Beneris

Project no:	**022936**
Project acronym:	**Beneris**
Project title:	**Benefit-risk assessment for food: an iterative value-of-information approach**
Instrument:	STP – Specific Targeted Project

Periodic Activity Report

Fourth project report (D48a)

Due date of deliverable:	**1 Oct, 2009**
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Dissemination level:	**PU**
Start date of project:	**April, 1st 2006**
Duration:	**3,5 years**

Organisation name of the lead contractor for this deliverable:
National Institute for Health and Welfare – THL (Jouni Tuomisto)

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Publishable Executive Summary

Beneris

Project acronym: Beneris
Project full title: Benefit-risk assessment for food: an iterative value-of-information approach
Contract no: 022936
Related to other Contract no: 022957/QALIBRA
Project duration: 1 April 2006 - 30 September 2009
Reporting period: **1 April 2009 - 30 September 2009**

Project objectives

The general objective of this project is to **create a framework for handling complicated benefit-risk situations**, and apply it for analysis of the benefits and risks of certain foods. The first food commodity to be used in the development of the methodology is fish. Some of the detailed objectives are listed below.

Objectives in developing benefit-risk analysis methods

- To develop Bayesian belief networks (BBN) to handle complicated benefit-risk situations, and to develop a decision support system (DSS) based on BBN.
- To develop improved methods for dose-response assessment, combining epidemiological and toxicological data, and apply them in combining epidemiological and toxicological information on fish contaminants (esp. dioxins and PCBs).
- To develop an integrated repository of surveillance, nutrient and food consumption data that is capable of receiving, analyzing, and disseminating the accumulated data for benefit-risk analysis and to key stakeholders.

Scientific objectives in food risks and benefits

- To estimate average nutrient intakes and food consumption in various subgroups based on national registries in three countries and to explore the use of the data in benefit-risk analysis.
- To estimate the health benefits of fish, and understand the effect of fish on different population subgroups (age, health, pregnancy etc.)
- To establish the association between external dose (intake) and internal dose (concentrations in the body) by analysing contaminants (PCDD/Fs, PCBs, PBDEs, organotin compounds, PCNs and Hg/methyl-Hg) from 100-200 placentas.
- To find out the effects of certain policy options on dietary habits and on intake of important nutrients and contaminants (e.g. vitamin D, n-3 fatty acids, dioxins, PCBs). As an example, does a restrictive recommendation on fish eating increase meat consumption?

Objectives in dissemination

- To integrate results into updated benefit-risk assessments, and evaluate the remaining uncertainties and their importance for decision-making.
- To develop an internet interface for publishing risk assessment results.
- To develop a method to publish entire benefit-risk models over the Internet using XML.
- To disseminate the results and to evaluate the relevance and usefulness of the work done in the project from the perspective of an end-user / authority.

Participants

Role	**No.**	**Name**	**Short name**	**Country**
Coordinator	1	National Institute for Health and Welfare (formerly: National Public Health Institute)	THL (formerly: KTL)	FI
Contractor	2	Delft University of Technology	TU Delft	NL
Contractor	3	Oy Foodfiles Ltd	FFiles	FI
Contractor	4	Food Safety Authority of Ireland	FSAI	IE
Contractor	5	National Food Institute / Technical University of Denmark	DTU	DK
Contractor	6	Food Safety Authority of Denmark	FVST	DK
Contractor	7	Lendac Ltd	Lendac	IE
Contractor	8	Fundación Privada para la Investigación Nutricional	FIN	ES

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Public website for the project: http://www.beneris.eu
See also: http://en.opasnet.org

Work performed

The fourth reporting period focused in finalising several major tasks that were still ongoing at the end of the third reporting period. These include D19 Contaminants in placenta, D21 Intake of contaminants: natl registries, D26 Evaluation of patterns, D36 Fetus contaminants from mother's diet, D39 Combined database, D38 Full benefit risk analysis of fish, D40 Full benefit-risk analysis: vegetables, D42 VOI analysis of fish, D43 Consumer reactions, D44 Third project meeting, D45 Evaluation of benefit-risk analysis in a food safety agency, and D46 End-user evaluation. In addition, the development of the user interface for Opasnet and Opasnet Base continued.

Results achieved so far and expected end results

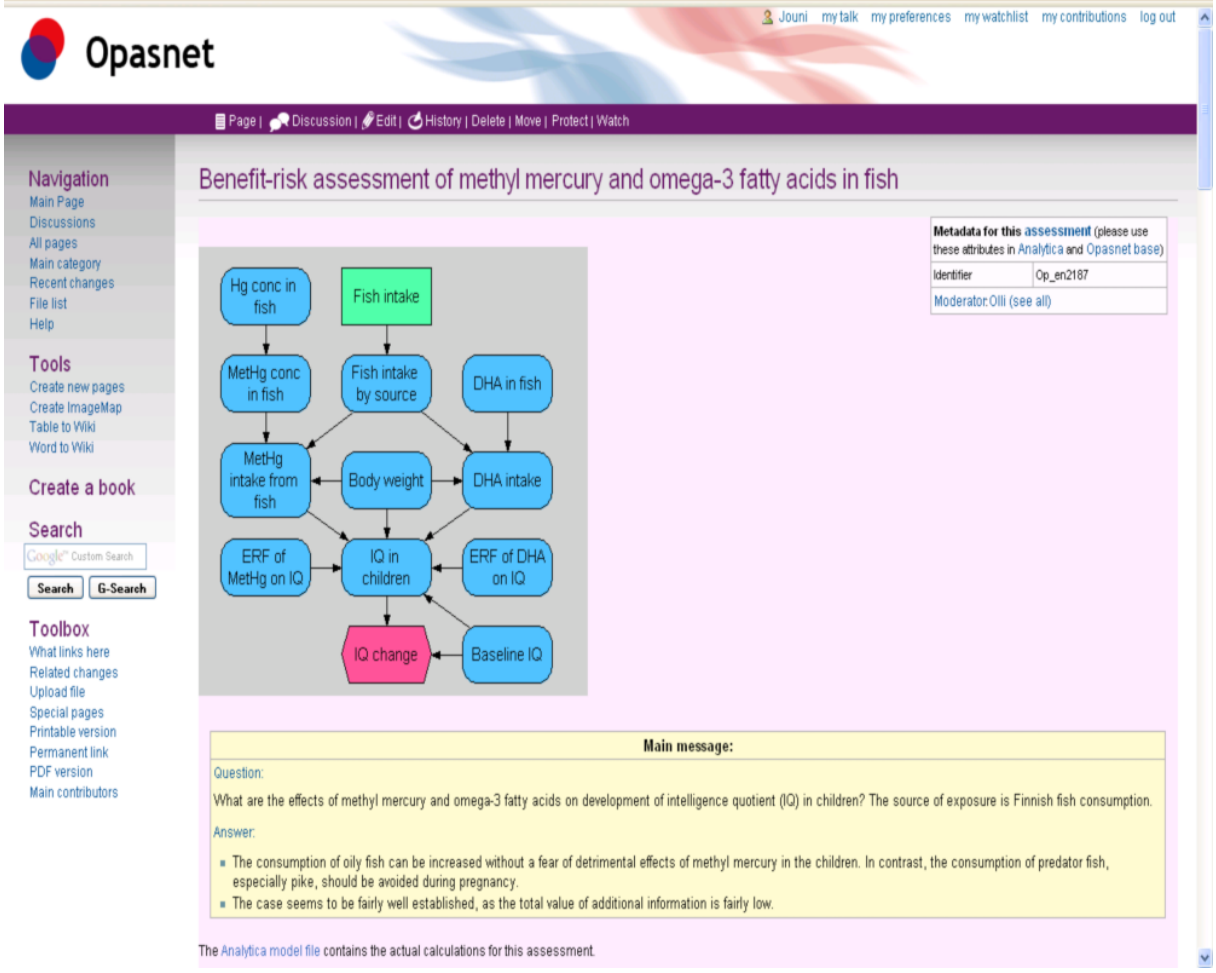
The new benefit-risk assessment method (open assessment) was described on the web workspace Opasnet (http://en.opasnet.org) , although this work will also continue after Beneris. The Beneris fish case study was described in Opasnet in two parts: a separate sub-assessment was performed about methylmercury and omega-3 fatty acids in children. Several assessment case studies are under way, also outside Beneris. The website is designed for assessments that are performed openly, allowing also for stakeholder participation. A database called Opasnet Base (http://en.opasnet.org/w/Opasnet_Base) was used to upload model results and nutrition studies performed in Beneris. The work has produced practical experience on this kind of collaborative work, and this experience has been used to develop the benefit-risk assessment methods further.

Intentions for use and impact

The methods and tools developed in Beneris were and are being offered to other projects, or real-life benefit-risk assessments. Opasnet workspace is available for this purpose. Several projects have already started to use the website for their own work: Intarese, Heimtsa, Hiwate, and Plantlibra (funded by EU); Claih, Bioher, and Hitea (funded by the Academy of Finland); and Bepraribean (European project on risks and benefits of food). We hope that it will become a place where several assessors are able to share their information and work collaboratively, thus producing better assessments than alone.

The main elements of the publishable results and the plan for using and disseminating the knowledge

The main products of Beneris are the improved methodology (open assessment) for benefit-risk assessments, the web workspace Opasnet for performing them in a collaborative way, and the Opasnet Base database containing ready-to-use information needed in assessments. Interested assessors have been identified and contacted for working with their own assessments using the website. These practical real-life examples will be a major method for disseminating the results of Beneris.



An example of a benefit-risk analysis performed in the project website with the Internet tools: Benefit-risk assessment of methyl mercury and omega-3 fatty acids in fish. This sub-assessment graph is shown as an example only, because the full fish case graph has more than a thousand nodes and would not fit on the page.

Section 1 - Project objectives and major achievements during the reporting period

The general objective of this project is to create a framework for handling complicated benefit-risk situations, and apply it for analysis of the benefits and risks of certain foods. The first food commodity to be used in the development of the methodology is fish.

The specific objectives of this project, and the progress related to them are described below.

Objectives in developing benefit-risk analysis methods

The exact objectives in the Description of work are:

- To develop Bayesian belief networks (BBN) to handle complicated benefit-risk situations, and to develop a decision support system (DSS) based on BBN.
- To develop improved methods for dose-response assessment, combining epidemiological and toxicological data, and apply them in combining epidemiological and toxicological information on fish contaminants (esp. dioxins and PCBs).
- To develop an integrated repository of surveillance, nutrient and food consumption data that is capable of receiving, analyzing, and disseminating the accumulated data for benefit-risk analysis and to key stakeholders.

The progress during the reporting period is described under these three bullet points. In addition, general progress with a new benefit-risk approach is described first.

Progress during the reporting period

<u>New approach</u>

The new approach has been described in previous reports. The last period of Beneris has been a time of writing down syntheses about different aspects of the method, and applying them in in practical cases. Relevant pages to look at for an overview of the method include the following, and links from those pages.

- http://en.opasnet.org/w/Open_assessment
- http://en.opasnet.org/w/Opasnet
- http://en.opasnet.org/w/Discussion
- http://en.opasnet.org/w/Open_participation
- http://en.opasnet.org/w/Assessment
- http://en.opasnet.org/w/Variable

In general, it can be said that the method itself has been established enough to be applicable, but there is a lot of work to be done to develop practices that participants are willing to use. This is because the benefit-risk analysis method was developed theory first, and Beneris fulfilled that task. The new projects need to develop these practices further.

The current status of the benefit-risk analysis method developed in Beneris was critically evaluated. There are still many critical issues that were not resolved in Beneris: credibility in the eyes of the user; difficulty in participating in a very different process than traditional assessment, and technical problems related to user interfaces of Opasnet and Opasnet Base.

On the other hand, Beneris was able to develop a web workspace for participatory benefit-risk assessments, and a database for detailed input data and results. This result offers a good starting point for new projects to develop these tools further. Indeed, there are several projects that are already using them.

BBN methods

The main development during this period was to add user-friendly functionalities in Uninet, the BBN software. These include the possibility to make saturated graphs and the possibility to save both unconditionalized and conditionalized samples of a BBN.

Improved dose-responses

TU Delft developed a new method for estimating the Cox model that leads to an explicit expression for the bias which depends only on the observed quantities and does not depend on the coefficients of excluded covariates under prevailing assumptions. A more detailed explanation is in WP1 and in Appendix "New approach to the missing covariates problem in the Cox regression".

