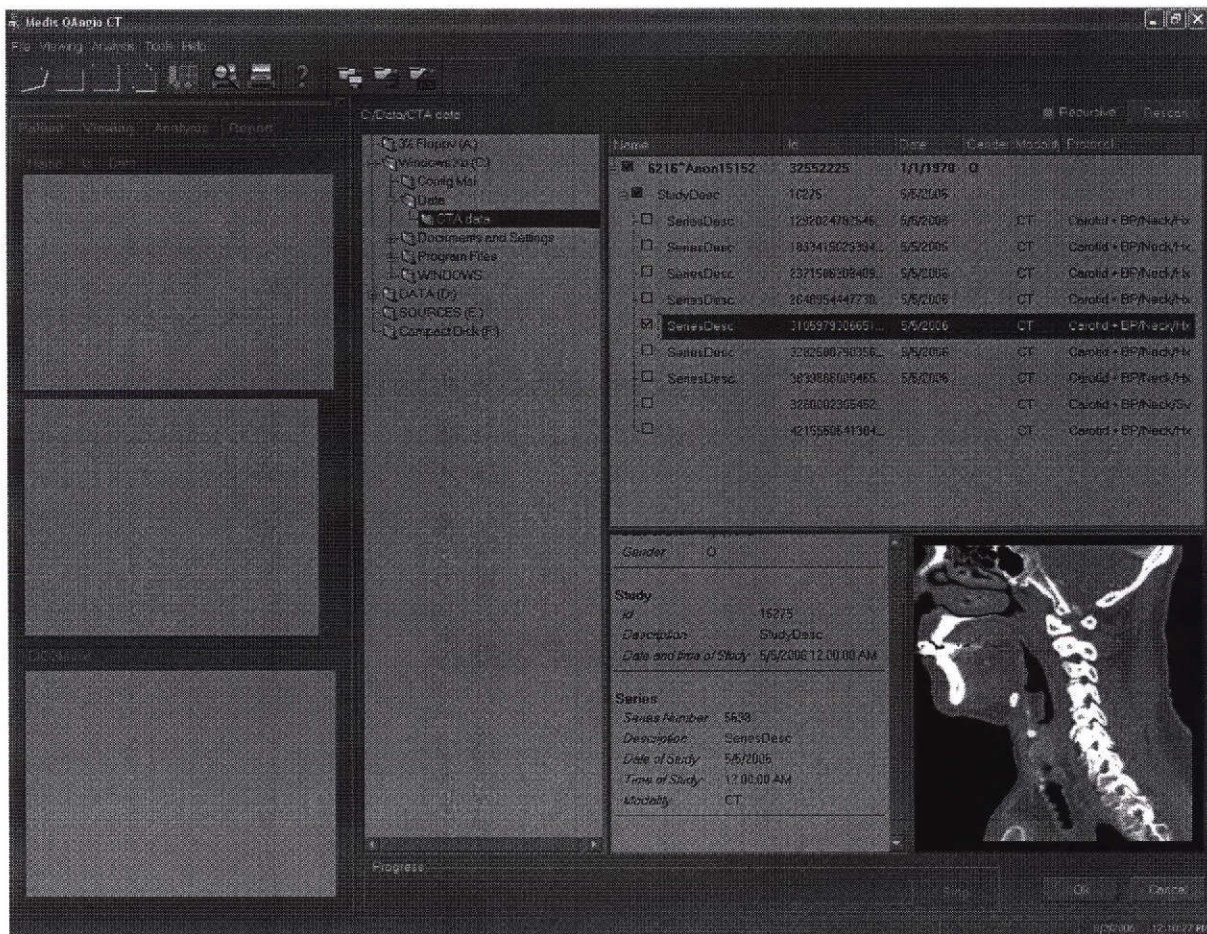
2.1 Selecting a Study

To start this quick tour, select one of the studies on your PC or network.

To select a study

1. Start the application by selecting **Start > Programs > Medis QAngio CT 1.0 > QAngio CT 1.0.**
2. Select **File > Open...** in the menu bar.

This shows the QAngio CT study browser window, which looks similar to the following.



3. Browse the directory structure and select a study.
4. Click OK.

This loads the study.

2.2 Reviewing Data

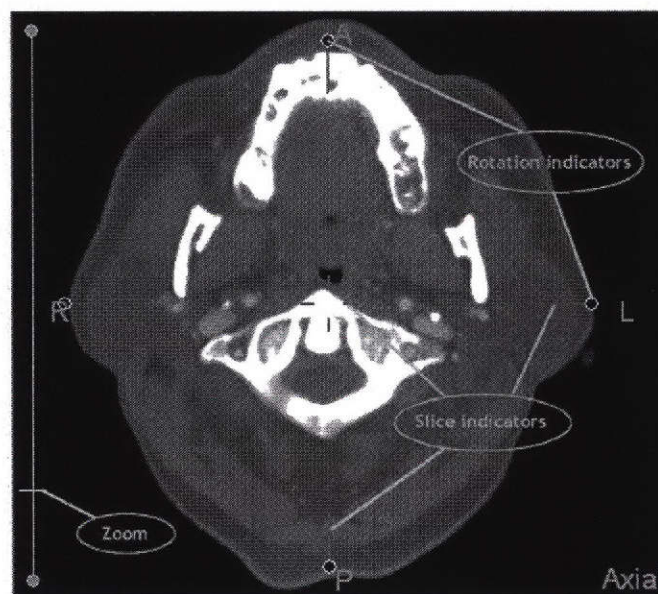
QAngio CT allows you to review the data in MPR views or using 3D volume rendering.

To load data into the viewer

1. Select the **Patient** tab in the workspace.
2. Select the study you want to analyze.
3. Double-click the thumbnail to load the data in the viewer.

To manipulate the MPRs

- Drag the slice indicators to change MPR slice positions
- Drag the rotation indicators to rotate the MPR
- Click in the image and drag the mouse up and down to scroll through the slices
- Zoom by dragging the zoom slider
- Pan by holding down the CTRL-key and dragging the image
- Change the window/level (W/L) using the middle mouse button




To manipulate the 3D volume rendering

- Rotate by using the left mouse button
- Pan by using the middle mouse button
- Zoom by using the right mouse button

2.3 Detecting Stenoses

The stenosis detection wizard guides you through the analysis.

To start the stenosis wizard

1. Select the **Analysis** tab in the workspace.
2. Click .

This opens the stenosis detection wizard, see figure on the right.

You can navigate through the wizard steps by clicking the **Back** and **Next** buttons, or selecting the corresponding button in the wizard time-line.

3. Click **Next** to go to the pathline detection step.

To detect the pathline

1. Click in one of the MPR images to position the proximal point.
2. Click in one of the MPR images to position the distal point.
3. Optionally, add or remove support points.

To add a support point, click **Add support point**, and then click in one of the MPR images to position the support point.

To remove a support point, select the support point, and then click **Delete support point** to remove the support point

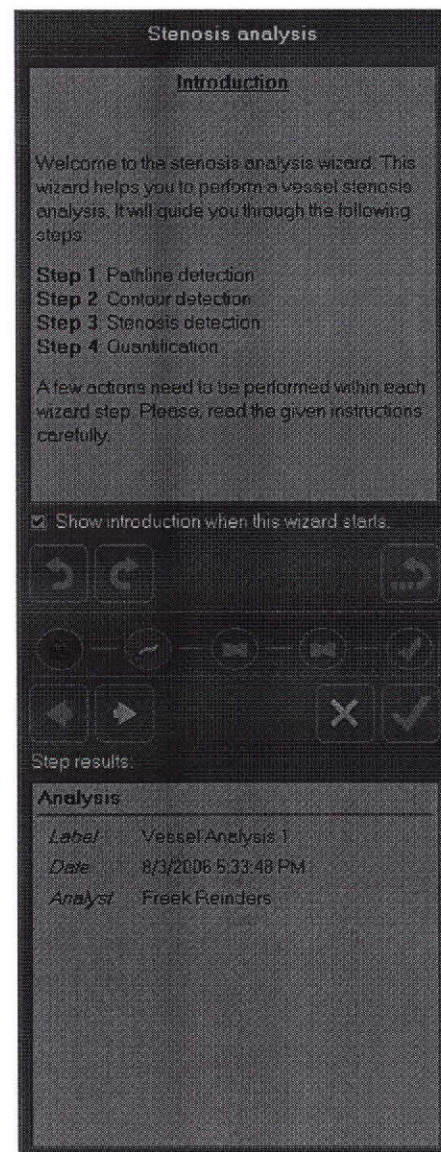
4. Edit the proximal, distal, and support points by dragging the corresponding markers.

N.B. Make sure the markers are located in or near the center of the vessel in **all three** MPR images.

TIP: Click the  buttons to simplify the editing of the markers.

5. Select the appropriate vessel type you want to analyze.

TIP: You can change the default vessel type in the options: **Tools > Options > Analysis**.



Getting Started

6. Click **Calculate** to detect the vessel pathline.
7. Review the calculated pathline.
When the pathline is not correct, repeat steps 3, 4 and 6.
8. Click **Next** to go to the contour detection step, or click **Finish** to automatically run through the subsequent wizard steps.

To detect the contours

The wizard automatically calculates longitudinal contours in four slices.


1. Edit the longitudinal contours.
TIP: Contour editing is W/L independent when you display the gradient images. Click **Gradient** or **Normal** to toggle between normal and gradient images.
2. Click **Calculate** to calculate the transversal contours.
3. Edit the transversal contours.
4. Click **Next** to go to the stenosis detection step.

To detect the stenosis

The wizard automatically calculates a reference vessel and the stenosis location.

1. Edit the stenosis markers in the stenosis diagram or in the longitudinal image.
2. Optionally, click **Flagging** to mark unrepresentative vessel segments for exclusion.
Use the left mouse in the stenosis diagram or in the longitudinal image.
Click **Flagging** again in order to edit the markers.
3. Click **Next** to go to the results step.

To review the results

1. The stenosis characteristics are displayed at the bottom of the wizard.
2. Edit the label of the stenosis.
3. Click  to analyze another stenosis in the same vessel segment.

The wizard will jump to the stenosis detection step, where you can repeat the actions described in 'To detect the stenosis'.

2.4 Viewing Analysis Results

QAngio CT allows you to review the previously performed procedures.

To review the analysis results

More Information

3 More Information and Support

This quick start manual provides all the information you need to perform a basic analysis in QAngio CT. You can find more detailed information and instructions for use in the documentation available on the CD-ROM. For support questions you can contact the Medis support team.

3.1 Additional Documentation

The QAngio CT CD-ROM features the QAngio CT installation manual, release notes, and the QAngio CT user manual. The QAngio CT user manual describes how you can work with QAngio CT in more detail.

3.2 Support

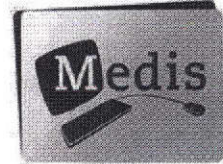
If you have any questions about QAngio CT or if you would like to make suggestions for improvements in the software or in the documentation, please send an e-mail to the Medis support team: support@medis.nl. Please mention "QAngio CT" and the version number in the subject field of your e-mail. To see what version of QAngio CT you have, select **Help > About** in the menu bar or press CTRL+A.

You can also contact the Medis support team by telephone:

North America and Mexico: +1 703 737 37 95, on working days 9.00-17.00 EST
Other countries: +31 71 522 32 44, on working days 8.30-17.30 CET

Appendix B

Product Data Sheet



QAngio[®] CT*

Fast Quantitative Analysis of Vessels in CTA Studies

CTA studies provide more information than the human eye can see at a glance. Cardiologists and radiologists have to find ways to get the information they need from the wealth of data that CTA studies provide.

QAngio[®] CT is a no-frills, intuitive software solution for the analysis of vessel abnormalities. It provides insight into vessel morphology and enables the fast and accurate quantitative analysis of cardiac and peripheral CTA studies.

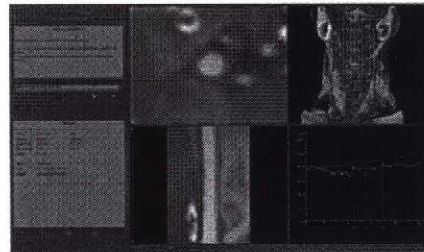
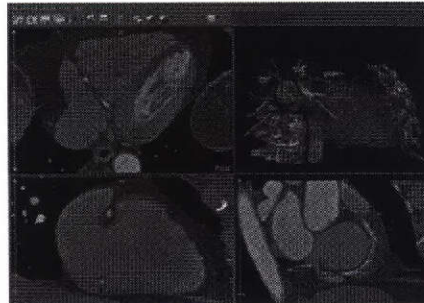
For this new CT solution, Medis has built on more than fifteen years of experience gained with automated segmentation in the cardiac quantitative analysis software solutions Qlvus[®] and QAngio[®] XA (QCA).

QAngio[®] CT Benefits

- Provides accurate and reproducible results
- Increases workflow efficiency and study analysis throughput
- Offers flexibility through vendor-independency

QAngio[®] CT Features

- Analysis of stenoses in CTA studies
- Available as integrated or as stand-alone solution
- Slice, MPR and CMPR views
- Manual or automatic determination of stenosis and reference segments
- Export of analysis results in PDF, DICOM SR or DICOM SC
- Floating license mechanism enabling efficient use of licenses by multiple users



* Work in progress

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QAngio is a registered trademark of Medis medical imaging systems in the Benelux.

QAngio[®] CT is based on advanced image processing algorithms developed at the Division of Image Processing, Department of Radiology, Leiden University Medical Center.

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Appendix C
Software Development Process Document.

Medis medical imaging systems bv

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Software Development Process Document

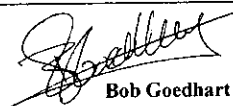
Doc. Version: v6c0 FINAL

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August 25, 2005

Owner: Dave Bierhuizen

Approval

Role	Name	Signature
VP Corporate R&D	Bob Goedhart	 Bob Goedhart

I am approving this document
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Distribution

1. R&D
2. M&S
3. I&S
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Leiden, The Netherlands

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Document Description

This chapter describes the document history an overview of the remaining open issues.

Version History

The following table presents an overview of the document version history.

Version	Date	Author	Remarks
v5c0	20040917	Dbie	Final. Approved by Bgoe (based on review).
v5c1	20050523	Dbie	PTQMS 129: Updated for Maintenance Release. Feedback Kras incorporated.
v5c2	20050531	Dbie	Review Bgoe (Removed Glossary, and refer to general Glossary only)
v5c3	20050803	Dbie	PTQMS 189: Uniform headers and footers.
v6c0	20050825	Dbie	Rework from inspection 168. Final and approved.

Summary of Changes

Since version v3c0, changes have been applied mainly to the integration part (section 4.5) and system test part (section 4.6). Open Issues

- Traceability from System Architecture Document to Module Requirements Document is not yet realized.
- Traceability from Module Requirements Document to Unit Test Report is not yet realized.
- The convention for unique identification should be moved to the General Naming Conventions.

Co-Authors

The following persons have contributed to this document:

- K. Rassels
- B. Goedhart
- H. Hollander
- N. van Wigger

Controlling Documents

- R&D Process Guide.

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Dependent Documents

- SDPD document templates.
- Software Development Plans of projects.

Typographical Conventions

The following typographical conventions are used in this document:

- To emphasize words or phrases, *italics* font is used.
- An important note is expressed using the following format:

Important note

Glossary

For a complete R&D glossary, refer to the Medis Glossary for Software Development [27].

1. Introduction

1.1. Purpose

The purpose of this document is to provide a methodology for Medis software development, which:

- Complies with regulatory requirements.
- Ensures reproducible development of Medis products.
- Enables effective cooperation between software developers and other key roles.

It identifies the various phases in the software development process, the different roles in the process and the necessary documentation that will be generated.

The methodology structures the different phases of analysis, design, implementation, integration, testing, validation, qualification and release of the software. This process (development life cycle) is derived from standard methodologies found in literature and can be considered an integral part of the Medis quality management system (QMS).

Refer to the R&D Process Guide [28] to understand the position of this document and the relation of the software development process with the other R&D processes.

1.2. Overview of the Document

Chapter 2 provides a global overview of the development process and produced documentation for a new (product) release. Chapter 3 provides an overview of procedures and conventions that are applied frequently in this software development process. Chapter 4 describes the software development process for a new (product) release in detail. Chapter 5 describes the user documentation. Chapter 6 describes the process for a maintenance release. Chapter 7 gives the document references.

1.3. Who Should Read What?

This software development process distinguishes a number of key roles, each of which should understand different aspects of the process. The R&D Process Guide [28] provides a list of key roles for R&D. The overview below provides the suggested reading for these key roles. Note that in practice one person may fulfill more than one key role.

The overview below provides the key roles in this process and suggested reading:

Key role	Suggested reading
Software engineer:	<ul style="list-style-type: none"> • Chapter 2 for a general overview of the development process. • Chapter 3 for a description of general procedures for creating, reviewing and managing the SRD and software development documents. • Section 4.2 for a description of the system requirements analysis steps. • Section 4.3.2 for a description of user interface prototyping. • Section 4.4 for a description of module development and testing.

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Medis medical imaging systems by**Confidential and Controlled Document**

Key role	Suggested reading
Software test engineer:	<ul style="list-style-type: none"> • Chapter 2 for a general overview of the development process. • Section 3.6 for a description of requirements traceability to test descriptions. • Section 4.4 for a description of module testing. • Section 4.6 for a description of system testing.
Software architect:	<ul style="list-style-type: none"> • Chapter 2 for a general overview of the development process. • Sections 3.1 to 3.5 for a description of general procedures for creating, reviewing and managing software development documents. • Section 4.1 for a description of recommended software development practices • Sections 4.3, 4.4, and 4.5 for descriptions of system design, module implementation, and system integration.
Technical writer:	<ul style="list-style-type: none"> • Chapter 2 for a general overview of the development process. • Chapter 5 for a description of creating user documentation.
Validation specialist:	<ul style="list-style-type: none"> • Chapter 2 for a general overview of the development process. • Section 4.6 for a description of scientific validation. • Section 4.7 for a description of the Scientific Validation Statement
Project manager:	<ul style="list-style-type: none"> • Complete document
Software test manager:	<ul style="list-style-type: none"> • Chapter 2 for a general overview of the development process. • Section 3.6 for a description of requirements traceability to test descriptions. • Section 4.4 for a description of module testing. • Section 4.6 for a description of system testing. • Section 4.7 for a description of system qualification.
Marketing and sales representative and product manager:	<ul style="list-style-type: none"> • Chapter 2 for a general overview of the development process. • Section 4.2 for a description of requirements analysis. • Section 4.3.2 for a description of user interface prototyping.
Installation and support engineer:	<ul style="list-style-type: none"> • Chapter 2 for a general overview of the development process. • Section 4.2 for a description of requirements analysis. • Section 4.3.2 for a description of user interface prototyping.
Quality coordinator:	<ul style="list-style-type: none"> • Chapter 2 for a general overview of the development process. • Chapter 3 for a description of general procedures and conventions for software development. • Section 4.6.4 for a description of the regulatory compliance process. • Section 4.7 for a description of system qualification.

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2. Process Description

This chapter provides the description of the software development process defined for Medis. This process is described by:

1. The process *phases and steps*
2. The output *SDPD documentation*, i.e. formal documentation that must be written for every product

In general, developing software applications demands the creation of the system requirements, the design, the implementation, and the application of test and validation methods. Medis applies this philosophy to object-oriented software development.

This process uses general definitions for software development and testing [27] .

2.1. Process Overview

Figure 2-1 provides the development process. The seven main phases are: *System Requirements Analysis*, *System Design*, *Module Development*, *System Integration*, *System Testing and Validation*, *System Qualification*, and *System Release*.

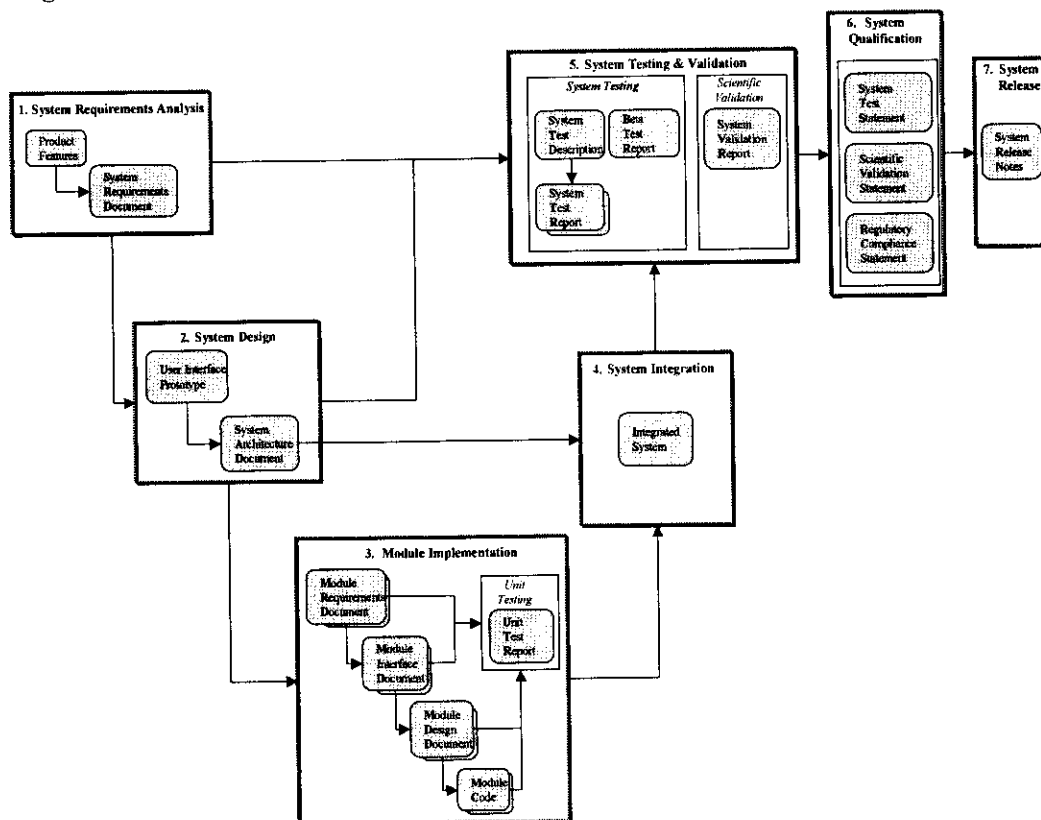


Figure 2-1: Overview of the software development process and the output work products.

Each shaded box is a type of work product of a phase in the development process:

- The documentation set consisting of descriptions and reports, and which is split into two levels:
 1. The documents at *system level* (SRD, SAD, STD, STR, BTR, SVR, STS, SVS, RCS, SRN), which are unique for each system.
 2. The documents at *module level* (MRD, MID, MDD, UTR) are specified for each module used by the system. There are as many document sets, as there are modules in a system. This number differs from one system to another. Note that modules can be shared by different systems. This demands a generic approach to design and implementation.
- Code of modules and (integrated) system.
- Product Features, held in a list or in a database (refer to [28]).

2.2. Software Test Process Overview

This section shows the overview and principle of software testing applied in Medis.

The overview of Figure 2-1 shows the integrated process of software development and testing. To understand how testing relates to development, Figure 2-2 provides another view, which has been adopted from [15]. It shows how the different levels of testing are applied to the development phases. Vertically, it is divided into 2 parts:

- *Left side* – the initiation of the test phase or writing of the tests.
- *Right side* – the execution of the tests.

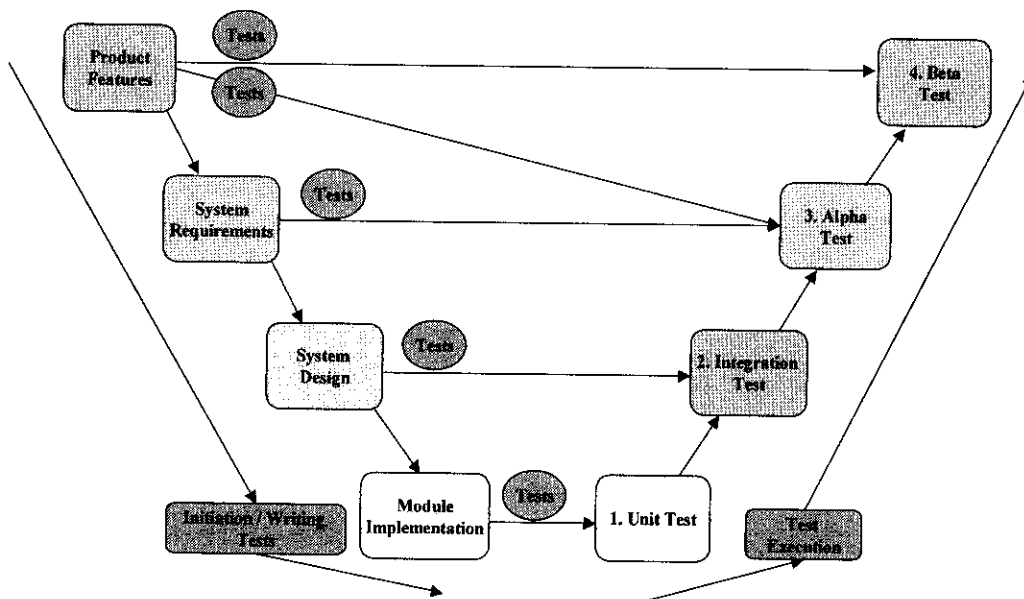


Figure 2-2: Test process relation to development phases.

From bottom to top, it has 4 levels:

1. *Unit Testing* of modules. Refer to section 4.4.5.2 for detailed descriptions.
2. *Integration Testing* involves testing the integrated system, i.e. the combinations of modules and their interfaces.

Medis medical imaging systems by

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3. *Alpha Testing* involves testing of the entire system functionality by Medis staff. Tests are defined and executed to demonstrate that all system requirements have been implemented correctly. From these results, it is demonstrated that all product features have been implemented. Refer to section 4.6.2 for detailed descriptions.
4. *Beta Testing* involves testing the entire system by end users to ensure that it is ready for delivery and use. Refer to section 4.6.2 for detailed descriptions.

General remarks:

- The effectiveness of the various levels of testing is monitored by collecting information about the types of defects found, and of the phases in which the defects originated.
- In each test phase, the software developers should run regression tests to ensure that software changes do not adversely affect the software and cause undesirable side effects.

3. General Procedures and Conventions

Many activities related to the software development process are covered by a number of general procedures and conventions used at Medis. These can be found in the R&D Process Guide [28] and the Medis Quality Manual [17]. In this chapter, their usage in the software development process is explained. Furthermore, general guidelines and supporting tools for document generation and inspection are presented.

3.1. Documentation

Guidelines, tools and templates to support development document creation are available:

1. The document content must adhere to document specific *Rule Sets*, see [24]. They are required to write and inspect the document. A violation of a rule is a defect.
2. Use an SDPD *template* [18] for the standard document organization, layout and text.
3. If a system is developed as part of a *framework*, refer to the documentation of the latter. Ensure that this documentation exists and is stable. If this cannot be guaranteed, no reference can be made.
4. Use the Medis *Best Practices Library* [26], containing examples of final SDPD documents that currently are of highest quality.

Guidelines for creating documents are described per document type in the next chapter.

3.2. Document Naming Conventions

Refer to the *General Naming Conventions* [25], which describes the naming scheme and storage structure for all R&D development documents.

3.3. Document Inspection

Inspecting documents and code is a powerful defect removal technique, but can be time-consuming. Medis uses a *Document Inspection Procedure* [23], which prescribes a workflow together with roles for document producer (author) and reviewers (inspectors), to systematically remove defects in software documentation and code.

Detailed guidelines for inspecting documents are described per document type in chapter 4.

3.4. Document Control

The R&D Document Control Procedure [19] applies to all SDPD documents. It ensures that:

- Document versions are identifiable.
- Documents are approved before their release.
- The document distribution is controlled.

3.5. Change Control

Change Control refers to the controlled way of changing a product, as well as development- and end-user documentation. Changes can be the result of solving problems or implementing enhancements.

Note that once an SDPD document has been inspected and approved, it will be baselined and brought under change control. This means that from now on every new change on this document must be handled by using the Change Control Procedure [21].

A complete workflow for implementing and tracing changes, together with roles in that workflow is described in the *Change Control Procedure* [21]. In this context the software change control board (SCCB) [22] is the authority to approve the changes.

When changes are made to a document, this can have consequences for other documents in the development cycle. Two different relations for a document under change are distinguished:

- *Controlling documents.* These documents directly influence the contents of the current document. In general, these are documents, generated in the previous step of the development process. A change to such a document may introduce a change in the current document. Thus, the current document *shall* be reviewed in case one of its controlling document changes.
- *Dependent documents.* These are documents, whose contents are directly influenced by the current document. In general, these are documents, generated in the next step of the development process. Thus, all of the dependent documents *shall* be reviewed in case the current document changes.

3.6. Convention for Unique Identification

SDPD documents contain specific *items*, i.e. *critical descriptions*, which must be uniquely identifiable to ensure traceability throughout system development.

3.6.1. Scope of the Convention

The following subparagraphs provide the scope of the identification convention.

3.6.1.1 Requirements for System and Module

- Each system requirement in the SRD must have a unique identifier for a particular system version. The same holds for a module requirement in the MRD, specified for a particular module version. It must be possible for dependent documentation, i.e. design- and test items, to refer non-ambiguously to a requirement. The reasons are:
 - ❖ The requirements coverage by design- and test items must be clear.
 - ❖ In case of a requirements change, the impact on the design- and test items must be traceable.
- It must be easy to insert, change or remove a requirement from the document with minimal impact on the existing set of requirements and on the dependent documentation.

- A change in SRD or MRD organization, e.g. insertion of a new chapter, must not influence the requirements identifiers.

3.6.1.2 Test Cases

- Test cases must be unique, and they must non-ambiguously refer to requirements.
- The convention for identification should allow multiple tests to relate to a single requirement, and vice-versa.

3.6.2. Description of the Convention

The following subparagraphs provide the description of the identification convention.

3.6.2.1 Requirements and Design Items

The format of requirements and design items is:

[<SystemModuleName>_<TypeRd>_<n>]

<SystemModuleName> is an abbreviated name of the system or module, consisting of one or more syllables, each of which has its first character capitalized. Examples are: MriMass, Qca, and ReadWrite.

<TypeRd> is the type of the requirements or design item with possible values:

- SR corresponds to a System Requirement
- MR corresponds to a Module Requirement
- OI corresponds to Other Items, i.e. those that do not fall in any of the above categories. For example, the SAD might contain constructions for which specific tests will need to be defined.

<n> gives the unique integer number of the item.

Examples: [Qca_SR_100]
 [ReadWrite_MR_25]
 [Mra_OI_39]

Rule 1: If a new set of items is created, the first item number will be 1 and must increase with 1 for each subsequent item.

An example of this rule applied to two requirements in an SRD, is given below.

[MriMass_SR_1] It shall be possible to calculate cardiac volume based on a single long-axis slice, using the monoplane area-length method.

[MriMass_SR_2] It shall be possible to determine the end diastolic phase and the end systolic phase automatically from the volume curve.

Rule 2: If a new item must be inserted into a set, the latter may not be renumbered. Instead, the number of the new item must be equal to the set's highest number + 1.

An example of this rule is given below. Here an extra requirement has been inserted between a set of two requirements.

[MriMass_SR_1] It shall be possible to calculate cardiac volume based on a single long-axis slice, using the monoplane area-length method.

[MriMass_SR_3] It shall be possible to calculate cardiac volume based on orthogonal long-axis slices, using the biplane area-length method.

[MriMass_SR_2] It shall be possible to determine the end diastolic phase and the end systolic phase automatically from the volume curve.

Rule 3: If an item becomes obsolete, it may not be deleted. Instead, its font must be changed to strikethrough. This is to avoid any confusion on the set's highest number.

An example of an obsolete item is:

~~[MriMass_SR_3] It shall be possible to calculate cardiac volume based on orthogonal long-axis slices, using the biplane area-length method.~~

Rule 4: If an item becomes obsolete, the remaining items may not be renumbered, and they must keep the same numbers.

3.6.2.2 Test Cases

The convention for the format of test cases is:

[<SystemModuleName>_<TypeT>_<n>]

<TypeT> is the type of test item with possible values:

- MT corresponds to a Manual Test item
- AT corresponds to an Automated Test item
- DT corresponds to a Duration Test item
- OT corresponds to Other Test items, i.e. those that do not fall in any of the above categories.