Intergrated repository (Opasnet Base)

The main properties of Opasnet Base are described on the Opasnet website (http://en.opasnet.org/w/Opasnet_base and http://en.opasnet.org/w/Opasnet_Base_structure). During this reporting period, we developed interfaces both for uploading data to Opasnet Base, and an interface to download data from it. In addition, it is now possible to utilise the data directly in an Analytica benefit-risk analysis model so that the model automatically downloads the input data it needs from Opasnet Base.

We also started to utilise Opasnet File, which is an additional feature of the data repository. It was not in the original plan, but we found it a very useful addition to the Opasnet workspace. It is a file management system that can be used for storing reports and other files that are important background information but are not actively edited, unlike e.g. assessments or models. The file management system makes it possible to automatically list all relevant files in any relevant page in Opasnet. This is a very efficient way of distributing background material. For examples, see e.g. http://en.opasnet.org/w/M-files.

Scientific objectives in food risks and benefits

The exact objectives in the Description of work are:

- To review the existing databases and their availability for chemical contaminant data in Europe, and integrate available data.
- To estimate average nutrient intakes and food consumption in various subgroups based on national registries in three countries and to explore the use of the data in benefit-risk analysis.
- To estimate the health benefits of fish, and understand the effect of fish on different population subgroups (age, health, pregnancy etc.)

- To establish the association between external dose (intake) and internal dose (concentrations in the body) by analysing contaminants (PCDD/Fs, PCBs, PBDEs, organotin compounds, PCNs and Hg/methyl-Hg) from 100-200 placentas.
- To combine existing and new data from food consumption databases with data on levels of contaminants in fish. The special emphasis is on children and the developing foetus.
- To estimate distributions of nutrient intake and food consumption relevant to benefit-risk analysis in a number of populations, and also the variability in exposure among various subgroups in the population.
- To identify food consumption patterns and food choices that determine the intake of those nutrients and contaminants that are related to benefit/risk-balance of a food item.
- To explore the usability of these patterns in another country than in which they were developed.
- To find out the effects of certain policy options on dietary habits and on intake of important nutrients and contaminants (e.g. vitamin D, n-3 fatty acids, dioxins, PCBs). As an example, does a restrictive recommendation on fish eating increase meat consumption?

Progress during the reporting period

Nutrient intakes and existing databases

The food intake data obtained from the partners have been uploaded to Opasnet Base. Contaminant intakes have been estimated in e.g. D21 (Intake of contaminants: natl registries) and D36 (Fetus contaminants from mother's diet) have not yet been uploaded. This reflects the fact that there are still developmental needs in Opasnet Base for future projects: the calculation of estimates, and the uploading of the results, are still two completely separate tasks and take time to do them. We already have plans how to develop Opasnet Base into a tool that can be used to calculate new estimates based on existing data (in this case, national food intake data). This was not in the Beneris plan, but we have identified this an important developmental need for Intarese and Plantlibra projects, which continue the work.

Contamination research

Additional task of measuring the fat concentrations of placenta was undertaken. Based on this, new pollutant concentration estimates were produced, and these were compared with the mothers' pollutant intake.

Benefit-risk analyses

The full Bayesian belief network (BBN) model on risks and benefits of fish was finalised and uploaded to the project website. Different parts of the model were described in either the protected website or Opasnet, depending on whether the part was going to be a key scientific information to be published elsewhere or not.

The vegetable case was finalised in Spain, Finland, and Ireland. It assessed the benefits and risks of fortification of foods with folate, vitamin A, and vitamin C in children.

Objectives in dissemination

The exact objectives in the Description of work are:

- To integrate results into updated benefit-risk assessments, and evaluate the remaining uncertainties and their importance for decision-making.
- To evaluate the integration methodology by all partners and develop it further.
- To develop an internet interface for publishing risk assessment results.
- To develop a method to publish entire benefit-risk models over the Internet using XML.
- To develop methods to collect feedback from end-users about benefit-risk analyses.
- To enhance the availability of existing databases through this interface.
- To disseminate the results and to evaluate the relevance and usefulness of the work done in the project from the perspective of an end-user / authority.

Progress during the reporting period

There have been several streams of activities during the reporting period:

- End user evaluation was performed.
- The Beneris and Opasnet workspacess were utilised.
- Tools to publish models in the Internet have been developed.
- Beneris methods were presented in several meetings and via email. The project results were also written as scientific manuscripts.

<u>The Opasnet workspasce</u>

The descriptions of the fish case study were written to Opasnet (or Beneris website in the case of non-public material). The material was cross-linked in such a way that the actual BBN model had links to Opasnet; the assessment page in Opasnet had a link to the model file; and each variable page had a link to Opasnet Base, which contained the actual sample results of the variable.

End users were involved with a questionnaire to evaluate the contents of the assessment (D43 Consumer reactions) and also the Opasnet workspace and open assessment methods (D46 End user evaluation).

<u>Tools to publish models</u>

TUDelft developed the user functionalities in Uninet, the BBN software. For a detailed description, see WP5.

Opasnet workspace contains the model files, and they can be downloaded and run by interested people. However, the user must have the appropriate software to run the model. To overcome this problem, we applied Analytica Web Publisher to publish our models. It is a server-based platform that runs Analytica models. The user only needs a web browser, and all

the computing happens on the server side. The fish case study models can be viewed and run with AWP.

Dissemination of benefit-risk analysis methods and the case study of fish

The benefit-risk analysis methods developed in Beneris were presented and will be presented in several meetings. For a detailed list, see Section 2 Dissemination of knowledge. In addition, the work to publish case study material in Opasnet continued. The first sub-model to be published was about fish, methylmercury, and omega-3 fatty acids. This was later expanded by adding publishable parts of the full fish case study. Parts that are not yet publishable are described in the protected website.

Several research manuscripts were written about the results of the case studies and the methods developed in Beneris. A publication plan was developed together with Qalibra, and it is presented in WP6 Cluster activities. The actual publishing of the results will start 2010.

The methods and tools developed in Beneris will be disseminated in a workshop organised in Kuopio, Finland, February 15-19, 2010. The planning of this event was started. http://www.facebook.com/event.php?eid=119417187921&ref=mf

Section 2 - Workpackage progress over the period

This section describes the progress of work by workpackage.

WP1: "Method (top-down approach to risk-benefit analysis)"

WP leader	KTL/THL / Jouni Tuomisto
Partners involved	KTL/THL, TUDelft, FFiles, FSAI, DTU, FVST, Lendac, FIN
Workpackage objectives	• To introduce all Partners to the common methods to be used: integrated modelling and Bayesian belief networks. (Partners: all; D1, D15; year 2) • To develop Bayesian belief networks (BBN) to handle complicated benefit-risk situations. (Partners: THL, TUDelft; D8, D22; year 3) • To develop a decision support system (DSS) based on BBN. (Partners: TUDelft, THL; D25, D46, D48; year 4) • To develop improved methods for dose-response assessment, combining epidemiological and toxicological data. (Partners: THL, TUDelft; D8; year 1) • Apply the dose-response methods in combining epidemiological and toxicological information on fish contaminants (esp. dioxins and PCBs). (Partners: THL, TUDelft; D38; year 4 M42) • To integrate results from the previous workpackages into an updated assessment. (Partners: all; D38, D40; year 4 M42) • To evaluate the remaining uncertainties and their importance for decision-making. (Partners: TUDelft, THL, FIN; D38, D40; year 4 M42) • To evaluate the integration methodology by all Partners and develop it further. (Partners: all; D15, D35, D45; year 4 M41) • To produce risk assessments that will be used for Internet interface and Dissemination Workpackages. (Partners: all; D22, D38, D40; year 4 M42)

The work in this workpackage was organized under three main themes: **open assessment method**, **Bayesian belief networks** (BBN), and **improved dose-response**.

Starting point at beginning of reporting period

Main achievements of the 1st reporting period:

- Major new developmental areas for BRA method were identified and solutions suggested
- Work done in collaboration with Intarese
- A functional BBN was developed and tested with pilot data
- A draft method for combining epidemiological and toxicological data was developed in collaboration with Intarese

Main achievements of the 2nd reporting period:

- Improved the BBN model for benefit-risk assessments (model calibration)
- Improved the BBN software (especially its data mining capabilities)
- Data provided on contaminants intake from fish by Irish consumers
- Designed and developed Internet based tools to facilitate conversion and dissemination of benefit-risk assessment models and data to e.g. Mediawiki format.

Main achievements of the 3rd reporting period:

- The development of Opasnet website continued by launching assessments and adding new methods.
- The Opasnet Base (data repository) its functional state, and first data were uploaded.
- Improved dose-responses methods were developed for Cox proportional hazards model; the work for combining toxicological and epidemiological data was delayed.
- Interfaces for the website and the modelling software (Uninet, Analytica) were developed.
- Interfaces for data exchange between Opasnet Base and the modelling software were developed.

Main achievements of the 4th reporting period

- Documentation of the open assessment method was written to Opasnet.
- Cox proportional hazards model was improved.
- Additional functionalities for user input were developed (e.g. questionnaires)
- Opasnet File was opened to facilitate the use of background material (e.g. reports) in Opasnet

Progress towards objectives

FIN:
The analysis which FIN conducted for the vegetable case in children – studying fortification with folate, vitamin A and vitamin C – can be applied to produce assessments that may be disseminated via the Beneris portal.

FSAI:
FSAI has dedicated significant time during P4 in critically examining the WP1 approach to risk assessment and benefit:risk analysis developed under Beneris using the Pyrkilo methodology, and the transition to the open risk assessment approach using the Opasnet workspace. The outcome of this analysis is primarily articulated as D45, Benefit-risk analysis for a food safety agency (WP1) and D46, End-user evaluation (WP5), where the methodology developed under WP1 has been assessed not only by FSAI staff (primarily Iona Pratt) but also by a psychologist, Dr Jim Flynn, under contract to FSAI.

THL:
Most of the method development of benefit-risk analysis (in the form of open assessment) has been performed already before the fourth reporting period. Therefore, we focused on adding functionalities that actually make it easier to apply the methods developed. The new functionalities include evaluation form, Opasnet Base interface, and Opasnet File.

Previously, the only way of contributing was to get a user account in Opasnet and directly edit pages (or related talk pages) in the workspace. Many people were reluctant to do this for several reasons, including the following: lack of experience with wiki workspaces, a fear that other people will change the contents signed by the user, and uncertainty about where and how to write a particular piece of information.

To overcome these problems, THL developed additional ways of contributing. Now it is possible to create questionnaires inside Opasnet pages. The moderator of an assessment can ask the users questions related to that particular page. The users don't need a user account,

and their responses cannot be changed afterwards by other users. An example of a questionnaire is http://en.opasnet.org/w/End_user_evaluation .

THL has uploaded more data into the Opasnet Base (formerly known as data repository), and Opasnet base is now in full use. THL will continue uploading data into the base, promoting and extending the use of the open assessment method as useful data becomes available for everyone.

We also started to apply Opasnet File, which is an additional feature of the data repository. It was not in the original plan, but we found it a very useful addition to the Opasnet workspace. It is simply a file management system that can be used for storing reports and other files that are important background information but are not actively edited, unlike e.g. assessments or models. The file management system makes it possible to list all relevant files in any relevant page in Opasnet. This is a very efficient way of distributing background material. For examples, see e.g. http://en.opasnet.org/w/M-files.

TU Delft:

During the last period of the project TU Delft finalized its work on the missing covariates problem in the Cox regression initiated in the previous years. To recall, Cox proportional hazard model is the most widely used regression model for analyzing censored survival data in epidemiology including data coming from the case-control studies. It allows to identify significant variables affecting disease, death or survival, estimate the regression coefficients of these variables and also to infer about the relative risk. It is commonly known that the conclusions drawn from the Cox model are wrong if some of the pertinent covariates are omitted. The most commonly reasons for neglecting covariates are: 1) simplification of the problem studied, 2) lack of awareness of the importance of covariates, and 3) inability to measure covariates.

The properties of the bias in coefficient estimates resulting from omitting covariates in the Cox model have been studied since early 1980s. However, all formulas for the bias derived until now are of little use in practice since they depend on the coefficients of the omitted covariates which are usually unknown. With regard to this problem TU Delft developed a new method for estimating the Cox model that leads to an explicit expression for the bias which depends only on the observed quantities and does not depend on the coefficients of excluded covariates under prevailing assumptions. A report describing the main details of this approach is attached to this document (see Appendices / "New approach to the missing covariates problem in the Cox regression").

Moreover, during the reporting period, TU Delft improved and also developed new features in its Bayesian belief network (BBN) software UNINET. However, since these new functionalities support the dissemination of results of the benefit-risk assessments modelled with BBNs, they are described under the work of WP5.

Deviations from the project workprogramme, and corrective actions taken/suggested

FSAI:

FSAI has not contributed actively to any of the open risk assessment activity on Opasnet, and in depth evaluation of the integration methodology has been restricted by the fact that the method has been under continuous development and in a process of change. The original objective had been that the application of the benefit:risk analysis methodology in the work of a food safety agency would be explored by the FSAI, and it would have been of considerable value to us to do so in our recent national assessment of the risks and benefits of folic acid fortification of food. However, the methodology emerging under WP1 was not sufficiently

mature enough test this formally (via Opasnet) during the lifetime of the Beneris project. No corrective action can now be taken to remedy this situation.

Deliverables

No.	Name	WP	Due (project month)	Date of submission: Actual	Date of submission: Fore-seen	Reasons for deviation and re-cuperative measures	Indicative person-months: Estim.	Indicative person-months: Used	Lead contractor(s)
D33	Consumer info on case results	**1**	24	15 Dec, 2009		Consumer info will be about the final case study. It will be pub-lished in "International Innnova-tion"	1	0.5	THL
D35	Pyrkilo guide 3	**1**	26	Aug 6, 2009		Was delivered after the final ad-justments to the data repository sections had been made.	3	1	THL
D45	Application of BRA to FSA	**1**	40	15 Dec, 2009	-	FSAI undertook an assessment of the method as part of the D45. Evaluation of the method by a FSA was delayed, given the fact that evolution of the method has also been delayed.	2	0.5	FSAI

Milestones

None in this reporting period.

WP2: "Database"

The work done in WP2 is described in detail below, under the sub-workpackage titles.

Deliverables

No.	Name	WP	Due (project month)	Date of submission: Actual	Date of submission: Foreseen	Reasons for deviation and recuperative measures	Indicative person-months: Estim.	Indicative person-months: Used	Lead contractor(s)
D19	Contaminants in placenta	**2**	17	May 15, 2009 (first version) 15 Dec 2009 (resubmission)		In addition to the original study plan, some further analyses of placentas were undertaken. The statistical analyses were finalised in September 2009.	17	19	THL
D21	Intake of contaminants: natl registries	**2**	18	15 Dec, 2009		The deliverable has been adjusted to include only Finnish data, because the PCDD/F concentration data that has been requested from the Commission during P2 has still not been delivered.	1	2	THL (FVST)
D26	Evaluation of patterns	**2**	20	15 Dec, 2009		Delayed due to data delays from DG Sanco. Will be done for Finland only with data in the Opasnet Base.	2	2	THL
D36	Fetus contaminants from mother's diet	**2**	27	15 Dec, 2009		Delivery delayed because new chemical analyses had to be performed.	2	2	THL
D39	Combined database	**2**	33	15 Dec, 2009		The database exists but delay is due to database interface and data management.	2	2	THL, DTU

Milestones

(Presented by sub-workpackage below.)

WP2.1: "Food intake studies"

WP leader	FSAI / Iona Pratt
Partners involved	KTL/THL, FSAI, DTU, FVST, FIN
Workpackage objectives	• To review the existing databases and their availability for chemical contaminant data in Europe, and integrate available data. (partners DTU; D7; year 3) • To estimate average nutrient intakes and food consumption in various subgroups based on national registries in three countries and to explore the use of the data in benefit-risk analysis. (partners FSAI, THL, DTU, FIN; D7, D10, D11, D14; year 2) • To estimate distributions of nutrient intake and food consumption relevant to benefit-risk analysis in a number of populations, and also the variability in exposure among various subgroups in the population. (partners FSAI, THL, DTU, FIN; D7, D10, D11, D14; year 2) • To identify food consumption patterns and food choices that determine the intake of those nutrients and contaminants that are related to benefit/risk-balance of a food item. (partner THL; D27; year 3) • To explore the usability of these patterns in another country than in which they were developed. (partner THL; D26; year 4 M41) • To find out the effects of certain policy options on dietary habits and on intake of important nutrients and contaminants (e.g. vitamin D, n-3 fatty acids, dioxins, PCBs). As an example, we will test the hypothesis whether a recommendation to restrict fish eating would increase meat consumption. (partners THL, TUDelft; D38; year 4 M42)

Starting point at beginning of reporting period

Main achievements of the 1st reporting period:

- Data collecting and computation completed on food consumption data for Finnish, Spanish and Irish populations, as classified by gender, age classes, various food stuffs and fish species. In addition, some nutrient intakes from Finnish and Spanish populations were classified as above.

Main achievements of the 2nd reporting period:

- Provision of detailed data on contaminant concentrations in fish and on pollutant intakes by Irish consumers
- Food consumption data for different age groups of the Irish population made available
- Distributions of food consumption and nutrient intakes in adults, children, and pregnant women have been calculated and reported
- Food consumption patterns and food choices identified for Finnish adults
- Acquired survey-based food consumption data and fish species-specific intake data for Spain

Main achievements of the 3rd reporting period:

- Food intake data from Spain (related to WP4) was collected.
- Mercury and fatty acid data from Ireland was collected.
- Food intake patterns in Finland were analysed.
- Food intake data from Ireland (related to WP4) were evaluated but dropped.

Main achievements of the 4th reporting period

- Additional data were collected for the vegetable case study.

- Several manuscripts were written about food and contaminant intakes.
- Food intake data was uploaded to Opasnet Base.

Progress towards objectives

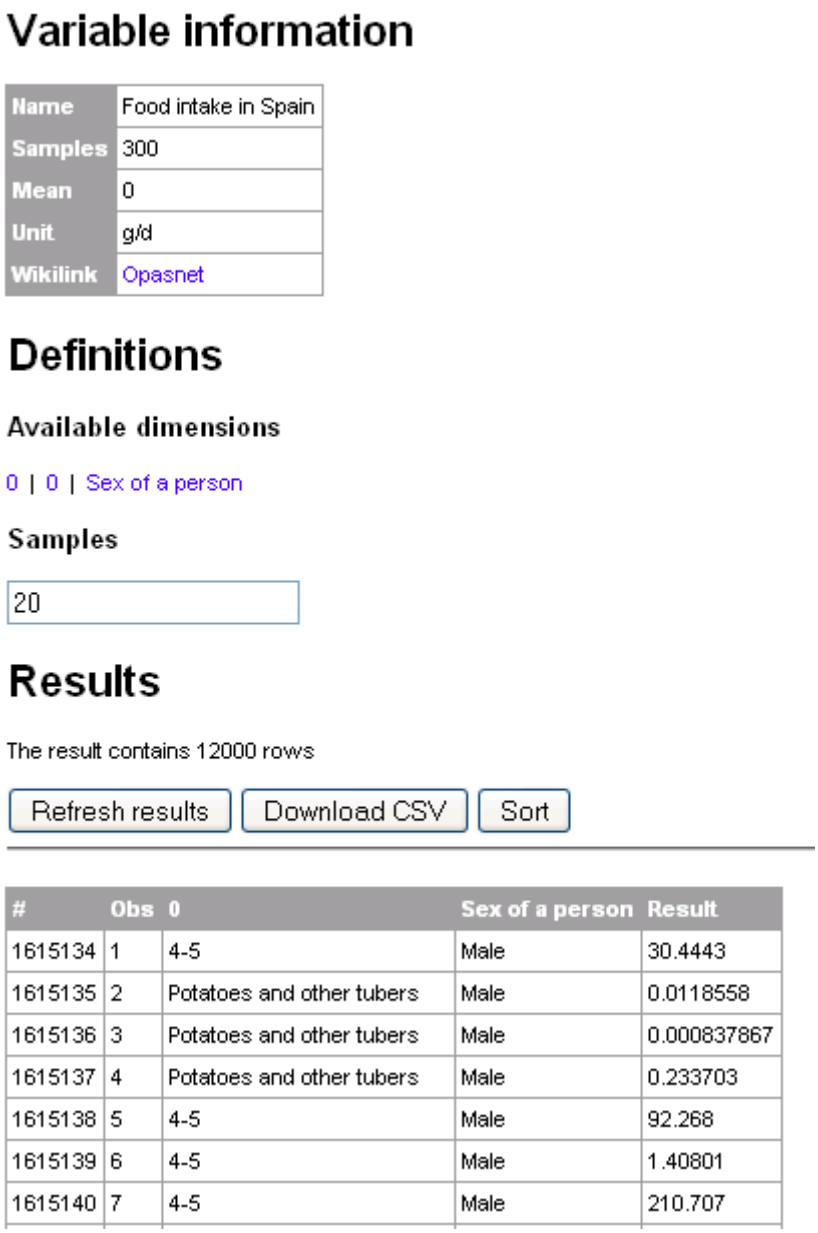
FSAI:
During P4, FSAI has provided individual consumption data for vegetables by young children in Ireland, together with intake data for folate, vitamin A and vitamin C (from vegetables and other dietary groups) for the same population group, and also information on fortification levels of these nutrients in certain food groups. These data have contributed to the database, and have also been used in the 2nd benefit: risk case study. Provision of these data had been thought to present considerable difficulties for FSAI during P3, as Iona Pratt only had access to summary data and was unaware that a nutritionist colleague was able to provide these data at individual level.

THL:
D21 (Intake of contaminants: national registries) has been prepared in a form of a manuscript "Intakes of polychlorinated dibenzo-p-dioxins and furans, polychlorinated biphenyls, polybrominated diphenylethers, and mercury from food in Finnish children: risk assessment implications" by Karjalainen AK, Kiviranta H, Sinkko H, Tuomisto JT, Kronberg-Kippilä C, Virtanen SM, Hallikainen A, Hirvonen T has been written. The manuscript is nearly ready for submitting. The manuscript compares the estimated contaminant intakes to national or international guideline values.

D26 (Evaluation of patterns) has been prepared in a form of a manuscript "Modelling the intake of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs): impact of energy underreporting and number of reporting days in dietary surveys" by Hirvonen T, Sinkko H, Hallikainen A, Kiviranta H, Pietinen P, Valsta L, Tuomisto J. This is further work based on D14 (Dietary patterns) and D20 (Intake of contaminants in children). This manuscript is also nearly ready for submitting.

THL has created webpages for all the three food intake studies (Denmark, Finland, Spain). Some of the webpages display links to the Opasnet database that can be queried to draw random samples from statistical distributions based on original data. These samples will thus be available for anybody with an internet connection.

See the figure below as an example of the data available.



Variable information

Name	Food intake in Spain
Samples	300
Mean	0
Unit	g/d
Wikilink	Opasnet

Definitions

Available dimensions

0 | 0 | Sex of a person

Samples

20

Results

The result contains 12000 rows

Refresh results | Download CSV | Sort

#	Obs	0	Sex of a person	Result
1615134	1	4-5	Male	30.4443
1615135	2	Potatoes and other tubers	Male	0.0118558
1615136	3	Potatoes and other tubers	Male	0.000837867
1615137	4	Potatoes and other tubers	Male	0.233703
1615138	5	4-5	Male	92.268
1615139	6	4-5	Male	1.40801
1615140	7	4-5	Male	210.707

Deviations from the project workprogramme, and corrective actions taken/suggested

FSAI:
In relation to leadership of this WP, the situation is still that the main responsibility for this now rests with THL. This is considered appropriate since THL have the necessary expertise and overall vision of the Beneris strategy and are in a position to coordinate the work on food intake studies in the most effective manner.

Milestones

None in this reporting period.

WP2.2: "Contaminant concentration"

WP leader	KTL/THL / Terttu Vartainen
Partners involved	KTL/THL, DTU
Workpackage objectives	• The general objective is to find out association between external dose (intake) and internal dose (concentrations in the body). The immediate objectives are (partners THL, DTU; D19, D20, D36; year 4 M42) • To analyse contaminants (PCDD/Fs, PCBs, PBDEs, organotin compounds, PCNs and Hg/methyl-Hg) from 50-200 placentas. (partners THL, DTU; D19; year 4 M38)

Starting point at beginning of reporting period

Main achievements of the 1st reporting period:

- The preparation and chemical analysis of 130 placenta samples for methyl mercury (DTU) and other pollutants including PCDD/Fs, PCBs, PBDEs, organotin compounds, and PCNs (KTL/THL) has started.

Main achievements of the 2nd reporting period:

- Placental contaminants analyzed by KTL/THL for seven groups of persistent organic pollutants (PCDD/F, PCB, PBDE, PBB, PCN, DDE, OT)
- Started studies of association between intake and internal dose
- Placentas also analyzed for the concentrations of Hg, Se, As, Cd, and Pb (DTU)
- Analysis of 130 placentas for methyl mercury finalized (DTU)

Main achievements of the 3rd reporting period:

- Statistical analyses based on the pollutant concentration studies were performed.
- The need for new chemical analyses (fat concentrations) was identified. (These analyses started on the fourth year.)