Examples: [Qca_MT_12]
[ReadWrite_AT_15]
[CtMass_DT_390]

Rules 1 to 4 for requirements and design numbering apply to the test item numbering as well.

3.6.3. SDPD Document Traceability

Figure 3-1 gives an overview of traceability between SDPD documents. A document at the start of an arrow contains or refers to a table that links its contents to the contents of the document at the end of the arrow. As an example, the UTR contains a cross-reference table of its test descriptions to the requirements items in the MRD.

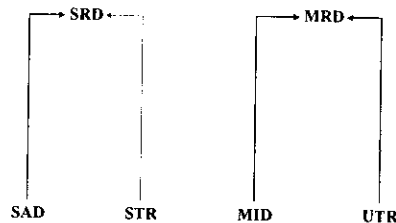


Figure 3-1: SDPD document traceability.

In the following SDPD documents, specific tables are defined to ensure traceability:

1. *System Architecture Document*

A requirements traceability table to provide for each requirement in the System Requirements Document, the architecture mechanism, data model element, module, or a combination, that fulfills this requirement. Details are given in section 4.3.2.

2. *Module Interface Document*

A requirements traceability table to provide for each requirement in the Module Requirements Document, the interface design that fulfills this requirement. Details are given in section 4.4.3.

3. *Unit Test Report*

For each test item in the Unit Test Report, those module requirements, covered by the test item, are listed. Details are given in section 4.4.5.2.

4. *System Test Report*

For each test item in the System Test Report, those system requirements, covered by the test item, are listed. Details are given in section 4.6.

4. Software Development Process

This chapter describes the software development process. It starts with a number of good practices in software development, which are proven and therefore highly recommended in Medis.

Subsequently, for each phase in Figure 2-1, process descriptions together with the output SDPD documents are given.

4.1. Recommended Practices in Software Development

This section recommends a number of proven practices in software development, which have been adopted from Kruchten [11]. The value of these practices should be recognized and considered during organizing and planning the development work in a Medis project.

4.1.1. Constructing Prototypes

Constructing a system prototype aims to explore the feasibility or usability, or to request user feedback, and thus reduces risks during development. Different types of prototypes can be distinguished:

- *Rapid prototype*, which helps understanding and formulating system requirements.
- *User interface prototype*, which supports the design of the user interface and allows for early user feedback.
- *Experimental prototype*, which demonstrates the technical feasibility of a design.

Prototypes are especially useful in the requirements analysis and the design phases.

Note that a prototype is 'throwaway' code, which means it can only be used to communicate and demonstrate ideas. It may not be used to develop the product.

4.1.2. Iterative, Incremental, and Timebox Development

The Medis software development process is a variation on the *waterfall model*. This means that the entire process goes through the development phases *linearly*: first *all* requirements are defined, then designs are made, and then code is written and tested. The underlying assumption is that requirements no longer change when the design phase begins.

A problem with implementing the *waterfall model* in a straightforward manner is that development risks are pushed to later development phases, where it is costly to undo mistakes made in earlier phases.

Modern approaches have enriched the waterfall model so that it can adapt to specific circumstances during the project lifetime. They acknowledge that it should be possible to:

- Revisit earlier development phases in the project, e.g., requirements analysis, based on new insights in later phases.
- Build in small steps.

- Redefine priorities if necessary, e.g. because of unexpected events.

The challenge here is to have an adaptive development project, which is still controlled so that it meets the constraints of functionality, quality, and time. From literature (refer to [13]) it is known that such adaptive methods can make large projects more manageable and can prevent project risks to become costly mistakes.

Therefore, R&D project managers should consider enhancing the waterfall model for their project by adding one- or a combination- of the following three variations: iterative development, incremental development, or timebox development. The differences and their benefits are given below.

Iterative Development

Iterative development is a controlled reworking of the system in order to make improvements. Iterations can be made in each phase of the development process. In general, an iteration provides feedback to earlier steps in the development process. For instance, during module design, a defect could be detected in the architecture design. The latter is then first reworked such that module design can be done. The benefit of iterative development is that project risks are dealt with in early iterations, thereby avoiding the high impact of defects that manifest later in the project. The principle of iterative development is shown in Figure 4-1. The gray arrows represent the standard waterfall model. The white arrows have been added to represent feedback flow. However, only direct feedback is given here. In reality, more feedback relations exist, including those within the boxes.

It is recommended to focus on requirements analysis in the first iteration(s) and to gradually shift the focus to subsequent steps (system design, module implementation, etc.) in later iterations.

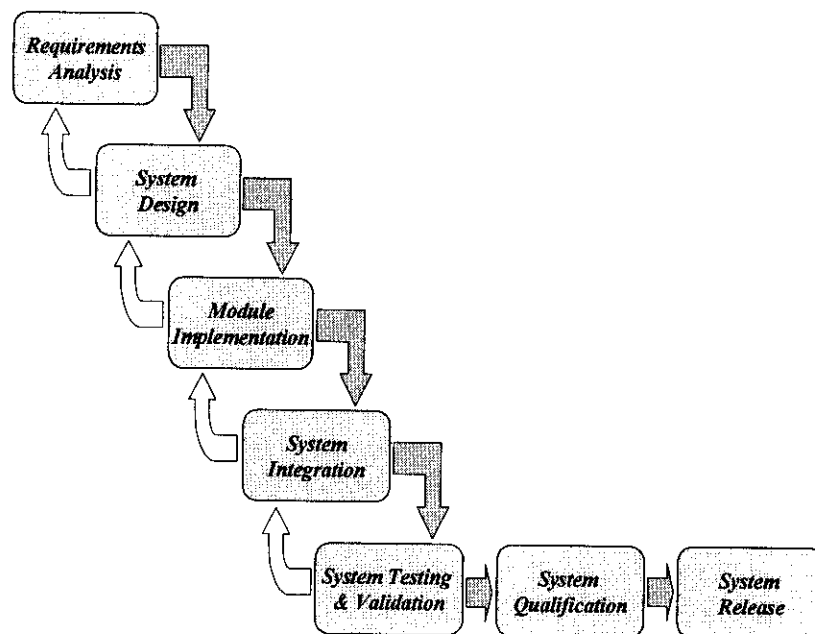


Figure 4-1: The principle of iterative development.

Incremental Development

Incremental development aims to make progress in small steps to get early results. Each increment consists of a working (sub)system, supporting a subset of the (sub)system functionality. The selected requirements are those that have high user priority. The principle of incremental development is shown in Figure 4-2. Each increment is a working system with partial functionality, and is built according to the standard waterfall approach.

It is recommended to perform planning and requirements analysis only once, and to repeat the subsequent steps (system design, module implementation, etc.) to create the increments.

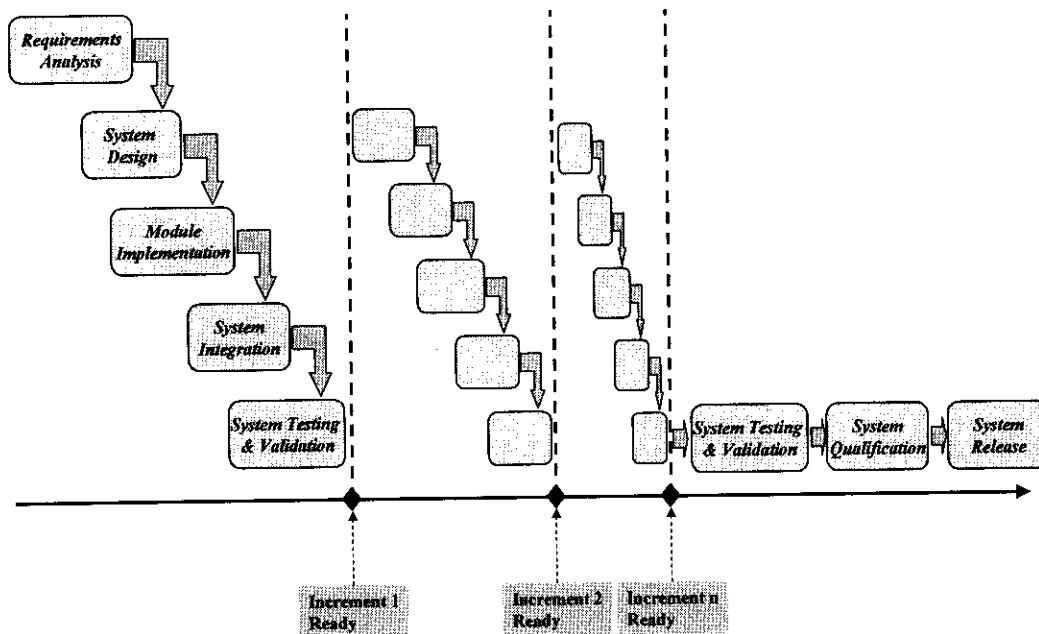


Figure 4-2: The principle of incremental development.

Timebox Development

Timebox development aims to develop the system when the time schedule is the primary constraint. With timebox development, the project manager specifies the maximum amount of time, typically four to six weeks that it will take to release the next baseline of the system. Developers implement and test the most important requirements first, and the less important requirements as time permits. There are no deadline extensions. Timebox development keeps the project's focus on the most important requirements, prevents the project from being almost complete for a long time, and maintains an ongoing urgency in the development team. Therefore, timebox development can reduce the development schedule as it is demonstrated in literature [13].

However, timebox development is suitable for projects where requirements can be prioritized and implemented relatively independently, and where the customer is willing to drop functionality instead of quality.

The principle of timebox development is shown in Figure 4-3. At the end of each timebox, the work products are evaluated for completeness. Incomplete work products are rescheduled and reprioritized for the next timebox.

It is recommended to perform planning and requirements analysis only once, and to perform the subsequent steps (system design, module implementation, etc.) using timeboxes.

Note that Figure 4-3 shows a single development trajectory only. However in practice, a project could develop several modules that are in a different development phase.

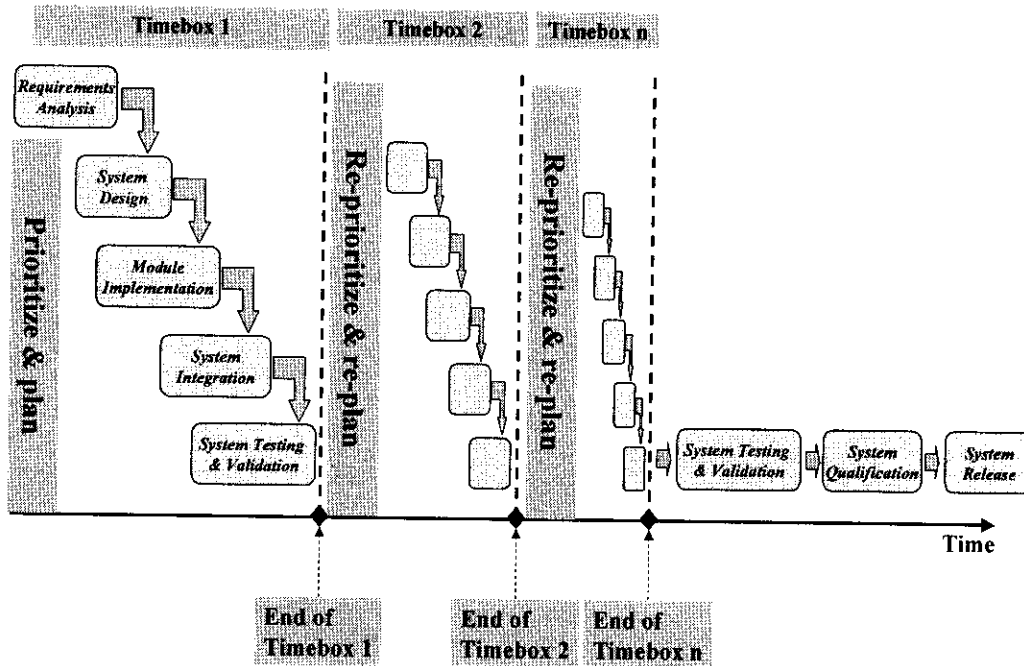


Figure 4-3: The principle of timebox development.

Recommendation

→ Develop iteratively in case there is a considerable development risk with using the waterfall model: due to requirements that cannot be made stable, or due to the complexity or criticality of certain system parts.

→ Develop incrementally in case there is a need or opportunity to deliver early to the market or to get early feedback from the market.

→ Develop using timeboxes in case the schedule is the primary constraint and the customer is willing to drop functionality instead of quality.

4.1.3. Requirements Management

It has shown to be difficult to completely and accurately delineate system requirements before the start of the development. Consequently, requirements may change during development because they become clearer and more understood. This demands the need of requirements management, which is a systematic approach to:

- Defining, organizing, and documenting the requirements of the system.
- Establishing and maintaining the agreement between customer / user and the development team in the presence of changing requirements.
- Evaluating the impact of a change in requirements.

- Preventing scope creep, which is the continuous expansion of the scope of the project. This is usually caused by the loss of the project's original objectives during development.

→ *Manage requirements according to [28].*

4.1.4. Component-Based Architectures

A well-defined architecture has the following features:

- It meets its requirements.
- It is maintainable, and extensible.
- It allows dividing the work among (teams of) developers.
- It encapsulates hardware and software dependencies.

Component-based development supports the above features. A component is a nearly independent, and replaceable part of a system that fulfills a clear function in a well-defined architecture. A *component-based* architecture enables:

- The reuse and customization of existing components.
- The choice of commercially available components.

→ *Develop system modules using components.*

4.1.5. Software Configuration Management

In order to maintain the integrity of the work products during software development and the product release, the software configuration has to be controlled. This should incorporate:

- Planning and execution of the configuration management activities [28].
- The identification of configuration items [28].
- The approval of SDPD documents [20] and the creation of software baselines [28].
- The control of changes to software baselines [21].

→ *Manage the software configuration according to [28].*

4.1.6. Software Quality Verification

Software defects are much more expensive to find and repair later in the development and after deployment. Therefore, verification must be initiated early in the software lifecycle. SDPD document and code inspection, unit testing, and system testing will decrease the risks associated with delivering poor quality software.

→ *SDPD documentation must be inspected (refer to [23]). Software must be tested and validated (chapter 4). It is recommended to review or inspect (parts of-) the module code (MC) after it has been tested.*

4.2. System Requirements Analysis

4.2.1. Process Description

Purpose

- Agree with the customer and users on what the system must do.
- Scope the system. It should be clear what the system, and possibly different versions, should be able to do and what it should not do.
- Provide sufficient understanding to developers of what the system must do.
- Provide input to testers for developing test plans.
- Provide input to technical writers for writing user documentation.
- Provide a basis for defining the system user interface.
- Provide a basis for planning the software development.

Input

- A system vision, based on domain experience and new developments in the field.
- A set of desired system features.
- Possibly, a system prototype (see also paragraph 4.3.2) as input to formulating the system requirements.

Output

- The SRD.

Key involvement

- M&S representative and product manager, to provide new system features and enhancements, and to provide input to-, and feedback on system usability.
- Software engineer, to create the SRD.
- Software engineer, to construct a system prototype.
- Software test engineer, who participates in the inspection of the SRD, to check the testability of the requirements.
- Technical writer, who participates in the inspection of the SRD, to acquire insight in what needs to be documented.
- Project manager, to track progress of the requirements writing and to ensure the timely delivery of the SRD.

Description

Every system development must be based on documented system requirements.

The SRD captures a set of requirements that apply to a version of the product.

Creating a system prototype would be useful in order to:

- Get early user feedback on system requirements.

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- Better understand system requirements.

Process steps

Figure 4-4 gives the system requirements analysis steps, which are based on [10]. The software engineer, M&S representative, and product manager are the key roles in this process.

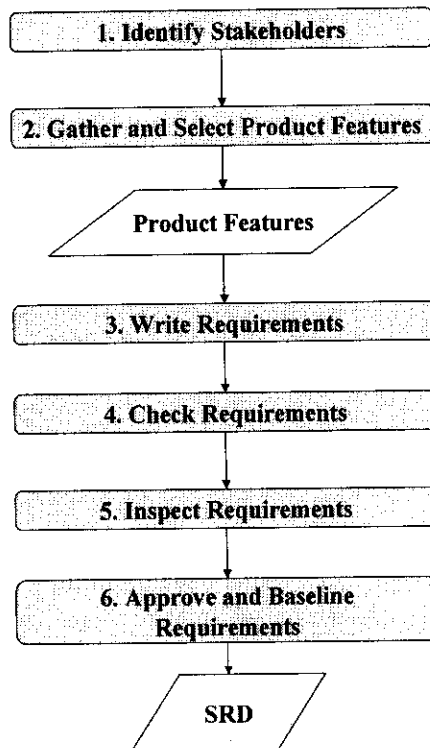


Figure 4-4: System requirements analysis steps.