Main achievements of the 4th reporting period

- Fat-based concentrations of pollutants were measured in the placenta study.
- A draft manuscript was written about the placenta results and their relation to mother's contaminant intake.

Progress towards objectives

THL:
After delivering D19 and during the work on D36 it became obvious that the original measurements on placenta which produced fresh-weight-based concentrations did not meet all the criteria imposed by work on highly lipophilic compounds. Therefore it was decided in June 2009 at the final meeting of the BENERIS-QALIBRA consortium that fat-based concentrations will be essential. In Budapest it was decided that the fat content be measured during the summer and early fall of 2009. The measurements were carried out, and thereafter the work has focussed on re-delivering D19 and re-calculating the associations between calculated/estimated intake and internal dose measured as placental concentrations.

In parallel with the deliverables, we are working on the manuscripts for scientific papers about the occurrence of POP in placenta and about the associations between the estimated intake and the measured concentrations in placenta.

Deviations from the project workprogramme, and corrective actions taken/suggested

THL:
Deliverables D19 and D36 were delayed due to the need for further original analyses (please see above). Now the situation has been corrected, and D19 and D36 have been finalised together with the P4 report.

Milestones

None in this reporting period.

WP2.3: "Contaminant intake studies"

WP leader	KTL/THL / Tero Hirvonen
Partners involved	KTL/THL, FSAI, DTU, FIN
Workpackage objectives	• To combine existing and new data of food diary data with data of contaminants. The special emphasis is on children and the developing foetus. (partners THL, DTU, FIN, FSAI; D20, D29, D30; year 3)

Starting point at beginning of reporting period

Main achievements of the 1st reporting period:

- A probabilistic intake estimation method (Monte Carlo simulation) has been developed and tested, using data from WP2.1 and WP2.2.

Main achievements of the 2nd reporting period:

- Calculated and reported the food intake of subpopulations (D18), intake of contaminants in children (D20), and the food intake of pregnant women (D18 and 29-30)
- Calculations of contaminants during pregnancy
- Detailed data made available on contaminant concentrations in, and their intakes from fish by Irish adults.
- A review on toxicity data of methylmercury in progress
- Database for intake of and critical contaminants (PCDD/F, PCB, Hg) in fish was derived from published data

Main achievements of the 3rd reporting period:

- Intakes of contaminants (D29, D30) per age and sex were analysed.
- Intakes of contaminants by the fetus from mother's diet were analysed but not finalised, because a need for further chemical analyses was identified.

Main achievements of the 4th reporting period

- Correlation of fetus contaminant concentrations and mother’s diet were analysed.
- Impact of underreporting and survey methods on intake pattern estimates was studied.

Progress towards objectives

THL:
Contaminant contents of D36 (Fetus contaminants from mother’s diet) were reanalyzed in order to get the contents per gram of fat. Results, tables and figures have been redone. Report has been finalised together with the P4 report..

THL and its collaborator, the Finnish Food Safety Authority (Evira), have created a manuscript about the evaluation of food patterns (D26), entitled as "Modelling the intake of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs): impact of energy underreporting and number of reporting days in dietary surveys".

Deviations from the project workprogramme, and corrective actions taken/suggested

THL:

Contaminant contents of D36 (Fetus contaminants from mother's diets) were reanalyzed in order to get the contents per gram of fat. This has further delayed the original timetable. Other reasons for the delay have been the lack of working time of the statistician as well as the unification of National Public Health Institute (KTL) with another governmental institute which has brought unexpected work tasks to the personnel (these two reasons have been reported in the 3rd period report).

Milestones

Name	WP no.	Due (project month)	Actual achiev. date	Foreseen achiev. date	Reasons for deviation and recuperative measures	Lead contractor(s)
Intake of different contaminants in different subpopulations is compared with the TDI values of EC and WHO.	**2.3**	not determined	15 Dec, 2009		Was dependent on D21.	THL
Food consumption advice is given for relevant subpopulations.	**2.3**	not determined	15 Dec, 2009		Was dependent on D33.	THL

WP2.4: "Database work"

WP leader	DTU / Ole Ladefoged
Partners involved	KTL/THL, DTU, Lendac
Workpackage objectives	• To develop an integrated repository of surveillance, nutrient and food consumption data, (DTU, THL; D39; year 4 M41) • To develop a robust system capable of receiving datasets from multiple sources on an ongoing basis, (THL; D39; year 4 M41) • To develop a rapid analytical tool for deriving intake estimates for key contaminants and essential nutrients to address the overall aims of the project. (TUDelft, THL; D29, D30; year 3) • To develop tools for making the accumulated data readily available to key stakeholders involved in risk analysis including the European Food Safety Authority and national authorities. (THL; D39; year 4 M41)

Starting point at beginning of reporting period

Main achievements of the 1st reporting period:

- Based on the evaluation of existing work on food databases, it was concluded that the collection of data for benefit-risk analyses should be designed so that there is a special emphasis on the applicability and simplicity of the data.

Main achievements of the 2nd reporting period:

- Report on available data for fish consumption and concentrations in Denmark, Finland and Ireland (D7)
- The overall structure of an integrated repository of data has been outlined, developed, and implemented in close collaboration with Intarese project. The database has been set up for testing and further development.

Main achievements of the 3rd reporting period:

- The concentrations of methyl mercury, cadmium, lead, arsenic, total mercury and selenium in 130 human placentas were analysed.
- The second version (with an improved and more flexible structure) of Opasnet Base (data repository) was launched.
- The interface for downloading data from the new version was developed.
- The first interface version for uploading data to the repository was developed.
- The first data were uploaded to the repository.
- Methods to link assessments in Opasnet and data in Opasnet Base were developed.
- Intake estimate methods for contaminants were developed and applied (D29, D30).

Main achievements of the 4th reporting period

- Interfaces for uploading to and downloading from Opasnet Base were improved.
- Case study results were uploaded to Opasnet Base.
- File management system was added to Opasnet.

Progress towards objectives

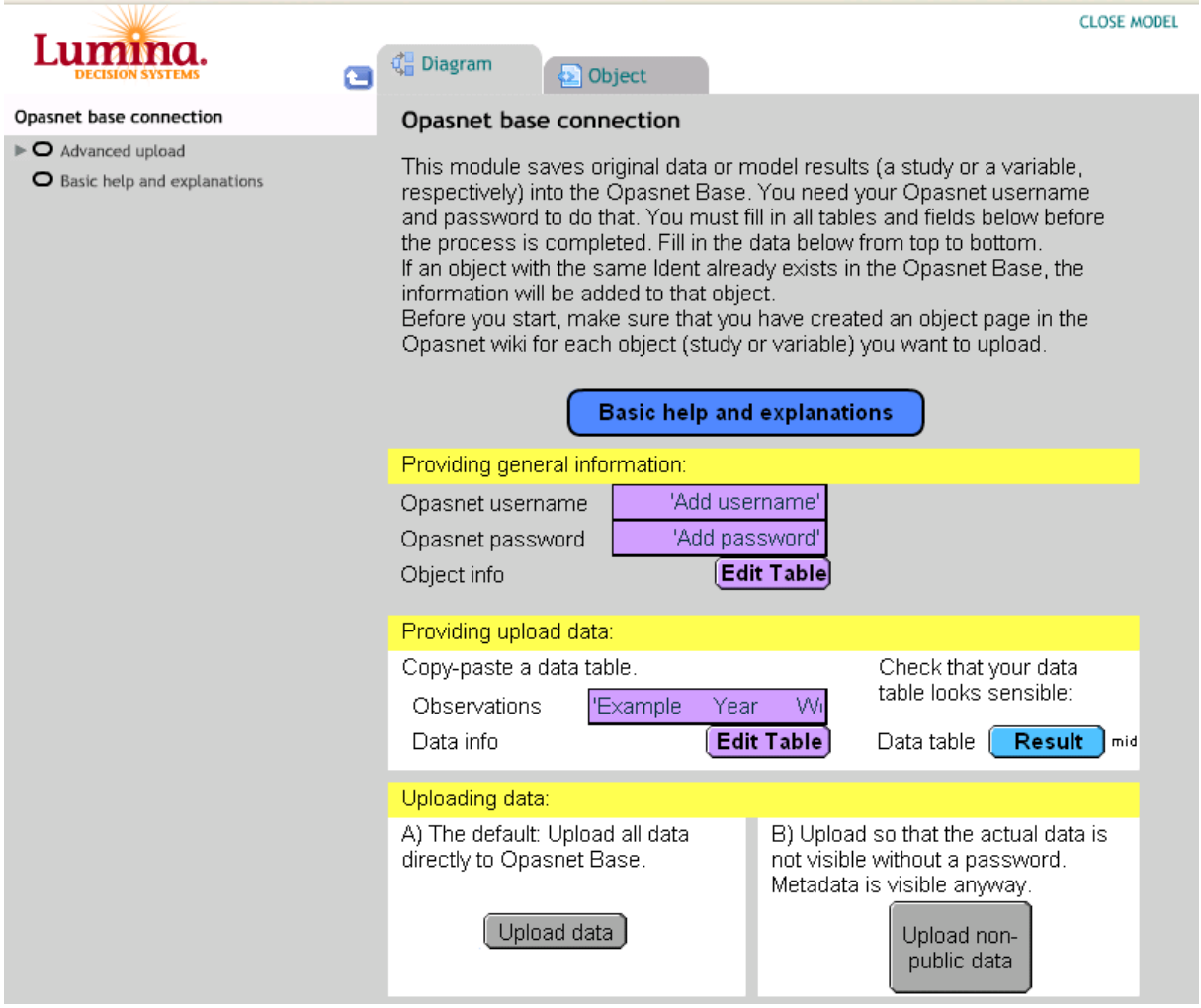
Opasnet Base has been described in detail in the third period report, and also in D39: Combined database. Only a brief description is given here, with a focus on work that has been performed during the fourth period.

Opasnet Base is a part of Opasnet and a storage and retrieval system for results of variable and data from studies. It is designed to be flexible enough to store information in almost any format: probability distributions or deterministic point estimates; spatially or temporally distributed data; or data with multiple dimensions. It can be used as a direct source of model input data, thus making it possible to use shared input information sources such as population data, climate scenarios, or dose-responses of pollutants. Opasnet Base can be accessed via links from Opasnet variable and study pages (e.g. the meta data box), via a web interface and via the model Opasnet base connection.ANA.

During the fourth reporting period, THL further developed the user interface of the database. A common problem is that the data stored can be very large (e.g. the Spanish food intake data alone contains 252,000 rows). The interface is needed so that the user can restrict to e.g. a specific food item, age group, or sex. This reduces the download time considerably and gives more usable results to the user. A figure of the interface is shown with WP2.1.

We also started to utilise Opasnet File, which is an additional feature of the data repository. It was not in the original plan, but we found it a very useful addition to the Opasnet workspace. It is a file management system that can be used for storing reports and other files that are important background information but are not actively edited, unlike e.g. assessments or models. The file management system makes it possible to automatically list all relevant files in any relevant page in Opasnet. This is a very efficient way of distributing background material. For examples, see e.g. http://en.opasnet.org/w/M-files.

THL also developed the user interface for researchers who want to upload their results into the database. Now there exists a web form to which the data can be copied and pasted, so that the user does not need any modelling tools to upload data. There are several different upload modes depending on the size and format of the data. A new feature is also that if the user has Analytica modelling software, the user can upload a whole model with a large number of variables at the same time.



The main page of the interface for uploading data into the Opasnet Base.

Deviations from the project workprogramme, and corrective actions taken/suggested

None.

Milestones

None in this reporting period.

WP3: "Case 1: Fish"

WP leader	FFiles / Henna Karvonen
Partners involved	KTL/THL, TUDelft, FFiles, DTU, FIN
Workpackage objectives	The general objective is to perform risk-benefit analysis on fish based on the methods developed in WP1; nutrition and contaminant information collected in WP2; and benefit dose-responses derived in this WP. We will estimate the dose-response slopes for different health benefits of fish including uncertainty around these estimates. A key task is to quantify the cardiovascular benefits of fish on different population subgroups, like cardiovascular patients vs. healthy adults, using the large body of published literature. Other potential benefits of fish include beneficial effects during pregnancy and early childhood on childhood development, allergies, and osteoporosis. All of these effects will be reviewed, prioritized and the most important effects and their uncertainties will also be quantified. (THL, TUDelft, FFiles; D38; year 4 M42)

In general, WP3 aims at performing benefit-risk analysis on fish consumption based on methods developed in WP1 and data on consumption and contaminants collected in WP2. TU Delft has had the main responsibility of developing the Bayesian belief network, while KTL/THL, together with FFiles, has prepared the preliminary case study.