1. *Identify Stakeholders* - It is essential to identify the different stakeholders in the system requirements. Each stakeholder type may have a specific set of requirements and viewpoints. Possible stakeholders are: end-users, product distributors, M&S representatives, product managers, development partners, Medis staff of other projects, etc.
2. *Gather and Select Product Features* - Collect all the required product features from all possible sources. Possible sources are: interviews, workshops, user observation at work, prototypes, problem reports and change requests, M&S representative, product manager, support team, competing products, existing designs and specifications, etc. Select product features for the version of the system to be developed.
3. *Write Requirements* - Write the SRD.
4. *Check Requirements* - This is an informal review by the different stakeholders to ensure that the requirements are well scoped, and complete.
5. *Inspect Requirements* - This is the formal review done by predefined roles.
6. *Approve and Baseline Requirements* - This ensures that the SRD is accepted and stable enough to serve as a baseline for the system design phase. The SRD is now under change control.

Related processes

- The *design process* uses the system requirements to design the system user interface and the system architecture.
- The *system test and validation process* uses the system requirements to develop high-level test- and validation plans.
- *Project management* (refer to [28]) uses the system requirements to plan and execute the system development.

4.2.2. Documentation

The System Requirements Document (SRD) specifies the requirements and basic functionality of the system as a whole.

The SRD describes what the system should do, not how.

The SRD contains the description of requirements for:

- The *hardware and software* of the system; what does the system consist of?
- The *functional requirements* of the system. They specify the functionality of the software that the developers must build into the product to enable users to accomplish their tasks.
- The *non-functional requirements* of the system. These include performance goals and descriptions of quality attributes. The latter augment the product's functionality by describing the product's characteristics that are important to users and to developers. These characteristics include usability, portability, integrity, efficiency, and robustness. Other non-functional requirements describe external interfaces between the system and the outside world, and design and implementation constraints. Constraints impose restrictions on the choices available to the developer for the design and implementation of the product.

Refer to [14] for more details on functional- and non-functional requirements.

The description of the requirements of the system must be usable as direct input to the System Test Description (STD). Each requirement receives a unique ID, which will correspond to one or more IDs in the STD, specifying how this requirement is tested. The prescriptions for unique requirements identifiers are given in paragraph 3.6.2.1.

Guidelines for Writing

- Create the SRD, based on a standard SDPD template [18].
- A software engineer with requirements engineering skills should write the SRD.
- The document content must adhere to the document specific *Rule Sets*, see [24]. They are mandatory to write and inspect the document. A violation of such rule is a major defect.
- Consult the Medis' *Best Practices Library* [26] for an example SRD.

Guidelines for Inspection

- The inspection moderator must ensure that the inspection team represents the following roles: an M&S representative and / or product manager, a software engineer, a software test engineer, and a technical writer. Preferably, an I&S representative should participate too.

- If the SRD applies to system architecture, the inspection team should exclude: an M&S representative and product manager. However, the team must include the roles of a software engineer, software test engineer, and an I&S representative.
- Use the SRD rule set and checklist [24] to inspect the SRD.

4.3. System Design

4.3.1. Process Description

Purpose

- Transform the requirements into a design of the system user interface and into a high-level system design, such that implementation can begin.
- Decompose the system into modules, such that they can be developed separately and independently.

Input

- The SRD.

Output

- The user interface prototype (UIP).
- The SAD.

Key involvement

- M&S representative and product manager to provide input to- and feedback on the user interface prototype.
- Software engineer, to design user interface layout and behavior.
- Software architect, to establish the overall software architecture.
- Software engineer, in case a system prototype is constructed (refer to section 4.3.2).
- Technical writer, to establish user interface terminology and check if the user interface is according to standard conventions.
- Project manager, to track progress of the system design and to ensure the timely delivery of the UIP and the SAD.

Description

The software engineer is responsible for creating a design of the user interface, based on system requirements, and on guidelines for designing a user-friendly interface.

The focus of the system design is the creation of the architecture. The software architect will assess the framework architecture, if existing, and determine which architecture mechanisms need to be present and added, and what the main system decomposition will be. System decomposition will identify the modules that need to be developed. Preferably, programmatic interfaces of these modules are already identified during the design process.

The construction of a system prototype serves to:

- Provide better understanding of the system usability.

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- Help demonstrating the technical feasibility of architecture design.

Related processes

- The *module implementation process* uses the designs of user interface and architecture to design, implement and integrate the modules of the system.
- The *system test and validation process* uses the design of the user interface to develop detailed test- and validation scripts.

4.3.2. System User Interface Design

4.3.2.1 Process Description

Purpose

- The purpose is to visualize the user interface to users, software engineers, and other persons involved in product development. They can give essential feedback on the user interface, before the development team commits to implementing the system.

Input

- The SRD, including the use cases of the application.

Output

- Baselined user interface prototype (UIP).

Key involvement

- Software engineer. This person has knowledge of user interface styles, and has skills to rapidly develop the prototype using any suitable tool.
- M&S representative and product manager to provide input to- and feedback on the UIP.
- Project manager, to track progress of the design and to ensure the timely delivery of the UIP.

Description

Figure 4-5 gives the steps for designing the user interface.

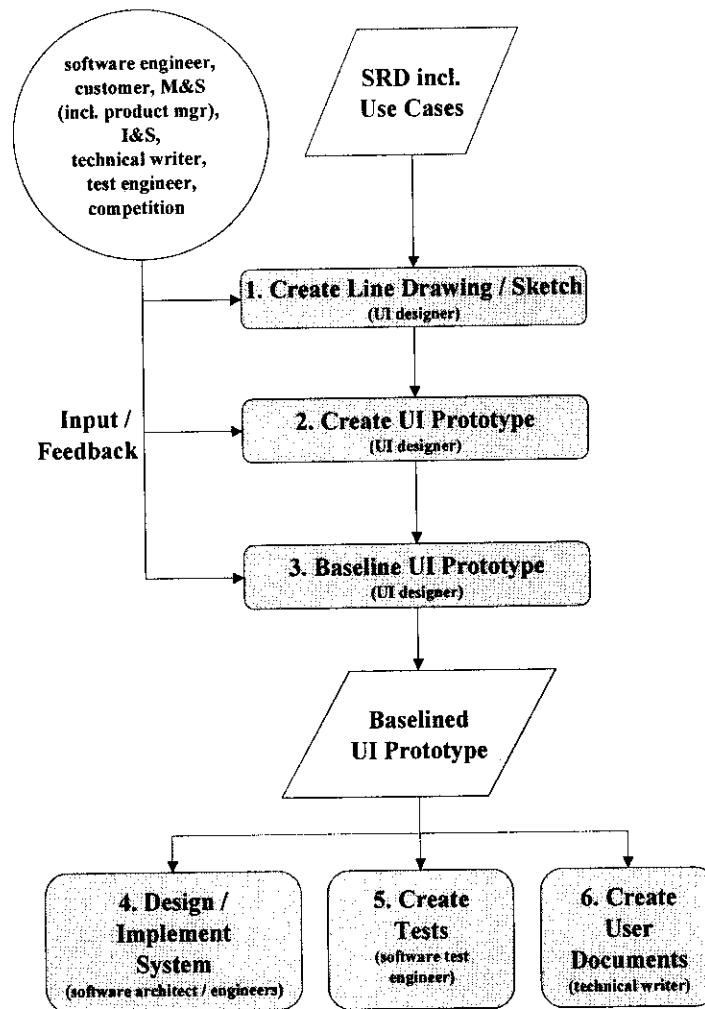


Figure 4-5: User interface design steps.

1. *Create Line Drawing / Sketch* – The use cases in the SRD provide the basis for designing the user interface workflow. The software engineer creates the workflow and initial drawings or sketches of the dialogs. In a number of iterations, preferably using sessions in which customer, users and / or user representatives provide feedback and other input, the drawings are improved. Competing products may provide useful input too. The process will stop once involved persons are excited about the result.
2. *Create User Interface Prototype (UIP)* – In this step, the software engineer builds an interactive prototype of the application. Its purpose is to present the look-and-feel to the user so that the latter can provide valuable feedback. As such, the prototype should be *shallow*, i.e. implemented functionality behind the screens should be limited, and *wide*, which means the prototype should support *all* key functionality. Similar to step 1, the creation of the UIP should be iterative, until all involved persons are excited about the result.
3. *Baseline UIP* – The UIP (code) is approved and baselined, implying that the development team commits to developing the application based on the prototype. Subsequent requests for change must be controlled.

4. *Design / Implement System* – System architecture design and module implementation can commence.
5. *Create Tests* – The software test engineer(s) start(s) developing the system tests based on the baselined UIP.
6. *Create User Documents* – The technical writer starts developing user documentation based on the baselined UIP.

In principle the user interface prototype is 'throwaway' code. This means that the software engineers should ensure that the final code of the application complies with quality standards and, if necessary, reengineer the interface prototype.

4.3.3. System Architecture Design

4.3.3.1 Documentation

In the System Architecture Document (SAD), a high-level description is given of the system as a collection of software modules and their dynamic behavior. Further, the SAD provides the major design decisions. The descriptions should demonstrate that the system's requirements are fulfilled.

The software architect identifies the software modules and their interrelations. In addition, (s) he identifies the responsibilities and interfaces of the modules. Note that interface details are omitted in the SAD. These are detailed in individual module interface documents.

Guidelines for Writing

- Use the SAD template [18].
- Generally, the system is built, based upon an application framework, which provides a set of base modules and mechanisms for communication, error reporting and fault management. Make sure the documentation of that framework is available and fully understood.
- The module graph and major structures must incorporate the relations with the common product framework. This means that used module interfaces of the common product framework must appear in the diagrams of the SAD.
- If application specific mechanisms, not provided by the common application framework, are needed, these mechanisms should be identified and described in this SAD.
- Use UML.

Guidelines for Inspection

- The inspection team should consist of staff familiar with architectural design, and staff concerned with the design of the system modules. It is not meaningful to invite end users, or medical domain experts in the inspection team, since this type of document is relevant to system construction only.

4.4. Module Implementation

4.4.1. Process Description

Purpose

- Designing, programming and testing the modules of the system. Refer to [25] for a definition of a module.

Input

- The SAD.

Output

- MRDs, MIDs, MC and UTR.

Key involvement

- Software engineer, to design, implement, and test modules.
- Software engineer, to integrate modules.
- Software architect involved in taking design decisions.
- Project manager, to track progress of the module implementation and to ensure the timely delivery.

Description

The software engineer is responsible for detailing the module interfaces, and designing, implementing, and testing the modules.

The software architect maintains the overview over module designs, and ensures that the integrity of the architecture is maintained. Further, the software architect participates in taking appropriate design decisions.

Related processes

- The *system integration process*.
- *Project management* tracks progress of the implementation and ensures the timely system delivery.

4.4.2. Module Requirements Analysis

4.4.2.1 Documentation

The Module Requirements Document (MRD) specifies the functionality of a module as a whole and the interfaces with other modules.

Similar to the SRD, the MRD describes what a module should do, not how.

The MRD contains the description of:

- The hardware demands made by the module; what does the module require?
- The functional requirements of the module; what should the module do?

- The non-functional requirements, what are the constraints of the module?

Guidelines for Writing

- Use the MRD template [18].
- Also, have a look at the guidelines for the SRD.

Guidelines for Inspection

- Reuse the Rule Set for inspection of the SRD [24]. However, the intended readership should exclude M&S representative, product manager, and end users.

4.4.3. Module Interface Design

4.4.3.1 Documentation

The Module Interface Document (MID) specifies the programmatic interfaces of a module. The MID can be seen as an agreement between module- and system developer. It is created *before* the design and implementation of the module, based on the MRD and based on the architecture of the system(s) the module will be integrated with. Specifying interfaces in an early phase of developing modules is seen as an important step in system design.

In UML [4], an interface is a model element, which defines a set of behaviors (a set of operations) offered by a class, module, or component.

The external behavior of a module is defined by the set of interfaces it realizes. When a module realizes an interface, it makes a commitment to support each operation defined by the interface. In turn, an operation may be realized by:

- An operation on a class contained by the module; this operation may require collaboration with other classes or modules.
- An operation on an interface realized by another module.

Note that all dependencies of one module on another should be solely on module interfaces¹. Using pure interface dependencies allows flexible frameworks to be designed with the use of replaceable design elements.

The format of the MID is particularly suited for object oriented development. However, for non-object oriented development, the principles still hold and minimal changes to the format are needed.

The description of the functionality of a module will be such that it can be used as direct input to detailing the tests in the Unit Test Report (UTR).

Guidelines for Writing

The following module interface design guidelines should be taken into account:

- Use the MID template [18].
- As an alternative to using the MID template, it is allowed to generate the interface specification from code header files. Doing this has the advantage that the specification

¹ A common principle of reusable object-oriented design: *Program to an interface, not an implementation* [5].

can be synchronized easily with any future change of the code. A convenient tool is Doc-O-Matic, which generates online HTML help from header files. Use the template described in [18] to generate online help.

- The intention must be to stabilize interfaces early in development. This enables software developers to simultaneously work on modules.
- Interface operations must always return result codes.
- Interface modeling could be supported using the following diagrams in UML:
 1. Sequence diagrams.
 2. Collaboration diagrams.

Guidelines for Inspection

Preferably, the MID should be inspected by a software architect, and a software engineer.

The following guidelines for inspecting the MID hold:

- Ensure that each interface serves a clear, and unique purpose. In general, an interface should not become too 'wide', i.e. providing more than one service, and not too 'small', i.e. a service is fragmented over different interfaces. Experience and understanding of the module purpose should help with this judgment.
- Ensure that the interface operations adhere to naming conventions, as prescribed in the coding standards.
- Ensure that terminology in the interface specification is not tied to a single application, or even to an image modality, if the intention is to develop a general-purpose module.

4.4.4. Module Design

4.4.4.1 Documentation

The Module Design Document (MDD) describes how the required functionality, formulated in the MRD, and specified in the MID, will be realized. Medis applies UML to model the design classes. The MDD contains:

- The design of the module in terms of class diagrams and sequence diagrams.
- The algorithms used in the module.
- The state transition diagrams.
- The error handling of the module.
- Communication of the module with other modules, what messages/data this module can receive and how these messages/data should look like.

The MDD could include one or more of the following diagrams in UML:

- Component diagrams.
- Class diagrams.
- Interaction diagrams.
- State chart diagrams.

Guidelines for Writing

- Use the MDD template [18].
- Ensure that a realization is made for each interface offered by the module, described in the MID.
- The level of detail will be low for the first versions of this document. Initially, only major classes with relationships may be distinguished. In subsequent iterations, the MDD could be further detailed to a level at which:
 - All class methods and their parameters are designed
 - Class associations are fully specified
 - Class interactions and state transitions are fully specified
- Make a distinction between module elements that have public visibility, i.e. the interface, and those that are not visible, i.e. the module implementation.
- The use of UML is strongly recommended to model the design.

Guidelines for Inspection

Preferably, a software engineer, having the role of module implementer, should be in the inspection team.

The following guidelines for inspecting the MDD hold:

- Ensure that the design is complete, understandable and correct
- Ensure that the design implements the interface, described by the MID

4.4.5. Module Coding and Unit Testing

4.4.5.1 Module Coding

The source code of the modules (MC) is implemented based on the MID and the MDD. Unless otherwise prescribed, it will be implemented in C++.

Guidelines for Writing

- Use the coding standards [16] to write the code.
- Use plug-ins and other code generation tools, to create code according to the coding standards.

Guidelines for Inspection

- Use the coding standards, and the code review checklist [24] to inspect the code.
- The version history (in the version control system) of the inspected and reworked source code files should be updated with a comment, which includes the Inspection ID.

4.4.5.2 Unit Testing

Purpose

The Unit Test phase is low level testing and one of the most important aspects of software testing. This step will help software engineers to detect software bugs at an early stage of the software development life cycle and to improve the software quality.

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Unit testing provides the test framework at a low level to be used within projects during the software development cycle.

Input

- SAD
- MRD
- MDD
- MID
- Module Code (MC)

Output

- Unit Test Report (UTR)

Note: Each project has to deliver one UTR, providing the unit test results of all modules developed in that project.

Key Involvement

- *Software engineer* - The R&D project members responsible for the development and maintenance of the code and test code of a certain module.
- *Project manager* - Person who plans and manages the software project.

Description

Software engineers create test stubs to test code. After the test run, the software engineer will fix the detected bugs. Consequently, the tests are repeated and bugs are fixed until the code is free of bugs. This may require several iterations.

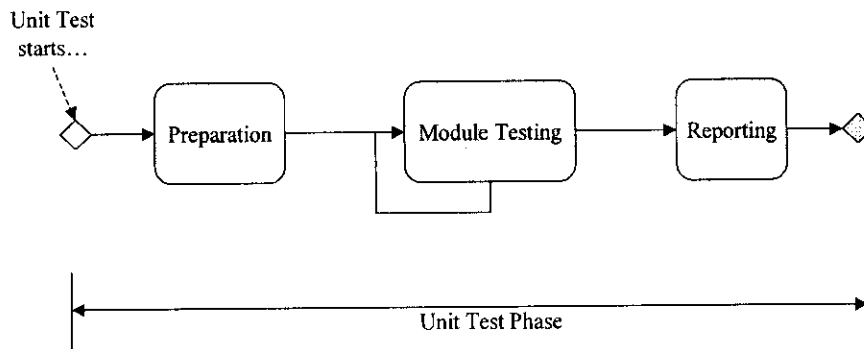


Figure 4-6: Unit Test phase.

This is white box testing and is performed at module level.

The Unit Test phase workflow consists of 3 blocks as shown in the above figure. This section will zoom into each block and describe corresponding activities, roles, responsibilities and deliverables in detail.

1. Preparation

Entry criteria shall be checked.

2. *Module Testing*

The created modules are to be tested using test stubs (as described in [31]).

All modules shall pass the test and meet the acceptance criteria.

In this block, software engineers may iterate their test methods (regression testing) as much as needed.

At the end of each iteration and / or milestone, all modules shall pass the test and meet the acceptance criteria.

Note 1: There is no reporting needed for the intermediate test results during the iterations. However, a complete set of test results must be baselined for each milestone.

Note 2: The software engineer should conduct tests of both: created code and dependencies (interfaces), when a dependency with other project modules exists.

3. *Reporting*

At this point, the project manager will check off the exit criteria.

When the Unit Tests for *all* modules (there can exist one or several modules) are successful, the Unit Test results of the project shall be reported in a *single* document, called a Unit Test Report (UTR).

Since this block is the final step within the Unit Test phase, the project manager shall finalize and approve the UTR.

Remark: Module testing shall be redone when the developed code changes.

Entry Criteria

Entry criteria shall be fulfilled when entering the test Unit Test phase.

1. The SAD has been approved, according to [20].
2. The MRD, MDD and MID have been approved, according to [20].
3. Acceptance criteria have been defined.
4. A properly configured development environment has been set up.
5. Properly configured test environment and defined test tools have been set up.

Exit Criteria

Exit Criteria shall be fulfilled when exiting the test phase.

1. All modules are working as required / designed (MRD shall be covered)
2. Acceptance criteria are fulfilled.
3. UTR is completed and approved based on [20].

Note: One of the entry criteria for the "Source Code Review Check List" (see [6]) is that the components and modules have to be tested.

How to Define Unit Test Acceptance Criteria

The acceptance criteria for the Unit Test phase can be specified in 2 different ways:

1. The minimum criteria shall be based on 100% function coverage on interface implementation level. E.g. all the module's functions should have been called once successfully (response as described in MID) in one-by-one order.
2. Additionally, 100% line coverage is recommended, however this is much more difficult to achieve.

In both cases, the main goal is that all test methods cover the MRD.

4.5. System Integration

System integration is the activity that comprises the assembly of all modules, as well as the creation of system configuration files, and communication with external systems. The key role is: software engineer.

For integration testing, see section 4.6.

4.6. System Testing and Validation

4.6.1. Process Description

Purpose

- Ensure that the system meets the requirements and intended use as described in the SRD.

Input

- The SRD.
- Integrated system.

Output

- The STP, STDs, STRs, BTRs.

Key involvement

- Project manager, to plan and execute the system testing and validation.
- Software test engineer to create the detailed test documents / scripts and to carry out the tests.
- Validation specialist, to ensure that the analysis algorithms produce the correct results.
- Quality coordinator, to ensure that regulatory requirements are met.

Description

The high-level system test plan is based on input from the requirements process.

The detailed test plan is based on user interface design, and integrated system. System tests are executed on a baseline of the software.

Quantitative analyses must produce correct results. The entire system must be scientifically validated before it is commercially released. The validation plan is based on input from the requirements process.

Related processes

- *Requirements analysis process.*
- *System integration process.*

4.6.2. System Testing Overview

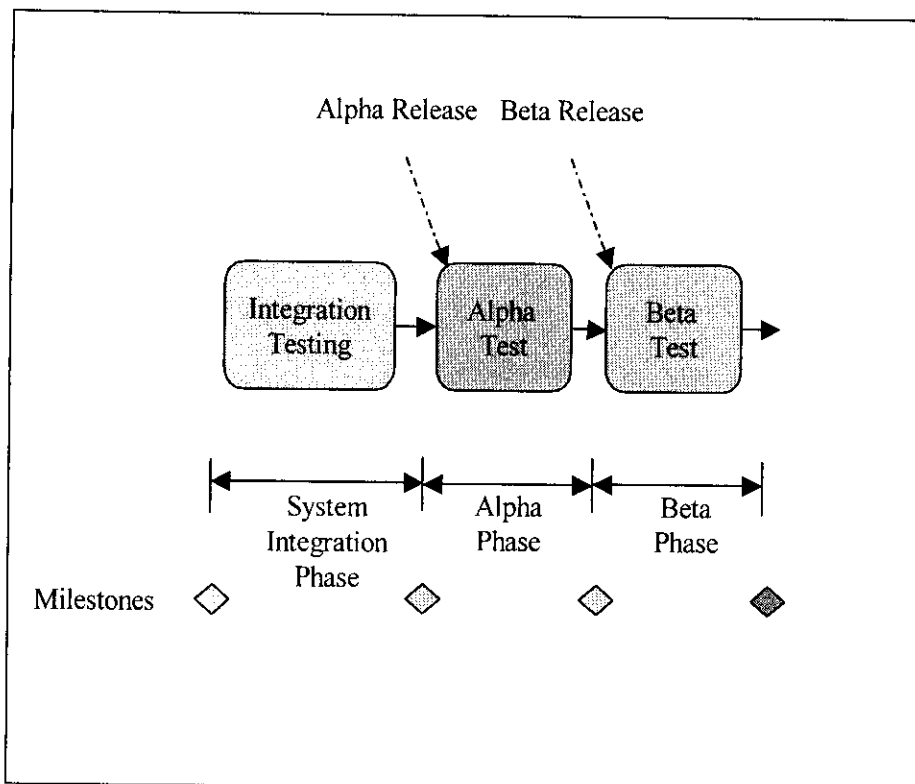


Figure 4-7: Process workflow of the System Test Phase.

Description

The above figure gives an overview of the high-level System Test Phase based on the V-model.

It is allowed and preferred to do Unit Testing (if applicable) at each phase. Reason: these tests have already been implemented and automated during the coding phase and running them is beneficial when the code is changed. The workflow consists of 3 major phases:

1. *Integration Test During the System Integration Phase*

This is the preparation of the prerequisites for Alpha Testing by testing the integrated system.

2. *Alpha Test Phase*

Alpha Testing involves testing of the entire system. Independent testers² accomplish alpha testing. This is an internal (Medis) test phase. In this phase, the developed software code might be changed in order to fix detected bugs.

3. *Beta Test Phase (Acceptance Test by the Beta Sites)*

² Independent testers should be persons, not involved in developing the system. For instance, these could be developers from other projects or staff from other Medis departments, or even external persons.

After the Alpha Test phase, the Beta Test phase will start. This is an Acceptance Test performed by the Beta Sites. Acceptance testing in this phase is planned during requirements analysis and accomplished or witnessed by intended system users (Beta Sites).

Relevant Reference Documents

- Refer to [32].

4.6.3. Scientific Validation

Scientific Validation proves the algorithmic correctness of the results of the Medis applications. Either a complete clinical validation can be performed resulting in a Scientific Validation Report (SVR), or a regression test to show that the software still generates the same results as recorded in the SVR.

4.6.3.1 Process Description

The validation specialist uses the scientific validation procedure [33] for validation of the algorithmic modules. In this process, an external party can play role.

4.6.3.2 Documentation

A Scientific Validation Report (SVR) contains the full description of the validation methods, the used data, the acceptance criteria, and the results.

4.7. System Qualification

4.7.1. Process Description

Purpose

- System qualification states that the commercial release of a system fulfils its demands.

Input

- All SDPD documentation produced by the project.

Output

- Signed *System Test Statement (STS)* – A conclusion that the product has passed the test criteria.
- Signed *Scientific Validation Statement (SVS)* – A conclusion that the product has passed the validation criteria.
- Signed *Regulatory Compliance Statement (RCS)* – A conclusion that the product complies with current regulatory standards and guidelines.

Key involvement

- Software test manager to create the STS.
- Validation specialist to create the SVS.
- Quality coordinator to create the RCS.
- Project manager, to collect the statements.

Description

The software test manager, validation specialist, and quality coordinator create the statements.

The project manager collects the approved and signed statements and stores them under the appropriate baseline. This is an input to the system release phase.

Related processes

- *System testing and validation process.*
- *System Release process.*

4.7.2. System Test Statement

In the system qualification phase, the software test manager creates a System Test Statement (STS). Refer to [32] and [35].

4.7.3. Scientific Validation Statement

The validation specialist creates the Scientific Validation Statement (SVS), which states that the software has been scientifically validated. It refers to the applicable SVRs.

4.7.4. Regulatory Compliance Statement

The quality coordinator creates the Regulatory Compliance Statement (RCS) [30], which states that the product is compliant with current regulatory standards and guidelines (European and American). It refers to all SDPD documents. To accomplish this, the regulatory compliance procedure [29] is used.

4.8. System Release

4.8.1. Process Description

The software engineers produce the System Release Notes (SRN).

4.8.2. Documentation

- The System Release Notes (SRN) are part of the user documentation set, and described in section 5.1.

5. User Documentation

This chapter describes the documentation set delivered with every software product. This set should be made complete and final before the release of the system.

The document descriptions include information on the audience, the format, the type of distribution, and the document type (optional or mandatory).

5.1. System Release Notes

This document provides a summary of important new functionality and enhancements as compared to the previous version of the application. It includes a paragraph on incompatibilities and known issues, and it lists workarounds.

Audience: system administrators and end users, Medis personnel (Marketing and Sales, Installation and Support)

Format: PDF

Distribution: on CD-ROM

Type: mandatory

5.2. Readme File

Provides important information required to correctly install or use the application.

Audience: system administrators, Medis personnel (Installation and Support)

Format: text file

Distribution: on CD-ROM

Type: optional

5.3. Installation and Configuration Manual

Lists system requirements and provides step-by-step instructions for installing the application.

If the installation process is entirely guided by an installation procedure, there may be no need for an installation manual. In this case, the system requirements will be listed in the release notes.

Provides step-by-step instructions for configuring the application, for example using settings in an INI file. Includes detailed descriptions of the configuration settings.

Audience: system administrators, Medis personnel (Installation and Support)

Format: PDF

Distribution: on CD-ROM

Type: mandatory

5.4. Conformance Statement

States the level of conformance to the DICOM standard. This document is required for applications that offer DICOM facilities. There is a predefined format for the conformance statement that can be found in the DICOM standards literature [9].

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Audience: distributors, system integrators, system administrators, Medis personnel,
(Installation and Support, Marketing and Sales)
Format: PDF
Distribution: on CD-ROM
Type: mandatory

5.5. Reference Manual for System Integrators

This document allows third parties to integrate Medis software with their own products. Depending on the product, this document may provide reference information on automation interfaces, command line interfaces, and scripting.

Audience: distributors and system integrators
Format: PDF
Distribution: upon request
Type: optional

5.6. CD Booklet

Contains instructions for locating the files on the CD, provides contact details, and includes the required legal and regulatory notices.

Audience: system administrators
Format: DOC
Distribution: with CD-ROM
Type: mandatory

5.7. CD Label

States the product name and version number, the copyright notice, provides contact details, and includes the CE marking.

Audience: system administrators
Format: CDR
Distribution: on CD-ROM
Type: mandatory

5.8. User Manual

The user manual offers an introduction to the application as well as step-by-step instructions for all tasks. It typically includes:

- Legal and regulatory information.
- Information on what is new in the latest version of the application.
- Quick tour (optionally as a separate Quick Start Manual if translated manuals are required, either by the customer, or because of EU language requirements).
- Overview of main areas in the user interface.
- Instructions for working with the application.
- Reference section (Typically includes lists of commands, shortcut keys, settings and any other type of information that the user must be able to look up quickly).

- Troubleshooting section.
- Index.

Users who first start using the software or who want to know the ins and outs of the software, will read a user manual. The linear structure of a user manual is perfectly suited for these purposes.

On the other hand, users who are already working with the software or who favor a hands-on way of learning to work with a software tool, will primarily access the on-line help. The hyperlinked structure of the on-line help allows users to browse the information instead of go through it in a linear way.

Audience: medical specialists and technicians, distributor personnel, Medis personnel (new employees)

Format: PDF

Distribution: on CD-ROM and on paper

Type: mandatory

5.9. On-Line Help

The on-line help is mainly accessed by users who are looking for reference information or who want to quickly look up how to perform a single specific task. This means that the information must be chunked into small, easily browsable pages. The range of navigation and indexing options available in WebHelp facilitates browsing. In addition, movies and animations may be used to enrich the on-line help, and context-sensitivity may be added.

Audience: medical specialists and technicians, distributor personnel, Medis personnel

Format: WebHelp

Distribution: accessible from the Help menu in the application

Type: mandatory

5.10. Tutorial

The tutorial offers an easy and intuitive way of learning how to work with an application for those who cannot attend Medis training sessions. Tutorials can be provided as separate help systems or, preferably, as animations.

It is an M&S decision whether the tutorials are offered as a standard part of the product (accessible from within the application or from the application CD) or as an optional extra, which is to be purchased separately.

Audience: medical specialists and technicians, distributor personnel, Medis personnel (new employees)

Format: WebHelp or Flash

Distribution: accessible from the Help menu in the application and the CD-ROM or available on a separate CD-ROM

Type: optional

6. Software Maintenance

The previous chapters describe the process to develop a *new release* of a product. However, in most cases an *existing* application needs to be maintained. Reasons to create a so-called *maintenance release* are: fixing bugs and implementing minor enhancements. To develop maintenance releases, we tailor the software development approach, described in the previous chapters.

6.1. Development Approach

To create a maintenance release, apply the Change Control Procedure [21]. With this procedure, each bug / enhancement is properly analyzed, implemented and verified:

1. Perform the analysis to get an overview of the impact on the code and the documentation (requirements, architecture, design, etc.).
2. Apply the V-model steps 1 to 4 (see Figure 2-1) in the prescribed order, and where applicable: first perform requirements updates, then design updates, then module implementation updates, and finally the integrated system updates.
3. Verify the implementation by (Unit) Testing the code changes, and by (peer) reviewing the documentation updates.

The above steps will produce an integrated system that includes the bug fixes and the enhancements. Subsequently, you will need to perform Regression Tests and re-validate the integrated system, and re-qualify the system before it can be released:

4. *System Testing and Validation*

- If required, and thus identified in the analyses of the bugs / enhancements, update the STDs. Perform Regression Testing based on relevant STDs, to demonstrate that the related requirements are met for the impacted functionality.
- If required, and thus identified in the analyses of the bugs / enhancements, update the validation scripts. Perform a re-validation [33] to show that the software still generates the same results as recorded in the SVR.
- It is highly recommended that a Beta Version be sent to the Beta Sites. Any (new) problems with the fixes and enhancements found at Beta Sites must be solved *before* System Qualification.

5. *System Qualification*

Update and approve the following statements: STS, SVS, and RCS.

6.2. Version Numbering

The creation of a maintenance release will result in to a minor update of the version number: e.g. from 4.0.1.0 or 4.0.2.0 (refer to [25]).