The different threads of work were described in more detail in the 1st-year report.

Starting point at beginning of reporting period

Main achievements of the 1st reporting period:

- A BBN developed for the full BRA of fish.
- Literature review on health effects of fish was completed. Evaluation of the most relevant health effect indicators of fish is under way.
- The preliminary BRA on fish was finalised and published.

Main achievements of the 2nd reporting period:

- Reviews on quantifiable cardiovascular health benefits of fish and omega-3 fatty acids (D16) and other health benefits of fish (D28) completed
- An improved, more sophisticated version of the BBN model for the case study (TU Delft)
- Collection of data needed for the new BBN model has been started (FSAI, FIN)

Main achievements of the 3rd reporting period:

- Health impact review about fish-related endpoints was performed (D28).
- Parts of the fish case study were described and published in Opasnet website.
- Data collection for completing the case study continued.
- The interface tools for combining models (in Uninet) and Opasnet website were tested.

Main achievements of the 4th reporting period

- The full fish case study was finalised.
- The case study descriptions were written to either Opasnet or the protected Beneris workspace.
- Value of information analysis was performed for the fish case study.

Progress towards objectives

Foodfiles:
Foodfiles has reviewed the existing data from clinical trials and epidemiological studies on the various health effects of fish in children. During this period, Foodfiles has written a review on the health effects of fish among children in developed countries for the further development of the benefit-risk analysis. The report has been finalized and is attached to the final report (see Appendices / "Health Effects Of Fish Among Children In Developed Countries").

Since several meta-analyses on the cardiovascular health and the effects of fish consumption or intake of fish oils in adults have been published during the recent years, we felt that a different perspective was needed for the meta-analysis of health benefits. Consequently, we included the effect of age on the health benefit assessment.

Furthermore, Foodfiles participated in the Final joint meeting of Beneris and Qalibra projects in Budapest on June 10-11th, 2009.

FSAI:
While FSAI was not involved in this WP, other than to provide data on levels of POPs, mercury and unsaturated fatty acids in fish (WP2), in the last phase of the study it has evaluated the results of the risk-benefit analysis on fish now available on Opasnet, and has reported on this in deliverables D45 and D46.

THL:
TU Delft has finalized the coding of the model. It now comes with the complete set of input information for the fish case study, and the results have been scrutinized at the THL. The full model now contains all sub-models for dealing with various health endpoints (cardiovascular, cancer, teeth development, central nervous system). THL has analysed variables of interests by conditioning their values (i.e. studying the potential policy options using what-if analyses), and these results are presented in deliverable D38 (Full benefit-risk analysis of fish). A manuscript to be submitted to a peer reviewed journal based on the results has been outlined in collaboration with other participants of this workpackage.

One submodel of the full case study, namely methylmercury and omega-3 fatty acids in children, was analysed and published separately in Opasnet: http://en.opasnet.org/w/MeHg-Omega3 . In addition, consumer reactions were collected based on this sub-assessment (see D43 in WP5).

A value-of-information (VOI) analysis was performed as a part of the fish case study (D42 Value-of-information analysis for fish). The screening analysis identified a small number of variables that seem to require further scrutiny, if the decision is to be improved with better knowledge. THL developed a new screening VOI method that can be applied directly on BBNs.

TU Delft:
The responsibility of TU Delft in this WP was to build and quantify a Bayesian belief network (BBN) model for the benefit-risk analysis of fish. The achievements of TU Delft in relation to the development of this model are described below.

The final scope of the fish case study is summarized below:

1. The assessment focuses on the Finnish population only.

2. There are five specific population subgroups of interest in this study: infants (0-2 years old), children and adolescents (2-18 years), adults (18-55 years), elderly (55+) and pregnant women (exposure to pregnant women is used as a proxy for foetal exposure).

3. Nutrients and environmental pollutants selected for the assessment include dioxins (PCDD/Fs), polychlorinated biphenyls (PCBs), mercury as methyl mercury (MeHg) and omega-3 fatty acids (EPA and DHA).

4. Health effects of fish encompass neurological effects during early development, developmental dental defects, cardiovascular disease and cancer.

5. Fish species covered in the study are domestic species only caught in Finland's inland waters and the Baltic sea. These species are: Baltic herring, vendace (sea/inland), whitefish (sea/inland), pike (sea/inland), perch (sea/inland), Atlantic salmon, pike-perch (sea/inland).

The process of developing the final BBN model was broken down into two main phases. In the first phase three separate BBNs were created - first describing the effect of prenatal exposure to methyl mercury and omega-3 fatty acids (DHA only) on the development of intelligence quotient (IQ) in children, second examining the impact of dioxins and PCBs on developmental dental defects in children, and third evaluating coronary heart disease mortality and cancer risk in adults exposed to all four fish compounds selected. In this way every benefit-risk situation, focusing either on adults or children, could be analyzed at a very detailed level. In the second phase, due to the presence of overlapping variables, all three models were integrated into a single BBN. The complete BBN for the fish case study developed in BENERIS is presented in Figure 1. It consists of 524 probabilistic nodes, 637 functional nodes and 1812 arcs.

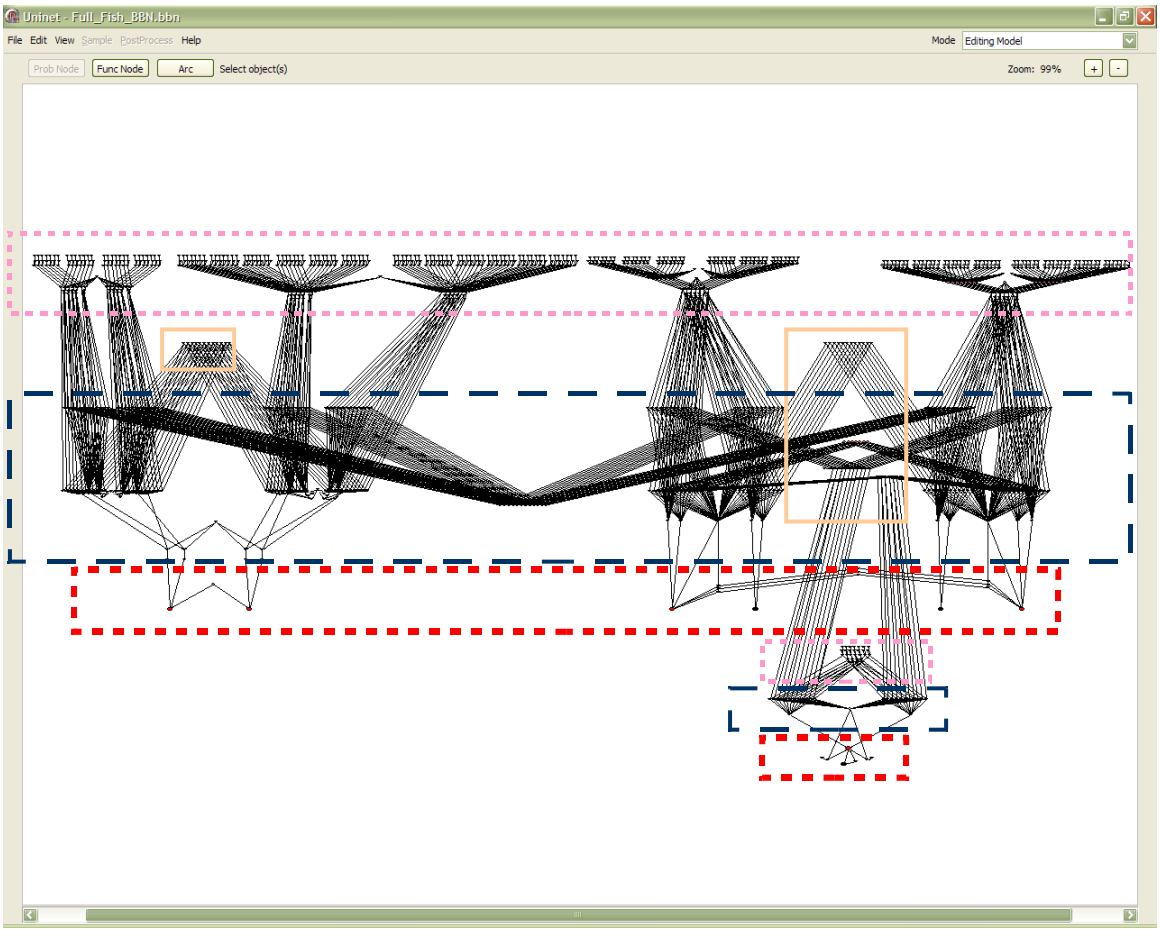


Figure 1: The BBN for the case study on fish in BENERIS; the pink doted squares cover fish consumption variables and demographic variables; the peach solid lined squares include variables representing concentrations of fish compounds; the blue dashed squares surround exposure variables and also personal/demographic variables; the red dotted squares contain exposure-response functions, baseline responses and health impacts.

The first sub-model was completed during the second year of the project while the other two were developed during the current reporting period. During the last six months TU Delft actively worked on acquiring missing data to complete the model and also analyzed and processed this data to describe the variables desired. Moreover, to facilitate the communication among project participants regarding the contents of the model and the results TU Delft described all model variables in the Opasnet website.

To quantify the model the data on the fish consumption and the content of nutrients and contaminants in fish collected in WP2 were used. Other data, on personal and demographic variables, exposure-response functions and other variables used at the intermediate steps of the assessment were gathered within WP3 and came from the literature search, Finnish databases and even from the in-house experts.

The detailed description of data and methods used by TU Delft to quantify the fish BBN is provided in the deliverable D38 on the full benefit-risk analysis of fish. However, the up-to date information about the fish case study can also be found through the Opasnet website http://en.opasnet.org/w/Benefit-risk_assessment_of_fish_consumption_for_Beneris.

Deviations from the project workprogramme, and corrective actions taken/suggested

None.

Deliverables

No.	Name	WP	Due (project month)	Date of submission: Actual	Date of submission: Foreseen	Reasons for deviation and recuperative measures	Indicative person-months: Estim.	Indicative person-months: Used	Lead contractor(s)
D38	Full benefit risk analysis of fish	**3**	32	15 Dec, 2009		Reasons for the delay relate to tool interfaces and data gathering.	3	6	THL TUDelft

Milestones

Name	WP no.	Due (project month)	Actual achiev. date	Foreseen achiev. date	Reasons for deviation and recuperative measures	Lead contractor(s)
Quantification of the effect of fish on cardiovascular disease and mortality. Identification of the need for further expert elicitation and other work. Feedback from of benefit-risk analysis.	**3**	18	April 2009		The expert needs have been identified. The information was collected using in-house experts during 2008-2009.	THL/TUDeflt

Recommendations for further research specifying the areas considered most important for the public health	**3**	24	15 Dec, 2009	Was dependent on D42.	

WP4: "Case 2: Vegetables"

WP leader	FIN Lluis Serra-Majem
Partners involved	KTL/THL, FSAI, DTU, FIN
Workpackage objectives	• To perform a preliminary benefit-risk analysis for vegetables in diet. A special focus will be on alternative sources of nutrients, such as supplements and food fortification. (THL, FIN; D40; year 4 M38) • To perform an updated benefit-risk analysis based on the preliminary analysis, the new intake data from several countries, and the redefined scope based on discussions among Beneris researchers. (THL, FIN; D40; year 4 M42)

Starting point at beginning of reporting period

Main achievements of the 1st reporting period:

- None (needed further development and application of methods in WP3).

Main achievements of the 2nd reporting period:

- Four exhaustive reviews to generate summary tables on the risk-benefit relationship of vegetable consumption, with focus on 1) health risk associated with vegetable intake due to contaminant contents 2) health effect [+ or –] of vegetable consumption 3) health benefits of supplements and fortified foods containing key vegetable nutrients 4) general health effects [+ or –] of vegetable consumption in adults.
- Case study 2 was scoped in the mid-term meeting in Helsinki.

Main achievements of the 3rd reporting period:

- The study protocol for the vegetable case study was finalised.
- The analyses were performed for the Finnish data (the work was finalised in the beginning of the year 4).
- The Spanish data were prepared for the analysis (to be done during year 4).

Main achievements of the 4th reporting period

- The vegetable case study was performed in Spain, Finland, and Ireland.