Note that a new release will result in to a major update of the version number: e.g. from 4.0 to 4.1, or even to 5.0 (refer to [25]).

7. Further Reading

Over the years, literature has proposed numerous methodologies for software development. Yourdon [7] and Jackson [2] describe well-known and frequently used approaches. These methodologies are traditional in the sense that they use a top-down or bottom-up approach. Worse, these methodologies cannot adequately support recent developments in software engineering, like object orientation, and the use of event mechanisms. Wirth [3] was one of the first to acknowledge the need for independent software units (which he called *modules*). Currently, there are a number of methodologies, which consider object orientation to be the basis of software development. Object-oriented analysis and design, described by Booch [6] and Rumbaugh [7], is probably the best-known methodology.

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8.1. External References

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8.2. Medis QMS references

16. C++ Coding Standard (CON 9418)
17. Medis Quality Manual (MAN 9102)
18. SDPD templates (TEM 9426a, ...)
19. How to use Doc-O-Matic: [SPI site](#) → Interesting Info
20. R&D Document Control Procedure (PRO 9412)
21. Change Control Procedure (PRO 9403)
22. Software Change Control Board (PRO 9411)
23. Document Inspection Procedure (PRO 9312)
24. Inspection Rule Sets for different document types:
 - General (CON 9312e)
 - SRD (CON 9312f)
 - SDP (CON 9312h)
 - User Document (CON 9312i)
 - Source Code (CON 9312j)
25. General Naming Conventions for SW Development (CON 9417)
26. Medis Best Practices Library, [SPI site](#) → Best Practices
27. Medis Glossary for Software Development (CON 9419)
28. R&D Process Guide (PRO 9429)
29. Regulatory Compliance Procedure (PRO 9408)
30. Regulatory Compliance Statement (TEM 9408a)
31. User Documentation Unit Testing (MAN 9438)
32. System Test Procedure (PRO 9436)
33. Scientific Validation Procedure (PRO 9428)
34. Scientific Validation Statement Template (TEM 9428a)
35. System Test Statement Template (TEM 9436a)
36. Product Development Process Document (PRO 9209)

Appendix A

Risk Analysis on Safety and Effectiveness

Medis medical imaging systems bv

Confidential and Controlled Document

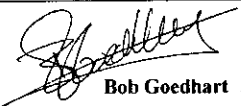
QAngio CT Version 1.0

Risk Analysis on Safety and Effectiveness Doc. Version: v1c0 FINAL

File: RiskAnalysisSafetyEffectivenessQAngioCT.doc

Owner: H. Hollander
January 12, 2006

Approval

Role	Name	Signature	
Project Principal	Bob Goedhart	 Bob Goedhart	I am approving this document 2006.01.12 15:29:00 +01'00'

Distribution

1. Medis Project- and Product Manager
2. QA team
3. Regulatory Authorities (Notified Body; FDA)



Medis medical imaging systems bv
Leiden, The Netherlands

QAngio CT
Risk Analysis on Safety and Effectiveness
Date: January 12, 2006 1 of 9

System version: 1.0
Document version: v1c0
Status: FINAL

Template: TEM 9408c Risk Analysis on Safety and Effectiveness

Preface

This document describes the risk analysis for a software product considered as a Class IIa medical device, according to the European Medical Devices Directive 93/42 [1].

The European Class IIa is comparable with the American FDA Class II controls and according to Global Harmonization Task Force proposals for classification [2], equivalent to Class B.

Medis' development processes and the resulting software product are in compliance with the ISO standard 13485 "Medical Devices" [3]. Before commercial release, European and American regulatory authorities (Notified Body / FDA) are notified of the product for market clearance.

Goal

This document is applicable for software products that not have been commercial released yet and is similar to the "Risk Analysis" chapter of Medis' PRO 9408 "Regulatory Compliance Procedure", described in Medis' QMS.

The "Risk Analysis on Safety and Effectiveness" is specifically used for notification activities to regulatory authorities, partners and clients of the safe use of the software product and the effectiveness of its application in image post-processing.

Intended audience

The document contains the identification of hazards in practical situations, the related occurrence- and severity assessments and consequently the risk reducing measures.

Therefore, it is assumed that the reader is familiar with safety fundamentals [4] and with risk management [5] related to the application of medical devices. Moreover it is assumed that the reader understands the concepts of medical image analysis and is familiar with principles of software engineering and basic computer terminology [6].

History of Creation

The following table presents an overview of the creation history of the document.

Version	Date	Author	Remarks
V0C1	January 5, 2006	H. Hollander	Initial version.
V0C2	January 9, 2006	H. Hollander	Version to review by Bgoe.
V1C0	January 12, 2006	H. Hollander	Final version.

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1. Safety Analysis

1.1. Software Product Identification

In general, the products of Medis medical imaging systems can be identified as stand-alone software packages for image post-processing. Particularly, the software package can be characterized as analytical software for the quantification of medical images. Furthermore the software is installed by Medis or by a trained distributor. Clinicians and analysts are trained to operate the software, to select a particular part of the image and to accept / reject quantification results.

1.2. Safety Characteristics

This document lists all the characteristics that can affect the safety of the product. The chapters A21 – A228 correspond to the questions mentioned in Appendix A of the Standard ISO 14971:2000 “Medical devices – Application of risk management to medical devices”[5].

A21 Intended Use? For all Medis software products the 'intended use' is the quantification of medical images. The user selects Regions Of Interest (ROI) within an existing medical image and with application of analytical software algorithms objective and reproducible data and diagrams can be presented.

Indications for Use? Installed on general-purpose computers the software can be applied in hospital areas to support clinical decisions or in core labs to study intervention effects.

A22 Intended patient contact? Not applicable. Software cannot make contact with the patient. The software does not drive or the hardware devices that directly influence the patient.

A23 Materials / components? Not applicable. Software is not a concrete substance.

A24 Energy delivered / extracted? Not applicable. Software does not deliver / extract energy.

A25 Substances delivered / extracted? Not applicable

A26 Biological materials processed? Not applicable

A27 Sterile / Microbiological controls? Not applicable

A28 Cleaned and disinfected by user? Not applicable

A29 Modify patient environment? Not applicable

A210 Measurements? The Medis software is an analytical software package for the quantification of selected region of interest within a medical image. The software algorithm calculates pixels and contains no measuring devices.

A211 Interpretative device? Existing medical images can be shown and with the installed Medis software the user can select region of interest within that image and make specific calculations based on a contour detection algorithm. The results of the calculations can be quantified and presented as in diagrams.

A212 Conjunction with medicines or other medical technologies? The software is installed on a PC or workstation. Safety demands for the PC or workstation are described in the manual. The PC or workstation and other devices located within the patient area and interacting with the software shall be either powered by a safety isolation transformer

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or connected via an additional protective earth terminal to system ground unless it is certified according to standard IEC60601-1 [7] or tested against the relevant safety standards. Medis advises the user to check the PC or workstation for proper use and to use a CE marked medical device.

- A213 Unwanted outputs of energy or substances? Not applicable
- A214 Medical device susceptible to environmental influences? Not applicable
- A215 Medical device influence the environment? Not applicable
- A216 Consumables / accessories? No consumables are part of the software.
- A217 Maintenance / calibration? Not applicable
- A218 Software? Software is installed by Medis or trained distributor. No modification to the software is allowed.
- A219 Restricted self-life? Not applicable
- A220 Delayed / long term use effects? Not applicable
- A221 Mechanical forces? Not applicable
- A222 Lifetime of the device? Software is not subjected to physical ageing. Technological progress should be regarded; e.g. the operating system can alter.
- A223 Single use / re-use? The software package is intended for re-use.
- A224 Safe decommissioning and disposal necessary? Not applicable
- A225 Installation and use require special training? Yes. Medis combines installation- and application training on site. Training is provided to distributors and end-users.
- A226 New manufacturing process needs to be established? Not applicable for software development process.
- A227 Successful application dependent on human factors such as the user interface? Yes, see hazard identification under 2.1 and application of Fault Tree Analysis under 2.2.
- A2271 Does the medical device have connecting parts or accessories? Not applicable, in terms of hardware as mentioned.
- A2272 A control interface? Yes, combined with hardware. Control is tested and validated.
- A2273 Display information? Yes, combined with hardware. Display info is tested and validated.
- A2274 Is the medical device controlled by a menu? The software contains menus and other controls. These menus and controls are tested and validated.
- A228 Mobile or portable? Not applicable in terms of grips, handles and wheels.

1.3. Conclusion Safety Analysis

It is Medis opinion, regarding the above safety characteristics, **QAngio CT**, version **1.0** is a safe software product. The level of concern for analytical software in image post-processing poses a low risk and does not introduce new hazards.

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2. Effectiveness Analysis

2.1. Hazards; Human-, Technical- and Software Errors

In the clinical practice of image post-processing 3 kinds of hazards can be distinguished; - technical errors (hardware failures) in the image acquisition equipment, - human errors made by clinicians (user misinterpretation), - software errors (bugs). Medis software is capable of reproducing the quantification results. These results support the clinicians for a more objective interpretation of the image. It is clear that Medis' software can influence the human errors; not the technical errors in the image acquisition phase.

For the effectiveness of the application, software errors are analyzed (Fault Tree Analysis [8]) to set development requirements for minimizing severity and probability (risk reduction).

2.2. Explanation of the Fault Tree Analysis (FTA)

Hazard Describes the potential source of harm.
Severity The degree of severity of the harm, taking into account the risk reducing measures. Can take on the next four possible values:

Catastrophic	Multiple deaths or serious injuries
Critical	Death or serious injury
Marginal	Injury
Negligible	Little or no injury

Probability The probable rate of occurrence of a harm-causing hazard, taking into account the risk reducing measures. Can take on the next five possible values

Irrelevant	Used for hazards which result primarily from external sources which cannot be (further) reduced within this project
Incredible	It is unthinkable the hazard will occur
Improbable	It is unlikely the hazard will occur
Occasional	It is possible the hazard occurs
Frequent	It is likely the hazard occurs

Risk Describes the combination of the probability and the severity. Can take on the next three possible (acceptable) values

PM	Pro Memoriam: used with 'irrelevant' probability
Acceptable	Generally accepted risk level - no further discussion required
Undesirable	This level requires documentation of the considerations to accept the risk
Intolerable	

These values follow from severity and probability defined the risk level:

	Catastrophic	Critical	Marginal	Negligible
Irrelevant	PM	PM	PM	PM
Incredible	Acceptable	Acceptable	Acceptable	Acceptable
Improbable		Undesirable	Acceptable	Acceptable
Occasional			Undesirable	Acceptable
Frequent				Undesirable

Risk reducing measures The measures taken to reduce the risk. These measures either reduce the severity, or the probability of the occurrence of the hazard.

2.3. Application of Fault Tree Analysis

The following tables need to be used in the Effectiveness Analysis:

Tables A and B summarize the Human- and Technical errors without use of Medis software;

Table C presents the analysis of software errors together with risk reducing measures;

Table D and E summarize the Human- and Technical errors with the use of Medis software.

	Hazard Application without Medis software	Severity	Probability	Risk	Risk reducing measures
A	HUMAN ERRORS: Summarized: All kinds of human errors (operator, clinician)	Critical	Occasional	Intolerable	Outside Medis scope; no interference
B	TECHNICAL ERRORS: Summarized: All kinds of technical errors (equipment, image acquisition process-ing)	Critical	Improbable	Undesirable	Outside Medis scope; no interference

	Hazard Application with Medis software	Severity	Probability	Risk	Risk reducing measures
	User manual and On-line help facility.				Document inspection avoid bad documentation
1	Unclear and inconsistent described operations	Marginal	Improbable	Acceptable	Is completed and clear
2	Missing a device description, an indication for use and the intended use	Marginal	Improbable	Acceptable	Is present on the welcome part of the manual
3	Missing a description of image processing functions supported by the system	Marginal	Improbable	Acceptable	Is present in the documentation and on the on-line help
4	Missing a description of quantitative clinical parameters, calculation methods, formulas and references to literature	Marginal	Improbable	Acceptable	Is present in the documentation and on the on-line help
5	Missing the required characteristics of the images the system is allowed to operate on	Marginal	Improbable	Acceptable	Is present in the documentation and on the on-line help
6	Missing the specifications about accuracy and precision of measurements	Marginal	Improbable	Acceptable	Is present in the documentation and on the on-line help
	System requirements without taken the following issue into account:				The system requirement document is inspected
7	Identification of the application about the version and the level of options in operation	Critical	Incredible	Acceptable	Identified by means of unique version numbers, documented in about box and splash screen
8	The identification of patient data in the system	Marginal	Improbable	Acceptable	The data is implemented and remains permanently visible for the operator
9	The identification of patient data mixed with other patient data;	Marginal	Improbable	Acceptable	The operator can take specific action to remove, change or skip the data
10	Image annotations permanently visible and displayed with images,	Marginal	Improbable	Acceptable	Operator must take specific actions to remove them

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11	Image processing functions able to provide diagnostically useful images	Marginal	Improbable	Acceptable	Operator judges if images are useful; he uses images processing to find the most optimal image
12	Image processing functions corrupt, interfere with existing software; the processing method affects user's interpretation	Marginal	Improbable	Acceptable	All image processing in the application do not affect the original diagnostic information
13	Measurements data and parameter settings visible; printed reports allow the operator to accept, reject or overrule this information	Marginal	Improbable	Acceptable	The operator can review and change data and settings during and after analysis
14	Error messages displayed on the console with warnings related to safety of the system	Marginal	Improbable	Acceptable	Presentation of hints about possible nature and cause of the error
15	Presentation of error messages when image characteristics differ from the required ones	Marginal	Improbable	Acceptable	The operator can take specific action to disregard the message
	Validation- and test documentation:	Marginal	Improbable	Acceptable	Test and validation reports contain a final statement
16	Without conducted state of the art engineering procedures	Marginal	Improbable	Acceptable	Procedures and literature references are used
17	Without plan, including test procedures and validation studies.	Marginal	Improbable	Acceptable	Indication of the used methods with pass/fail criteria are recorded and statistically analyzed

2.4. Summary Fault Tree Analysis

	Hazard Application with Medis Software	Severity	Probability	Risk	Risk reducing measures
D	HUMAN ERRORS: Summarized: All kinds of human errors (operator) Application with Medis software.	Critical	Incredible	Acceptable	With application of software, objective and reproducible analytical results reduces subjective interpretation and the occurrence of human errors
E	TECHNICAL ERRORS: Summarized: All kinds of technical errors (equipment, image acquisition / processing)	Critical	Improbable	Undesirable	The application of software does not reduce the severity and probability of all kinds of technical errors

2.5. Conclusion Effectiveness Analysis

In image post-processing the application of this commercially released analytical software product presents reproducible quantification results. The reproducibility of objective results reduces the risks of human errors from an **intolerable** level (Table A) to an **acceptable** level (Table D). Beside this risk reduction, the interpretation of the now acquired quantification results saves a considerable amount of time.

It is Medis opinion that the application of Medis software product **QAngio CT**, version 1.0 can be considered as effective with added value.

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2. Global Harmonization Task Force; Study Group 1, Doc NO11R22: 2003, "Principles of Medical Devices Classification".
3. ISO 13485:2003, "Medical Devices – Quality management systems – Requirements for regulatory purposes".
4. CEI/IEC 513:1994, "Fundamental aspects of safety standards for medical electrical equipment"
5. ISO 14971:2000, "Medical Device – Application of risk management to medical devices".
6. ISO/IEC 1506:1998, "Information Technology – Systems and software integrity levels".
7. CEI/IEC 601-1:1998, "Medical electrical equipment, Part 1: General requirements for safety".
8. IEC 1025: 1990, "Fault Tree Analysis".

4. Statement Risk Analysis

I certify, in my role as Quality Coordinator of Medis medical imaging systems bv, that all data and information in this Risk Analysis overview are accurate and that no material fact has been omitted.

I conclude to my best knowledge that Medis software product: **QAngio CT**, version **1.0**, can be regarded a safe product (see Section 1.2) with an effective application (see Section 2.5).

Role	Name	Signature
Quality Coordinator	H. Hollander	 <small>Digitally signed by Hans Hollander DN: CN = Hans Hollander, C = NL, O = Medis, OU = QA Location: Isiden Date: 2006.01.12 15:12:12 +0100</small>

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Appendix E
Validation Report.