Progress towards objectives

FIN:
FIN has conducted a thorough analysis of Spanish data in children aged 3 to 6 regarding vegetable consumption and the possible need to fortify non-vegetable foods so as to avoid inadequate intakes of folate, vitamin A and vitamin C. Given that the available data on vegetable intake in this age group shows that the intake is quite low, and that the percentage of intakes of these nutrients below the Estimated Average Requirements (EAR) in the lowest consumers is high, further analysis on fortification was conducted.

The analysis consisted of following the BENERIS protocol that was provided for use in this case study. The food fortification analysis was conducted in the three non-vegetable food groups that were specified for the “vegetable case”, which include:

I) Fruit juices, margarines, milks and yoghurt

II) All foods in option "I" and breads

III) All foods in option "II" and curl milks, milk puddings, breakfast cereals, jams, sweets, chocolates, soft drinks, biscuits, snacks, dressings, ice creams, cheeses and mineral waters.

The same procedure was conducted for each vitamin and for each food group as follows: With folate and vitamin A, we carried out fortification by adding step by step 1 µg nutrient per 100 kcal. With vitamin C, 1 mg was added per 100 kcal. Then we estimated the intake distribution for all age groups from 3 to 6 years, adjusting for intraindividual variability.

Please refer to Deliverable 40 for further details on these analyses.

FSAI:
FSAI has collaborated with THL on the benefit-risk analysis for vegetables in the diet of children. The primary contribution has been to provide vegetable consumption data for 6-year old Irish children, together with intake levels of folate, vitamin A and vitamin C (WP2). However, FSAI has specific data on the contribution of vegetables and other food groups to the intake of these nutrients, relative to intake from fortified foods (e.g. cereals) and food supplements, which are of value in the overall benefit-risk analysis. Irish data was used to run the case study for vitamin C in Ireland.

THL:
Benefit-risk analyses of vegetables were performed for the Finnish data with 3- and 6-year-olds for vitamins A and C and for folate in Finland. In addition, THL collaborated with FIN to perform the same analyses in Spain with Spanish data. Individual Irish data for 6-year-olds were obtained in the beginning of October, and THL also collaborated with FSAI to perform the model runs with Irish data. The analyses, figures and conclusions are described in detail in D40 (Full benefit-risk analysis: vegetables).

Deviations from the project workprogramme, and corrective actions taken/suggested

FSAI:
There was a delay in FSAI becoming involved in this part of the project, due to lack of clarity about the availability of the data. However, the case study was run successfully in Ireland. FSAI will continue to provide information to THL after the close of the project, for as long as is needed.

THL:
In the deliverable 40 (Full benefit-risk analysis: vegetables) some methodological assistance has been needed from the Finnish partner. The analyses were first performed for the Finnish data and according to the experiences to the Spanish data. During the spring 2009 the Irish individual food consumption data was under work and got ready in October. This has also delayed the analyses. Other reasons for the delay have been reported in the 3rd period: lack of working time of the statistician in Finland and the unification of National Public Health Institute (KTL) with another governmental institution which has brought unexpected work tasks for the personnel.

Deliverables

No.	Name	WP	Due (project month)	Date of submission Actual	Date of submission Fore-seen	Reasons for deviation and re-cuperative measures	Indicative person-months Estim.	Indicative person-months Used	Lead contractor(s)
D40	Full benefit-risk analysis: ve-getables	**4**	34	15 Dec, 2009		The work was repeated in Spain and Ireland after it was done in Finland.	2	3	THL

Milestones

None in this reporting period.

WP5: "Dissemination"

WP leader	FSAI / Iona Pratt
Partners involved	THL, TUDelft, FSAI, DTU, FVST, Lendac, FIN
Workpackage objectives	• To develop an internet interface for publishing risk assessment results. Specifically, (Lendac, THL; D17; year 2) • to develop a method to publish entire benefit-risk models over the Internet using XML; (Lendac, THL; D17; year 2) • to develop methods to collect feedback from end-users about benefit-risk analyses; (Lendac, THL, FSAI; D17, D46; year 4 M42) • to enhance the availability of existing databases through this interface. (THL D39; year 4 M41) • To disseminate the results and to evaluate the relevance and usefulness of the work done in the project from the perspective of an end-user / authority. (FSAI, THL, TUDelft; D31, D43, D46; year 4 M42)

Starting point at beginning of reporting period

Main achievements of the 1st reporting period:

- Beneris website was opened.
- A tool for transforming BRA models into web pages was developed.
- The planning of a Gordon conference was started.

Main achievements of the 2nd reporting period:

- Development of the Pyrkilo method towards the more sophisticated Open Assessment methodology
- Development of a website to outline project objectives, progress reports, news, events etc.
- Development of Internet based tools to facilitate conversion and dissemination of results of benefit-risk models (Lendac)
- Conversion of benefit-risk model data to Mediawiki format was completed
- Development and opening of the open assessment website (http://en.opasnet.org) in collaboration with the Intarese project.
- Conference about environmental health in the Valamo monastery (December 3-5, 2007) organized in collaboration with Qalibra project.
- Preliminary benefit-risk assessment on fish published in a peer reviewed journal (Leino et al. 2008)
- Workshop on evaluation of the methodologies arranged (Berlin, September 2007), with two participants from Qalibra
- Kuopio Open Assessment workshop in February 2008, with participants from Beneris, Intarese, Envirisk, Hiwate, and Heimtsa

Main achievements of the 3rd reporting period:

- Open Assessment Workshop 2009 was organised in February 2009.
- End-user evaluation (D31) was performed in spring 2009.

- The Beneris tools were made available to other projects. EU-wide Intarese, Heimtsa, and Hiwate and several Finnish projects are actively using them.
- Draft dissemination plan (D5) was written (and subsequently accepted in June 2009).
- Feedback tools were developed for the www.beneris.eu website.
- Guidance for model publishing in Opasnet was improved.
- Guidance for commenting and peer review in Opasnet (based on the mid-term review) was created.
- A model publisher (website that runs model without a need to install anything) was set up and first models made available.
- Background data (useful for several assessments) was made available via Opasnet Base.
- Collaboration with Brafo was continued by providing Beneris data to Brafo and commenting Brafo work.

The streams of dissemination activities and future plans of dissemination were discussed in detail in the 1st-year report.

Main achievements of the 4th reporting period

- Beneris methods and case study results and methods were presented in several meetings.
- An end user evaluation was performed.
- User interfaces were developed for the tools (Opasnet and Uninet).
- Opasnet was used to disseminate results of the fish case study and open assessment methods.

Progress towards objectives

FIN:
A poster on the BENERIS vegetable case study in Spain is being submitted for presentation at the meeting of the Spanish Federation of Food and Nutrition Societies (FESNAD), to be arranged in March 2010.

FSAI:
FSAI has undertaken an evaluation of the relevance and usefulness of the work done in the project from the perspective of an end-user / authority and has written a report on the outcome (a part of D46).

In P4 FSAI has re-evaluated the proposal to specifically look at communicating the outcome of the benefit-risk assessment of contaminants in fish, which was carried out using the Beneris methodology, to a test population of Irish consumers, and to test their reactions to the information. A decision was taken in year 4 not to proceed with this. FSAI has written a report on the outcome (a part of D43).

THL:
THL has carried out an end-user evaluation to get feedback and enhance the usability of the information accumulated in Opasnet (a part of D46 End user evaluation).

The main model variables have been published on the Internet , and the main model results have been uploaded to Opasnet Base. However, because the model is a subject of two or three scientific articles, the whole model cannot yet be published on the Internet, Instead, it is

available to Beneris and several other projects on the protected website Heande. http://heande.opasnet.org/wiki/Benefit-risk_analysis_of_fish

THL has also agreed about a publication plan in final meeting in June 2009, including joint publications with QALIBRA. See also WP6.

In September 2009, THL participated in a workshop where the QALIBRA tool was presented. The workshop continued with a BRAFO project workshop, where the QALIBRA tool was applied on BRAFO case studies. THL represented Beneris in both workshops.

THL has published a statistical summary for the use of Opasnet and Beneris wikipages as part of the end user evaluation (deliverable 43).

Beneris and Qalibra agreed on a dissemination strategy in the Final project meeting in Budapest in June 2009. The practical actions in the plan relate mostly to Opasnet, and therefore this mostly guides Beneris - and especially THL after the project has ended. The dissemination strategy has been sent to the Commission previously, and it is also available on Opasnet: http://en.opasnet.org/w/Dissemination_plan_for_benefit-risk_assessment_of_food .

THL developed the user interface of Opasnet Base (D39 Combined database). This is described in detail in WP 2.4.

THL has presented results of Beneris methods in several meetings (see Section 2 Dissemination of knowledge).

TU Delft:

UNINET is a standalone software application developed by TU Delft that implements non-parametric continuous-discrete Bayesian belief networks (BBNs) [1,2,3]. This specific type of BBN is used in BENERIS to model benefit-risk assessments and especially to describe and assess the benefits and risks associated with the consumption of fish. Recalling, Bayesian belief network is a directed acyclic graph (i.e. a set of nodes connected by directed edges such that there are no directed cycles) in which nodes represent univariate random variables relevant to the problem being studied and directed edges represent probabilistic or functional influences between these variables. In the BBN the direction of an arrow indicates the direction of the influence. Thus, the meaning of an edge drawn from node X to node Y is that node X has a direct influence on Y. In this case node X is called the parent of node Y while Y is called the child of node X.

Each node in the non-parametric continuous-discrete BBN is associated with an arbitrary, continuous or discrete, random variable and each probabilistic influence between parent and its child is represented as (by assumption constant) conditional rank correlation[1]. Functional influences between the variables are also allowed with the restriction that functional nodes cannot have probabilistic nodes as children. In order to quantify the non-parametric continuous BBN one needs to specify marginal distributions for all probabilistic nodes, a number of conditional rank correlations and also mathematical models associated with functional nodes. This information can be extracted from data or, if data is unavailable, elicited from experts.

The main point of BBNs is to make probabilistic inferences about the variables involved, that is, to answer probabilistic queries about them in the light of observed evidence, what is equivalent to calculating conditional probability distributions from the joint distribution over

[1] Conditional rank correlation is the Spearman's rank correlation in a conditional distribution.

all model variables. Thus, the inference in the BBN is also called conditionalization. In the non-parametric BBNs the joint probability distribution for probabilistic nodes is built using the joint normal copula that realizes the dependence structure specified via parent-child conditional rank correlations attached to the edges of the BBN. Since all calculations are performed on a joint normal copula conditioning in non-parametric BBNs can be done analytically. UNINET assists both analytic and sample-based conditioning. Analytic conditioning allows for conditioning on single values of probabilistic variables while a sample-based conditioning is applicable to both probabilistic and functional nodes and conditionalizes on intervals.

Dissemination of results of benefit-risk assessments using UNINET is crucial for the project. Therefore, during the final project meeting in June 2009 it was decided to allocate additional resources to TU Delft for the improvement of UNIENT so that it fulfils its dissemination task. The improved and new features developed in UNINET supported by examples are described below.

The sample-based conditioning functionality in UNINET is a mature and very useful feature, perhaps mainly because it is the sole method we have to conditionalize on functional nodes (the most crucial variables in benefit-risk assessments are functions of other variables, e.g. exposures, health impacts). The user interface to this feature has, however, been unnecessarily spartan, and some remarkable improvements have been made. Most crucially, the sample-based conditioning window now allows the export of the currently conditioned sample to a standard text file. This means that the sample can then be explored with any sample analysis software including satellite programs UNIGRAPH and UNISENS[2]. Additionally, a report can be now generated regarding the conditional sample. The report contains some general information about the conditional sample and about the input and output nodes[3] (node names, descriptions, etc.). The full range and conditioning interval of the input nodes is specified. For the output nodes, the mean, standard deviation, usual percentiles and the range are specified for both the unconditional and the conditional sample. Moreover, for output nodes of discrete nature, the states and their probabilities in both conditional and unconditional distribution are provided. Finally, by right-clicking on any node in the input or output node lists in the sample based conditioning window, the user can visualize both the conditional, and the unconditional histogram of that node. This is particularly useful for discrete nodes, where the mean and standard deviation are generally of less interest than the probabilities of each state, while the latter are difficult to display within a line of text.

The data mining functionality of UNINET has been also improved. Data mining is the process of extracting and analyzing information from large data sets, and its ultimate aim is to build a good, useful BBN model that represents the underlying data well. A good model is characterized by being sparse (the smaller the number of arcs the better) and by representing well known relationships (arcs exist in the right places and have intuitive directions). Achieving both aims can be quite difficult, especially as the model grows. The method used traditionally has been to build the model from a scratch. A different approach is to start with a saturated graph (in which each variable is connected with every other variable) and gradually deconstruct it (remove the less significant arcs). UNINET has now the ability to create a saturated graph, either from scratch or starting from an existing structure. The order of nodes can be specified by the user and hence the directions of arcs can be controlled.