QAngioCT Validation report

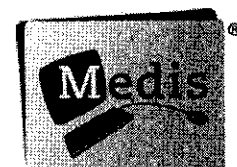
Preliminary

**Conclusions from this report
need to be verified on the final
version of the software**

Validation report
Author: Eelco Giele
Version V0C1

August 4, 2006

Medis medical imaging systems



1 Introduction

This is the QAngioCT validation report. QAngioCT is the Medis software solution for the quantification of lesions in the blood vessels using CT images.

By using a contrast agent the vessels (or better, the lumen of the vessels) become opaque for x-ray radiation and thus show up in the images made with a CT scanner. CT scans are a two stage affair, whereby a scan is made which is then reconstructed to a 3D volume. This volume is what is normally considered to be the output from the scanner. During the actual scanning and the reconstruction process there are several parameters that can be set and which influence the resulting volume.

QAngioCT reads the volume, gives an operator the option to select the vessel to be analysed and then analyses the vessel, calculating vessel cross section areas, the stenosis percentage and stenosis length. From vessel selection to calculation the software takes several steps in between. The first thing after the vessel section selection is the calculation of a path line. Most vessels are not straight but follow a tortuous path that, in that form, would be difficult to analyse. The path line follows the centre of the vessel and based on that line a multi planar reformat is used to create two volumes. One volume contains 4 longitudinal cross sections of the vessel and one volume contains a large number of transversal cross sections of the vessel. A first segmentation is performed on the longitudinal cross sections. If the operator agrees with these results a (far more accurate) segmentation is performed on each transversal slice. Both in the longitudinal and the transversal slices the detected contours can be corrected by the operator.

After the contour detection the cross sectional areas and the derivative values from those areas, like stenosis percentage and stenosis length are calculated from the contours. The image information is not used in these calculations.

This leads to two areas that need validation. The first area is the pure mathematical side of the software which calculates areas, stenosis percentage etc. from the contours. The second area is image-processing side with, amongst others, path line detection and contour detection.

QAngioCT development has been split in two phases. In the first phase development focuses on the analysis of peripheral and carotic vessels. In the second phase the analysis of coronaries will be included as well. Although both are closely related, the coronaries have a smaller diameter and more movement (due to the speed of the heartbeat there is a very high risk of movement artefacts in the image volume), therefore the coronaries pose their own set of problems for analysis.

This is a preliminary validation report; the software and calculation libraries are still being refined. Therefore, very few results are present and the results which are present are based on the current state of the library.

2 Methods and materials

2.1 Methods

Since the calculations in the software are performed as a two-stage process, contour detection and stenosis quantification based on those contours, it is possible to split the validation in those two parts as well.

2.1.1 Image loading

The basis for almost every measurement in an image (with the notable exception of relative measurements, like stenosis percentage) is the scale, often called the calibration factor. It enables the user or software to translate the arbitrary pixel-centre distances to real distances in SI units. The reconstructed volume from a CT scanner already contains the necessary calibration factors so manual calibration is not needed. Although these systems are calibrated and the results should be correct it is important to verify that this is actually the case. Therefore a validation takes place where acrylic phantoms are scanned and measurements on the images are performed in the software. These measurements are then compared with the actual size of the phantoms.

2.1.2 Path line detection and multi planar reformat No validation implementation yet

The path line and multi planar reformat (MPR) are responsible for the creation of the cross section images of the vessel. In case the MPR's are not perpendicular to the vessel, the cross sections will be larger than they are in reality, which affects all absolute measurements (relative measurements are not influenced unless the error in angle becomes so large that the plaque and the vessel are from different locations in the vessel).

Currently only a visual inspection of the path line is used.

2.1.3 Contour detection

Although the phantom scans can be used for contour detection validation, the similarity to the images of real vessels is limited. The phantoms consist of very nice straight segments and the lumen/vessel-wall contrast is very homogenous and although approximating those encountered in reality not exactly the same. Therefore the contour detection is validated by comparing the QAngioCT contours with golden standard reference contours in real CTA images.

For this purpose we use a set of 9 different scans of the various peripheral vessels and one scan of the phantoms. Since the contours are drawn on the cross sections of the vessels, these have to be calculated first. This is done using a multi planar reformat which in turn is based around the path line through the vessel to be analysed. To make certain that all the experts are drawing contours in the same images, the path line start and end point are given, resulting in identical path lines, identical multi planar reformats and thus identical images.

The images in which contours need to be drawn are prescribed for all the experts (5 slices per scan, 50 slices in total). From these different contours the average "golden standard" contour is determined as is the inter observer variability.

After the determination of the golden standard, these contours can be compared to the contours as detected by QAngioCT.

2.1.4 Quantifications

The quantifications are calculated from the contours, therefore there are no unknown or arbitrary parameters influencing the results. This means that if the contours are known, the quantifications can be analytically calculated and compared with the results from the software.

There are two types of comparison material. The first uses the raw contours and calculates the results from this and the second uses the scans from the phantoms. Especially with the last the full chain from

scanning via contour detection to numerical results can be validated. The first will be verified for each contour encountered, of the second the results are shown in a table.

2.2 Acceptance criteria

The acceptance criteria describe the maximum errors that the software is allowed to make. If the errors are larger than described in the acceptance criteria, the validation is considered to have failed for that particular item.

There are two types of errors: systematic and random. Random errors are "normal" errors, systematic errors on the other hand often indicate a problem in the algorithms with consequent over- or under-estimation.

2.2.1 Image loading, quantification

The only criterion for this is that everything functions correctly. If there are errors either in reading of the image information or the analytical part the validation will have automatically failed.

2.2.2 Contour detection

The contour detection itself is not directly validated. Although it is possible to calculate a measure for how closely two contours match, this gives no information (or only very indirect) on what this means for the subsequent measurements. Therefore the measurements, which are based on those automatically detected contours, are validated.

2.2.2.1 Area calculation

The area calculation results in an absolute value (in mm²). The limits for the error in surface area have been set to either 10% of the real area or the error caused by an increase or decrease in diameter of half a voxel. The CTA index indicates the value as calculated by QAngio CT, the TRUE index indicates that the actual value.

$$\frac{\text{abs}(A_{CTA} - A_{TRUE})}{A_{ref}} < 0.1 \quad (1)$$

$$\text{abs}(\sqrt{A_{CTA}} - \sqrt{A_{TRUE}}) < \sqrt{\pi} \cdot [\frac{1}{2} \text{ pixel}] \quad (2)$$

2.2.2.2 Stenosis percentage

The stenosis percentage is calculated as the area at the location of the stenosis (A_{STE}) divided by the vessel area (A_{VES}). This is usually interpolated from the vessel outside the stenotic area

For stenosis percentage the same limits have been chosen as for the area calculation. It is important to keep in mind that this means it is still possible for the validation to succeed for the area calculation but to fail for the stenosis percentage validation or the other way around.

$$\text{abs}(\%_{CTA} - \%_{TRUE}) < 0.1 \quad (3)$$

$$\frac{\left(\sqrt{\frac{A_{STE}}{\pi}} - [\frac{1}{2} \text{ pixel}] \right)^2}{\left(\sqrt{\frac{A_{VES}}{\pi}} + [\frac{1}{2} \text{ pixel}] \right)^2} < \%_{CTA} < \frac{\left(\sqrt{\frac{A_{STE}}{\pi}} + [\frac{1}{2} \text{ pixel}] \right)^2}{\left(\sqrt{\frac{A_{VES}}{\pi}} - [\frac{1}{2} \text{ pixel}] \right)^2} \quad (4)$$

2.2.2.3 Stenosis length

The length of the stenosis should be determined with a 10% accuracy. Since these lengths are far bigger than the pixel size, no leniency for errors in the half pixel range is provided for.

$$\text{abs}(L_{CTA} - L_{REF}) / L_{REF} < 0.1 \quad (5)$$

2.2.2.4 Systematic errors

There should be no systematic errors. Errors are considered to be systematic when the correlation between the measured and true values has an $R > 0.85$ and the average relative error exceeds 10%.

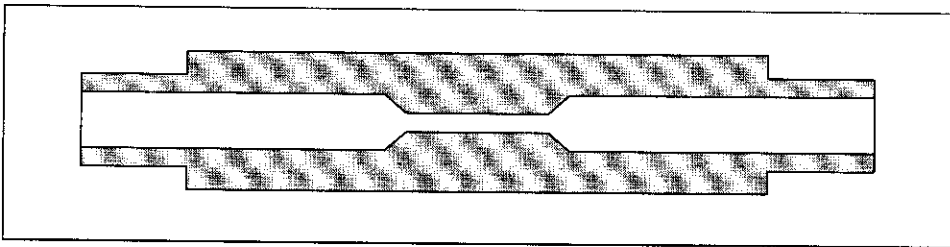
2.3 Materials

2.3.1 Phantoms

The phantoms used in this validation study were specifically designed for the validation of CTA and MRA images of the peripheral vessels.

The set of phantoms consists of 6 hollow perspex tubes with a stenosis in the centre. For CTA scans the phantoms are filled with diluted contrast agent with the dilution chosen so the same contrast between "vessel wall" and lumen is present as in patient CTA scans.

The stenosis is symmetrical and part of the perspex tube and therefore has the same intensity as the vessel wall. It does not simulate calcified plaque.



This set of phantoms is specifically meant for peripheral vessels; therefore the phantoms are fairly large.

Phantom number	Reference diameter (mm)	Reference area (mm ²)	Stenosis diameter (mm)	Stenosis area (mm ²)	Stenosis length (mm)	Diameter stenosis %	Area stenosis
1	6	28	3	7.1	20	50	75
2	6	28	4	13	20	33	56
3	9	64	4.5	16	20	50	75
4	9	64	2.5	4.9	20	72	92
5	12	1.1x10 ²	6	28	30	50	75
6	12	1.1x10 ²	8.5	57	30	29	50

2.3.2 Phantom scans

All six phantoms are placed in a box and scanned at the same time. The settings are chosen so the images resemble in vivo images. A series of parameters is used for the scans to represent the differences in settings used in a clinical setting.

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Series nr	Contrast	Angle	KV	Description	Reconstruction filter
6	2 percent	0	120	Baseline	Soft
7					Medium
8					Sharp
9	2 percent	0	135	KV high	Medium
10	2 percent	0	100	KV low	Medium
11	2 percent	45	120	Angle 45	Medium
12	2 percent	90	120	Angle 90	Medium
13	5 percent	0	120	Contrast	Soft
14					Medium
15					Sharp

2.3.3 In vivo images

A set of images has been selected that represents the different vessel anatomies that can be analysed with QAngio CT. By using different sources for the images and different brands of scanner the performance can be evaluated in the wide spectrum of images used in clinical practice.

Location	Internal name	Scanner Manufacturer
Carotids	Carotids (10171129)	Siemens
Carotids	Carotids (10171131)	Siemens
Carotids	Carotids (GE)	GE
Carotids	Carotids (LB686)	???
Coronary	Coronair (ToshibaMV1)	Toshiba
Coronary	Coronair (08260904)	Siemens
Legs	Legs (11011635)	Siemens
Legs	Legs (11011650)	Siemens
Legs	Legs (GrStudy001)	Siemens
Legs	Legs (GrStudy003)	Siemens
-	Phantom (07)	Toshiba

<This set has to be enlarged to include more vendors>

3 Measurements

3.1 Quantification

All result files containing contours also contain the measurements (area calculations). A special tool compares these results for all result files presented to it.

Number of files	Total number of contours	Errors
2	14	0

3.2 Phantoms

In the next table the results of the phantom the measurements are displayed together with the reference values.

Currently one set of phantom measurements has been performed. See table for the remaining sets.

Scan	Phantom																	
	1			2			3			4			5			6		
	ref area	sten area	sten %	ref area	sten area	sten %	ref area	sten area	sten %	ref area	sten area	sten %	ref area	sten area	sten %	ref area	sten area	sten %
Reference	28	7.1	75	28	13	56	64	4.9	92	113	57	50	64	16	75	113	28	75
6																		
7	26	7.7	70	26	12	55	62	5.1	92	115	56	51	61	14	77	115	28	76
8																		
9																		
10																		
11																		
12																		
13																		
14																		
15																		

3.3 In vivo images

There will be 9 different sets (as described in the materials and methods) and 3 operators. The following table contains example data!

Measurement results per slice

Slice number	Operator 1	Operator 2	Average	Relative difference	QAngioCT	Relative error
15	37	40	38.5	1.5/38.5	40	4%
24	37	42	39.5	2.5/39.5	40	1%
27	41	45	43	2/43	44	2.3%
43	28	30	29	1/29	27	7%
66	17	17	17	0	16	6%
Average				7.6%		

4 Recommendation

An increase in the number of data sets from different scanner vendors is needed.

5 Conclusion

These conclusions are based on the preliminary, and very limited in number, results in this report.

5.1 Quantification

All the calculations performed, based on the contours, are correct.

5.2 Contour detection

The results as found with the phantom are well within the margins set in the acceptance criteria.

The results of the in vivo images show that the automatic contour detection is comparable with that of an operator.

5.3 Final conclusion

If all results during the final validation perform as well as the current very limited set in the current version of the calculation library, this program is suitable for its intended use.

6 Appendix A: Golden standard protocol

This is the protocol the operators responsible for the golden standard contours had to adhere to. It minimises the

- Start the program
- The start and end point are predefined in the accompanying settings.xml. These should be loaded automatically
- Start path line detection without moving the begin or end point
- Calculate CMPR. Both longitudinal and transversal images will be displayed
- Select the transversal slice according to the table handed to you
- Draw the transversal contour
- Repeat selection of slice and contour drawing for all the slices indicated on the table
- Find the transversal slice with the minimum lumen
- Draw the transversal contour
- Find a slice which contains what you think is a good reference
- Draw the transversal contour
- Save the contours in a file (txt or xml format)

Appendix F
Literature

References for QAngio CT

- **Towards quantitative analysis of coronary CTA.** H.A. Marquering, J. Dijkstra, P.J.H. de Koning, B.C. Stoel, J.H.C. Reiber. 2005, *Int. J of Cardiovascular Imaging*. 21, 73-84
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- **Automatic Delineation and Lesion Quantification of Coronary CTA Images - NASCI 2004.** H. Marquering, J. Dijkstra, J. Geleijns, A. de Roos, J. H. Reiber. *The international Journal of Cardiovascular Imaging*, 2004, v. 20, issue 5, p. 420-421.
- **Automatic Segmentation and Quantitative Analysis of Coronary Arteries in MSCT Images - RSNA 2004.** H. Marquering, J. Dijkstra, J. Geleijns, A. de Roos, J. H. Reiber.
- **CT Image Quality of In-stent Restenosis - RSNA 2005,** H. Marquering, J. Dijkstra, Marion Persoon, Koos Geleijns, Wouter Jukema, Berend C. Stoel, Johan H.C. Reiber.
- **Quantitative In-stent Restenosis Measurements in CT Images - In Vitro Validation -- RSNA 2005,** H. Marquering, J. Dijkstra, Marion Persoon, Koos Geleijns, Wouter Jukema, Berend C. Stoel, Johan H.C. Reiber

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Memorandum

From: Reviewer(s) - Name(s) LOREN A. EARLE MBA

Subject: 510(k) Number K062386

To: The Record - It is my recommendation that the subject 510(k) Notification:

- Refused to accept.
- Requires additional information (other than refuse to accept).
- Is substantially equivalent to marketed devices.
- NOT substantially equivalent to marketed devices.
- Other (e.g., exempt by regulation, not a device, duplicate, etc.)

- Is this device subject to Section 522 Postmarket Surveillance? YES NO
- Is this device subject to the Tracking Regulation? YES NO
- Was clinical data necessary to support the review of this 510(k)? YES NO
- Is this a prescription device? YES NO
- Was this 510(k) reviewed by a Third Party? YES NO
- Special 510(k)? YES NO
- Abbreviated 510(k)? Please fill out form on H Drive 510k/boilers YES NO

Truthful and Accurate Statement Requested Enclosed

A 510(k) summary OR A 510(k) statement

The required certification and summary for class III devices

The indication for use form

Combination Product Category (Please see algorithm on H drive 510k/Boilers)

Animal Tissue Source YES NO Material of Biological Origin YES NO

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs)

No Confidentiality Confidentiality for 90 days Continued Confidentiality exceeding 90 days

Predicate Product Code with class: Additional Product Code(s) with panel (optional):

70- JAK, Class II

Review: Ruth Phily 2A05 9/29/06
(Branch Chief) (Branch Code) (Date)

Final Review: David A. Argonne 10/4
(Division Director) (Date)

Revised: 4/2/03

REVISED:3/14/95

THE 510(K) DOCUMENTATION FORMS ARE AVAILABLE ON THE LAN UNDER 510(K) BOILERPLATES TITLED "DOCUMENTATION" AND MUST BE FILLED OUT WITH EVERY FINAL DECISION (SE, NSE, NOT A DEVICE, ETC.).

"SUBSTANTIAL EQUIVALENCE" (SE) DECISION MAKING DOCUMENTATION

K 042388

Reviewer: Zarenka

Division/Branch: DRARD / RDB

Device Name: Q Ampir CT

Product To Which Compared (510(K) Number If Known): K040746

	YES	NO	
1. Is Product A Device	<input checked="" type="checkbox"/>	<input type="checkbox"/>	If NO = Stop
2. Is Device Subject To 510(k)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	If NO = Stop
3. Same Indication Statement?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	If YES = Go To 5
4. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?	<input type="checkbox"/>	<input type="checkbox"/>	If YES = Stop NE
5. Same Technological Characteristics?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	If YES = Go To 7
6. Could The New Characteristics Affect Safety Or Effectiveness?	<input type="checkbox"/>	<input type="checkbox"/>	If YES = Go To 8
7. Descriptive Characteristics Precise Enough?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	If NO = Go To 10 If YES = Stop <u>SE</u>
8. New Types Of Safety Or Effectiveness Questions?	<input type="checkbox"/>	<input type="checkbox"/>	If YES = Stop NE
9. Accepted Scientific Methods Exist?	<input type="checkbox"/>	<input type="checkbox"/>	If NO = Stop NE
10. Performance Data Available?	<input type="checkbox"/>	<input type="checkbox"/>	If NO = Request Data
11. Data Demonstrate Equivalence?	<input type="checkbox"/>	<input type="checkbox"/>	Final Decision: <u>SE</u>

Note: In addition to completing the form on the LAN, "yes" responses to questions 4, 6, 8, and 11, and every "no" response requires an explanation.

1. Intended Use: *Automated quantitative analysis of CT angiography image*
2. Device Description: Provide a statement of how the device is either similar to and/or different from other marketed devices, plus data (if necessary) to support the statement. Is the device life-supporting or life sustaining? Is the device implanted (short-term or long-term)? Does the device design use software? Is the device sterile? Is the device for single use? Is the device over-the-counter or prescription use? Does the device contain drug or biological product as a component? Is this device a kit? Provide a summary about the devices design, materials, physical properties and toxicology profile if important.

EXPLANATIONS TO "YES" AND "NO" ANSWERS TO QUESTIONS ON PAGE 1 AS NEEDED

1. Explain why not a device:
2. Explain why not subject to 510(k):
3. How does the new indication differ from the predicate device's indication:
4. Explain why there is or is not a new effect or safety or effectiveness issue:
5. Describe the new technological characteristics:
6. Explain how new characteristics could or could not affect safety or effectiveness:
7. Explain how descriptive characteristics are not precise enough:
8. Explain new types of safety or effectiveness questions raised or why the questions are not new:
9. Explain why existing scientific methods can not be used:
10. Explain what performance data is needed:
11. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

ATTACH ADDITIONAL SUPPORTING INFORMATION

510(K) Review

K06-2386

GENERAL INFORMATION

Company Name: Medis Medical Imaging Systems bv

Address: 9 Schuttersveld

Leiden

The Netherlands 2316XG

Dated: August 11, 2006

Received: August 16, 2006

Contact: J. I. Hollander, Quality Coordinator

Email: hhollander@medis.nl

Tradename: QAngio CT

Common Name: Analytic software package for CT

Intended Use: Automatic quantitative analysis of CT angiography images

Device to Which Equivalence is Claimed:

Manufacturer: Medis

Tradename: MRA-CMS

510(k) Number: K040746

Applicable Guidance: Software Contained in Medical Devices

Standard Questions:

1. Is the device subject to postmarket surveillance? No
2. Is a summary or certification of safety and effectiveness included? Summary
3. Is the device life supporting or life sustaining? No
4. Is the device implanted? (short term or long term) No
5. Does the device use software? No
6. Is the device sterile? No
7. Is the device for single, home or prescription use? Prescription
8. Does the device contain drug or biological products? No
9. Is the device subject to the Radiation Control Act or other Standards? DICOM

DETAILED REVIEW

Device Description:

Indications –

QAngio CT software has been developed for the objective and reproducible analysis of vessels in CTA images. It enables the quantitative analysis of CT angiograms based on automated segmentation. More specifically, QAngio CT can be used to quantify a number of lesion characteristics. It is intended for use as an auxiliary tool in assessing CTA studies in clinic practice and trials. The analysis results obtained with QAngio CT are to be interpreted by cardiologists and radiologists.

Technical Characteristics –

QAngio is an analytical software package for image post-processing that runs on Microsoft Windows XP. It can be installed on work stations or integrated in a PACS environment. QAngio is able to read DICOM CT images from all major vendors. Furthermore, it has an open architecture facilitating the exportation of results into DICOM SR files or to an xml general data base file for further statistical analysis of study results. Vessel analysis data, automatic or manual contour segmentation, detected stenosis and quantitative results can be saved in separate files enabling comparison of results by different users.

Laboratory and Clinical Data:

Medis conducted a validation study using phantoms consisting of hollow Perspex tubes with a stenosis in the center. For CTA scan the phantoms were filled with diluted contrast agent with the dilution chosen so the same contrast between vessel wall and lum was present as in patient CTA scans. A set of images that represents the different vessel anatomies that can be analyzed with QAngio was also selected and tested.

Labeling:

Labeling includes a printed user manual containing an introduction with warnings, standards and CE marking, a notification of intended use, a short description of QAngio and directions for use. Promotional material was included.

Software:

The company provided a description of their software development process including the system requirements analysis, system design, module implementation, system integration, testing and validation, quantification and release. A risk analysis was also included.

Substantial Equivalence:

Medis provided a tabular comparison of the features and specifications of the new device and the predicate. Both devices provide segmentation and quantification on 3D CTA data sets, automatic detection of 3D vessel contours, CSA values over the entire segment, percentage of diameter and area stenosis, volumes of stenosis, vessel and segment, automatic calculation of 3D reference contour and acceptance of images from major vendors. MRA-CMS is used for quantification of MR angiography images whereas QAngio is used for CT angiography images. Both devices accept DICOM images.

Recommendation:

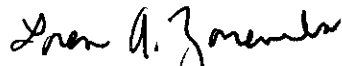
I believe that this device is substantially equivalent to:

90 – JAK

Classification should be based on:

892.1750 – Computed Tomography X-ray System

Class: II



Loren A. Zaremba
9-27-06

**SCREENING CHECKLIST
FOR ALL PREMARKET NOTIFICATION [510(k)] SUBMISSIONS**

510(k) Number: K062386

The cover letter clearly identifies the type of 510(k) submission as (Check the appropriate box):

- Special 510(k) - Do Sections 1 and 2
- Abbreviated 510(k) - Do Sections 1, 3 and 4
- Traditional 510(k) or no identification provided - Do Sections 1 and 4

Section 1: Required Elements for All Types of 510(k) submissions:

	Present or Adequate	Missing or Inadequate
Cover letter, containing the elements listed on page 3-2 of the Premarket Notification [510] Manual.	✓	
Table of Contents.	✓	
Truthful and Accurate Statement.	✓	
Device's Trade Name, Device's Classification Name and Establishment Registration Number.	✓	
Device Classification Regulation Number and Regulatory Status (Class I, Class II, Class III or Unclassified).	✓	
Proposed Labeling including the material listed on page 3-4 of the Premarket Notification [510] Manual.	✓	
Statement of Indications for Use that is on a separate page in the premarket submission.	✓	
Substantial Equivalence Comparison, including comparisons of the new device with the predicate.	✓	
510(k) Summary or 510(k) Statement.	✓	
Description of the device (or modification of the device) including diagrams, engineering drawings, photographs or service manuals.	✓	
Identification of legally marketed predicate device. *	✓	
Compliance with performance standards. * [See Section 514 of the Act and 21 CFR 807.87 (d).]	✓	
Class III Certification and Summary. **	NA	
Financial Certification or Disclosure Statement for 510(k) notifications with a clinical study. * [See 21 CFR 807.87 (i)]	NA	
510(k) Kit Certification ***	NA	

* - May not be applicable for Special 510(k)s.

** - Required for Class III devices, only.

*** - See pages 3-12 and 3-13 in the Premarket Notification [510] Manual and the Convenience Kits Interim Regulatory Guidance.

Section 2: Required Elements for a SPECIAL 510(k) submission:

//

	Present	Inadequate or Missing
Name and 510(k) number of the submitter's own, unmodified predicate device.		
A description of the modified device and a comparison to the sponsor's predicate device.		
A statement that the intended use(s) and indications of the modified device, as described in its labeling are the same as the intended uses and indications for the submitter's unmodified predicate device.		
Reviewer's confirmation that the modification has not altered the fundamental scientific technology of the submitter's predicate device.		
A Design Control Activities Summary that includes the following elements (a-c):		
a. Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis.		
b. Based on the Risk Analysis, an identification of the required verification and validation activities, including the methods or tests used and the acceptance criteria to be applied.		
c. A Declaration of Conformity with design controls that includes the following statements:		
A statement that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results of the activities demonstrated that the predetermined acceptance criteria were met. This statement is signed by the individual responsible for those particular activities.		
A statement that the manufacturing facility is in conformance with the design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review. This statement is signed by the individual responsible for those particular activities.		

Section 3: Required Elements for an ABBREVIATED 510(k)* submission:

	Present	Inadequate or Missing
For a submission, which relies on a guidance document and/or special control(s), a summary report that describes how the guidance and/or special control(s) was used to address the risks associated with the particular device type. (If a manufacturer elects to use an alternate approach to address a particular risk, sufficient detail should be provided to justify that approach.)		
For a submission, which relies on a recognized standard, a declaration of conformity [For a listing of the required elements of a declaration of conformity, SEE Required Elements for a Declaration of Conformity to a Recognized Standard, which is posted with the 510(k) boilers on the H drive.]		

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For a submission, which relies on a recognized standard without a declaration of conformity, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device.		
For a submission, which relies on a non-recognized standard that has been historically accepted by FDA, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device.		
For a submission, which relies on a non-recognized standard that has <u>not</u> been historically accepted by FDA, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device and any additional information requested by the reviewer in order to determine substantial equivalence.		
Any additional information, which is not covered by the guidance document, special control, recognized standard and/or non-recognized standard, in order to determine substantial equivalence.		

* - When completing the review of an abbreviated 510(k), please fill out an Abbreviated Standards Data Form (located on the H drive) and list all the guidance documents, special controls, recognized standards and/or non-recognized standards, which were noted by the sponsor.

Section 4: Additional Requirements for ABBREVIATED and TRADITIONAL 510(k) submissions (If Applicable):

	Present	Inadequate or Missing
a) Biocompatibility data for all patient-contacting materials, OR certification of identical material/formulation:	NA	
b) Sterilization and expiration dating information:	NA	
i) sterilization process		
ii) validation method of sterilization process		
iii) SAL		
iv) packaging		
v) specify pyrogen free		
vi) ETO residues		
vii) radiation dose		
viii) Traditional Method or Non-Traditional Method		
c) Software Documentation:	/	

Items with checks in the "Present or Adequate" column do not require additional information from the sponsor. Items with checks in the "Missing or Inadequate" column must be submitted before substantive review of the document.

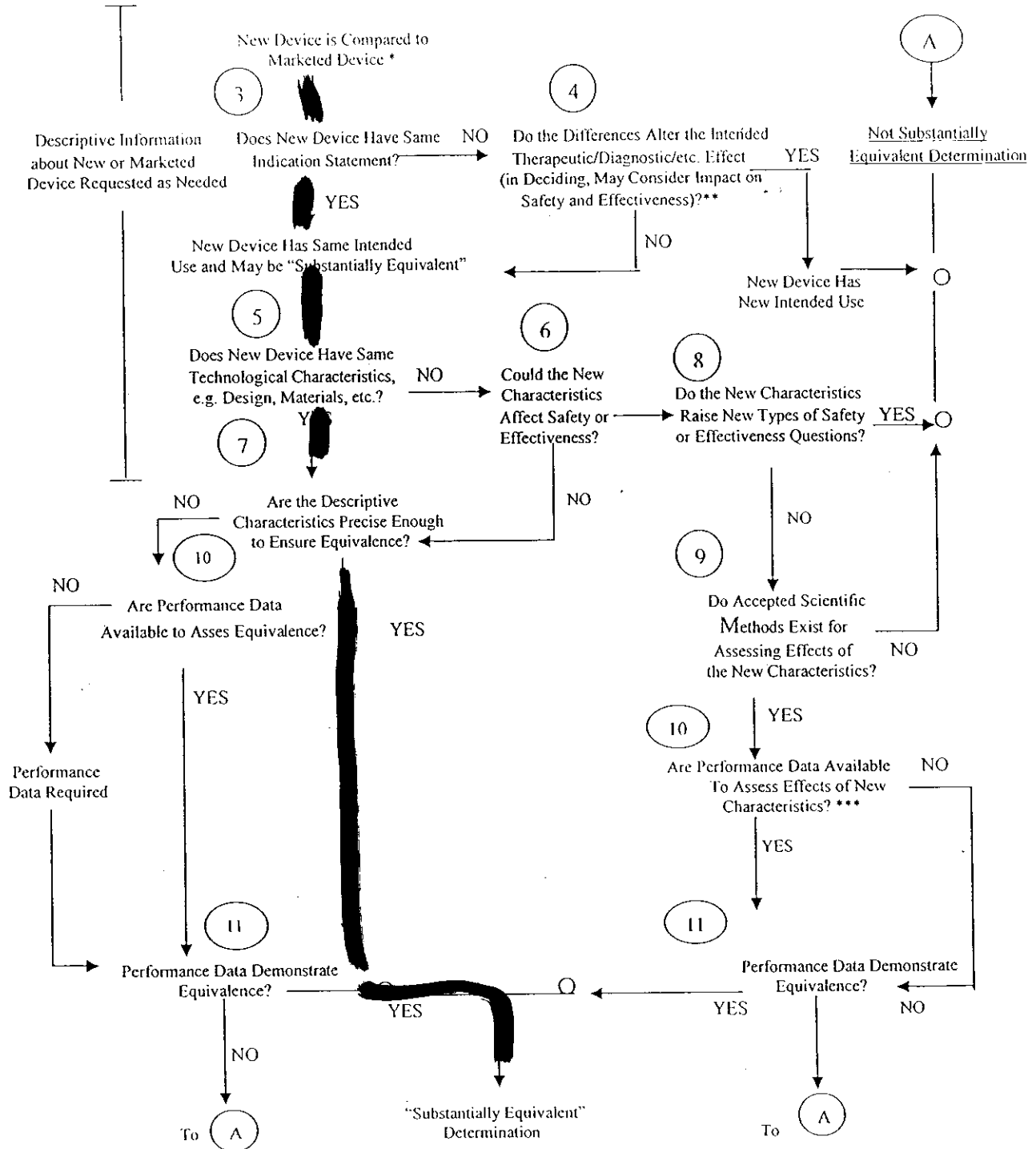
Passed Screening Yes No
 Reviewer: [Signature]
 Concurrence by Review Branch: _____
 Date: _____

Internal Administrative Form

	YES	NO
1. Did the firm request expedited review?		✓
2. Did we grant expedited review?		✓
3. Have you verified that the Document is labeled Class III for GMP purposes?	NA	
4. If, not, has POS been notified?		
5. Is the product a device?	✓	
6. Is the device exempt from 510(k) by regulation or policy?		✓
7. Is the device subject to review by CDRH?	✓	
8. Are you aware that this device has been the subject of a previous NSE decision?		✓
9. If yes, does this new 510(k) address the NSE issue(s), (e.g., performance data)?		
10. Are you aware of the submitter being the subject of an integrity investigation?		✓
11. If, yes, consult the ODE Integrity Officer.		
12. Has the ODE Integrity Officer given permission to proceed with the review? (Blue Book Memo #191-2 and Federal Register 90N0332, September 10, 1991.		

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510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



- * 510(k) Submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.
- ** This decision is normally based on descriptive information alone, but limited testing information is sometimes required.
- *** Data maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.