Consider data-mining a sample from a ten-dimensional distribution. UNINET mines ten random variables from the sample. The marginal distributions are taken directly from the sample and their underlying rank correlations calculated from data are stored (Image 1).

[2] UNIGRAPH supports the visual analysis of multivariate distributions while UNISENS is a program for sensitivity analysis.

[3] Input nodes are those on which we want to conditionalize while the output nodes are those for which we wish to see the effects of conditionalization.

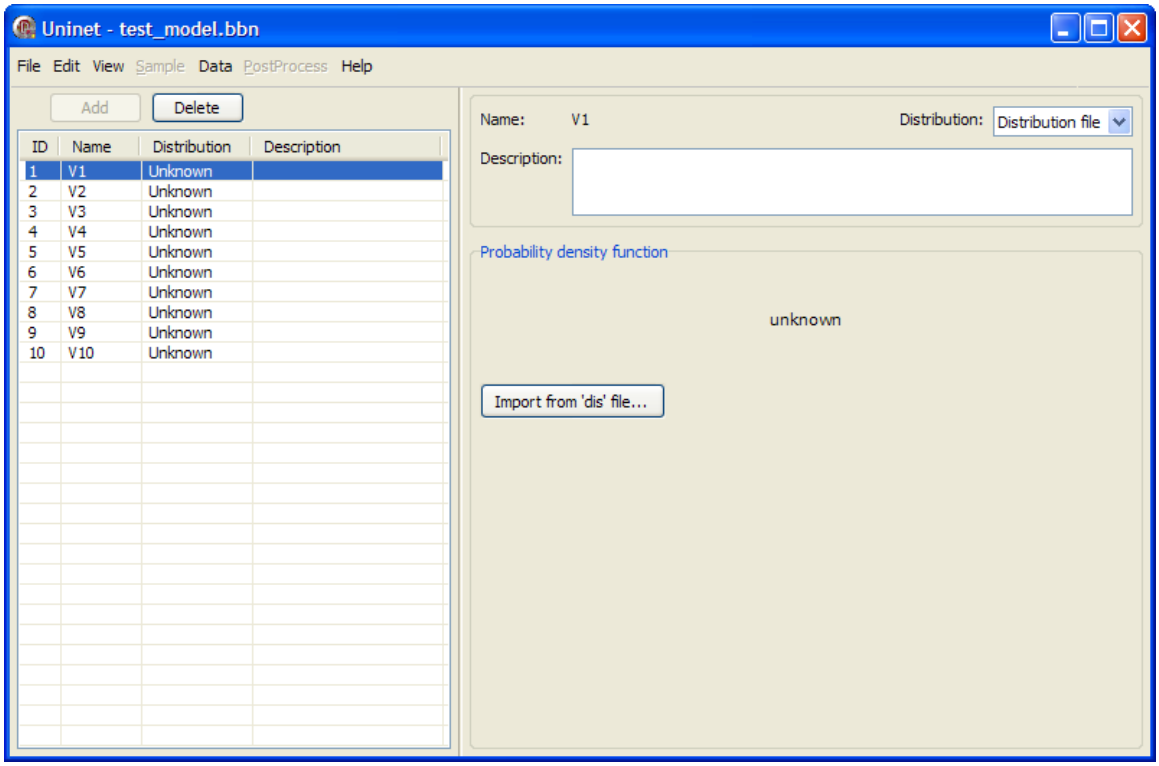


Image **1**

The adequacy of a data-mined model can be evaluated statistically by comparing the determinants of the rank correlation matrices (being a measure of multivariate dependence) in empirical and modeled distributions [4]. Two statistical tests for the determinant have been implemented in UNINET and are described below.

As mentioned before UNINET uses the joint normal copula to realize rank correlations between random variables, which were mined from the data. Therefore, before setting out to build a model, it is important to test whether the data can be adequately represented using the joint normal copula. In this test we compare the determinant of the rank correlation matrix of the original data (DER) with the determinant of the rank correlation matrix under the assumption of joint normal copula (DNR). For this test UNINET creates the sampling distribution of the DNR by simulation. If DER falls between the 5th and 95th percentile of this distribution, we consider that the data can be well represented using a joint normal copula. Image 2 presents the result of this test for our example. One can observe particularly good fit (as the test is applied to a sample generated with the normal copula).

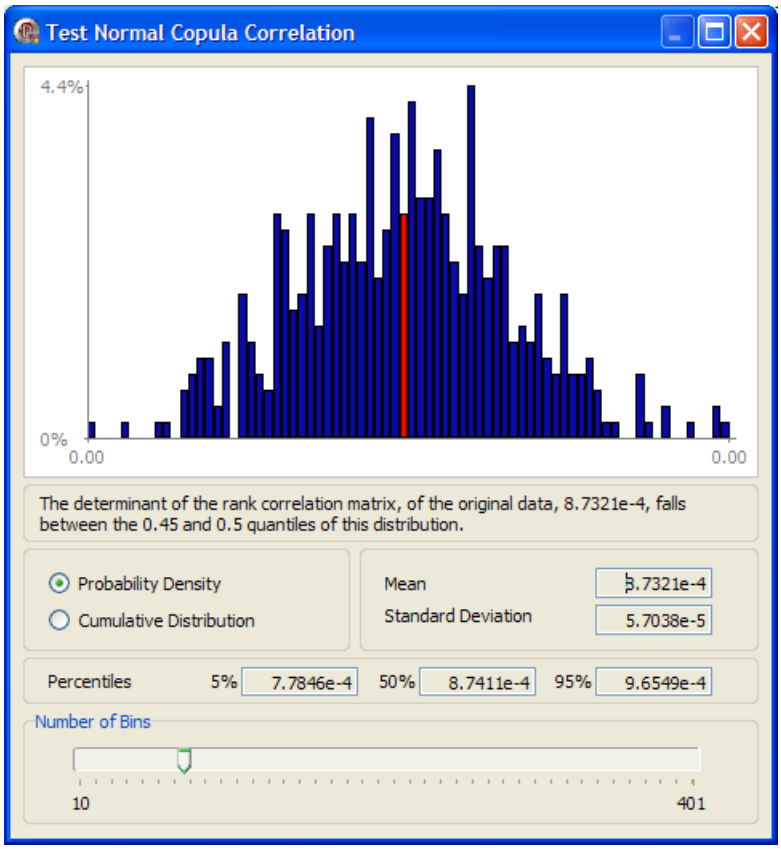


Image **2**

However, there are datasets that perform less well. Example of such data is presented in Image 3.

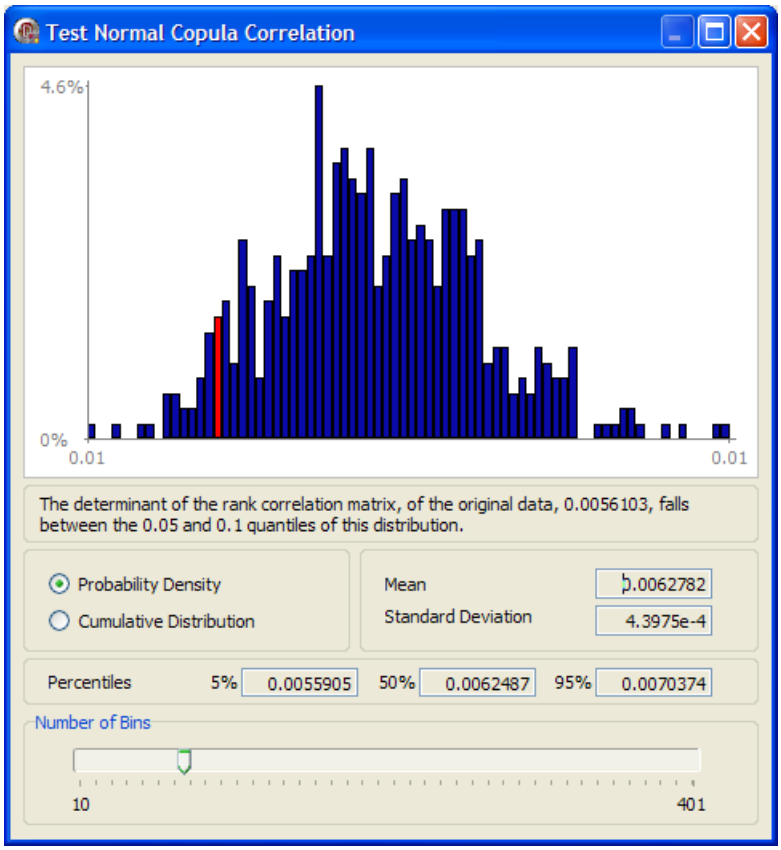


Image **3**

Suppose now that we are interested in developing BBN model which contains only eight variables out ten and we want to know which model structure adequately represents the data. We can start by creating a saturated graph. The list of variables chosen and their order is shown in Image 4.

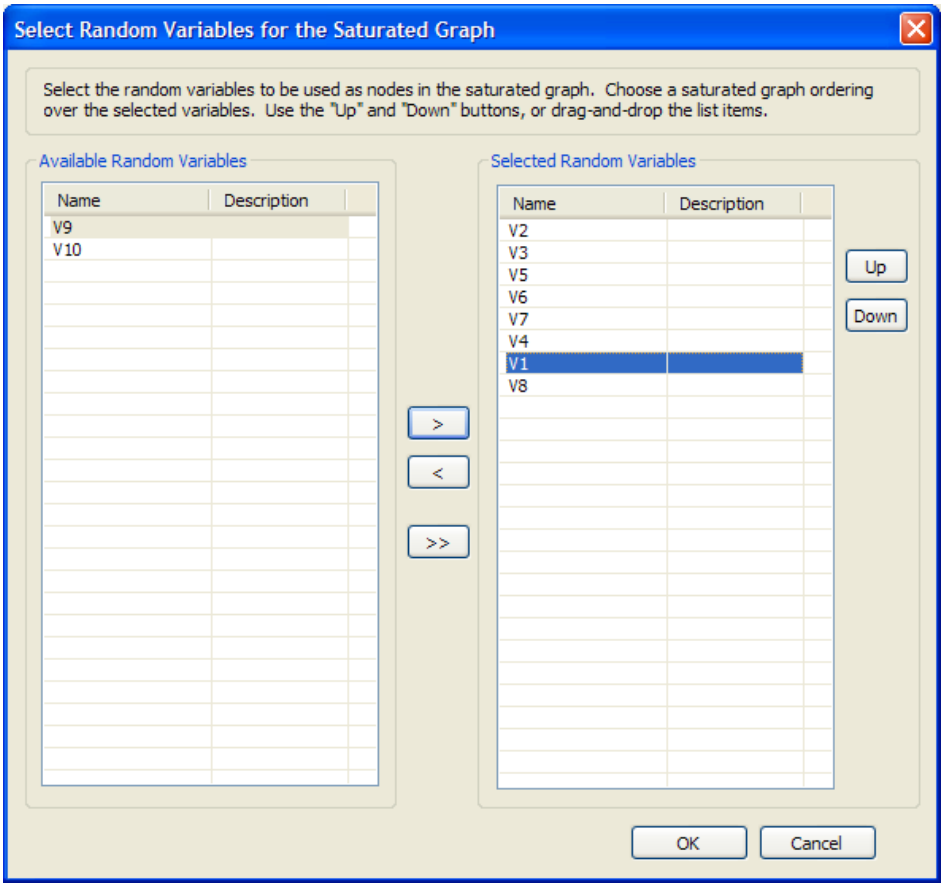


Image **4**

The saturated BBN is automatically created by UNINET with the nodes arranged in a circle. The user is able to choose the radius of that circle in a tool window visible on a screen. The program computes conditional rank correlations in the resulting model so that they match the underlying correlations, as mined from the data (Image 5).

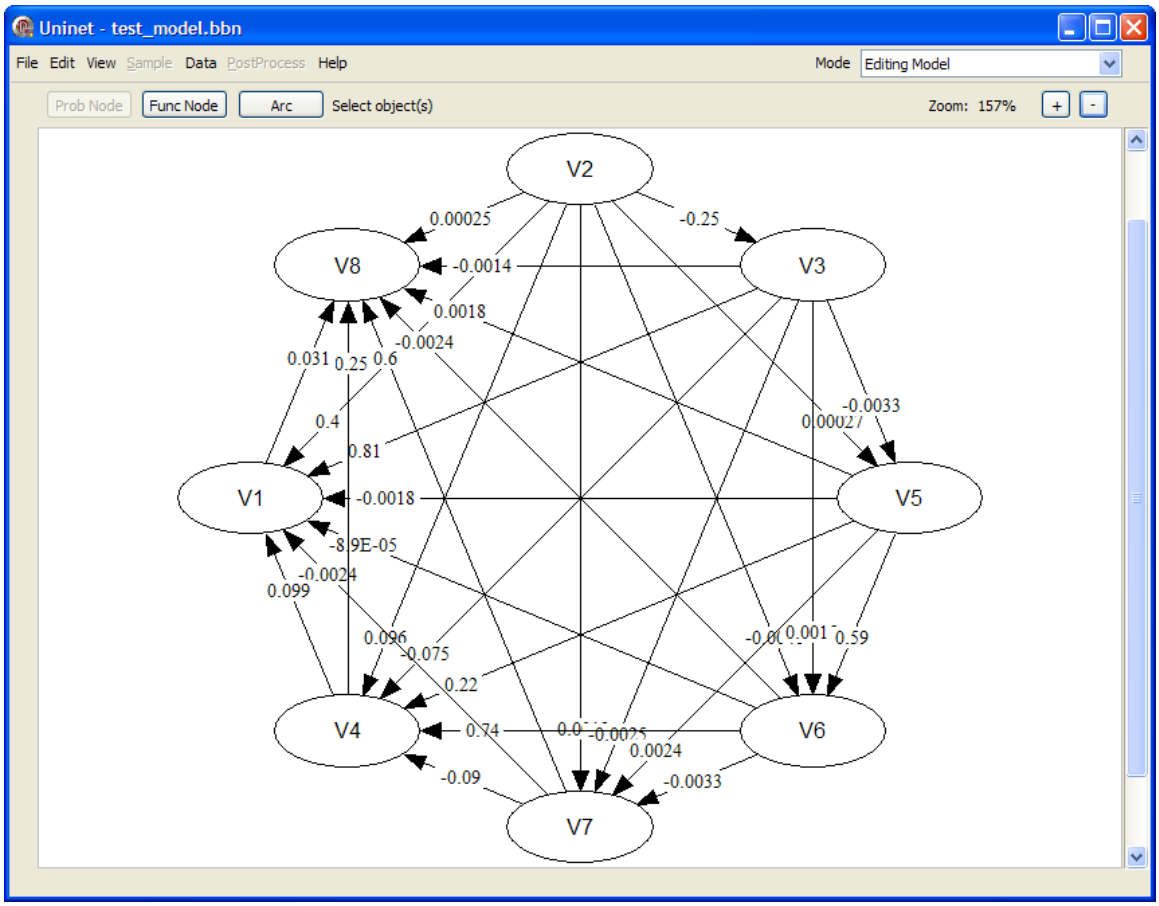


Image **5**

The other statistical test that has been implemented in UNINET allows to determine which arcs can be eliminated from the saturated graph such that the resulting model is still suitable to represent the data. In this test we compare the DNR (which represents the saturated model) with the determinant of the rank correlation matrix based on the BBN (DBBNR). If DNR falls between the 5th and 95th percentile of the sampling distribution of DBBNR, we consider that the model is a good representation of the underlying data (the correlations are well represented in the model). With a saturated model, of course, this match will be very good. In our example the determinant corresponding to the data correlation is almost equal to the median of the distribution of the determinant corresponding to the model correlation (Image 6).

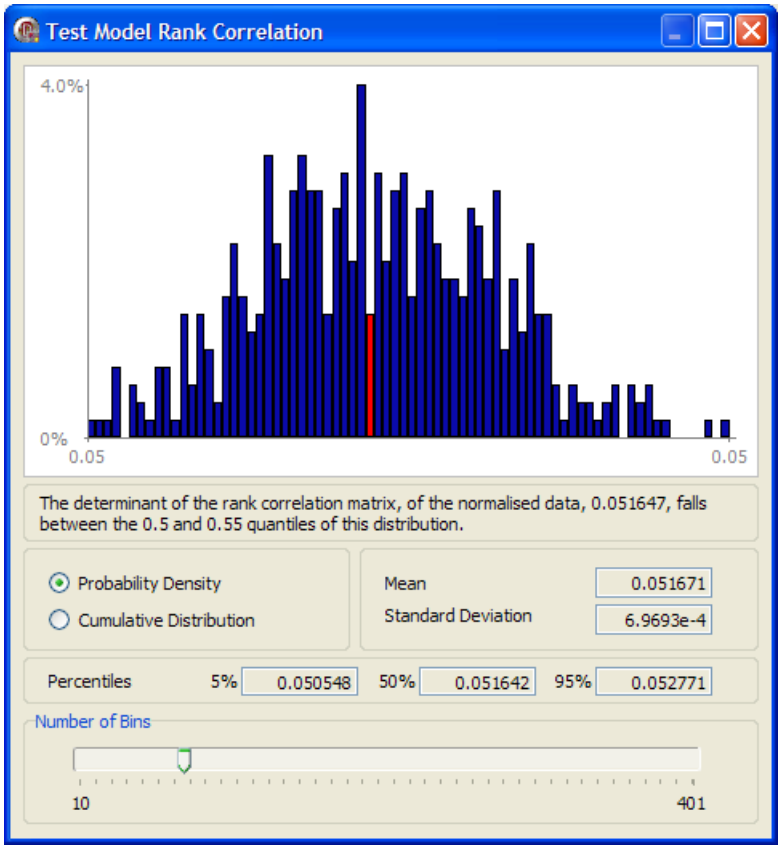


Image **6**

The situation can change quite quickly however. If we remove only one arc, between V4 and V1, we obtain...

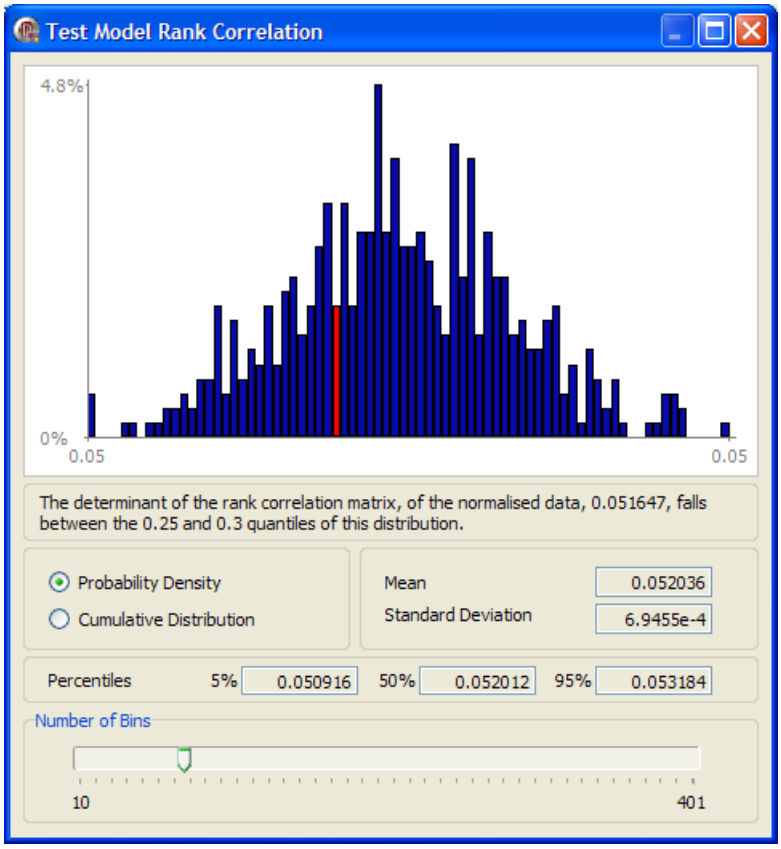


Image **7**

If we remove one of the more important arcs (V4 to V8) the model is rejected:

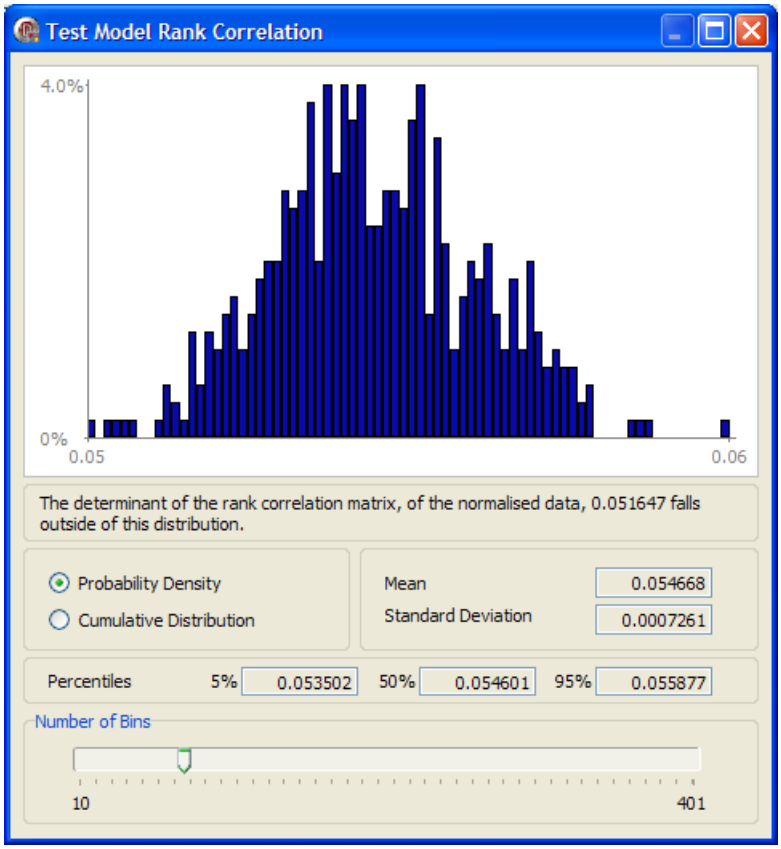


Image **8**

Once the determinant falls out of the confidence bounds, the model is no longer a good representation of the data.

The last improvement made in UNINET is related to the import/export model feature. UNINET has two main modi operandi, one of which, discussed above, is data-mining. In this mode the random variables are mined from a pre-existing sample, and their underlying correlations are at the basis of the model that the user creates using these variables. The creation/import of new random variables is, therefore, not allowed, as the new variables would not have a meaningful correlation with the existing model and the mechanisms that keep the underlying correlations in synch with the model would not apply to them. The second modus operandi does not imply a pre-existing sample, and the user can add random variables and correlate them freely. After a data-mining model is brought to a satisfactory form, the user may however wish to extend this model in some way by creating new variables or importing (sub)models from elsewhere. The new feature allows a data-mining model to be transformed into a "standard" model, that is a user-defined random variables BBN model. The transformation is irreversible (the connections between the model and the data-mined correlations are irrevocably broken) but of course a backup is made. After the transformation, all functionality related to standard models is available.

References:

[1] Kurowicka D., Cooke R.M. Distribution-free continuous Bayesian Belief Nets. In Proceedings of the Mathematical Methods in Reliability Conference, 2004.

[2] Hanea A.M., Kurowicka D., Cooke R.M. Hybrid method for quantifying and analyzing Bayesian Belief Nets. In Proceedings of the 2005 ENBIS5 Conference, 2005.

[3] Hanea A., Kurowicka D. Mixed non-parametric continuous and discrete Bayesian Belief Nets, in Advances in Mathematical Modeling for Reliability by T. Bedford et al., 2008.

[4] Hanea A.M., Kurowicka D., Cooke R.M., Ababei D.A. Mining and visualizing ordinal data with non-parametric continuous BBNs. Paper accepted for publication in Computational Statistics and Data Analysis.

Deviations from the project workprogramme, and corrective actions taken/suggested

FSAI:
As indicated in earlier reports, the ongoing development of the Pyrkilo method for risk:benefit analysis and the increasing focus of the Beneris project on Open Risk Assessment (ORA) has reduced FSAI's input to WP5 in a major way, and leadership and responsibility for dissemination was taken over by THL in year 2, although FSAI was nominally the workpackage leader for WP5

Lendac:
Input from Lendac was not possible due to postponement and alteration of project dissemination aspects. This change was identified before P4 and discussed with THL and Lendac, and it was according to the updated plan approved by the coordinator.

Deliverables

No.	Name	WP	Date of submission: Due (project month)	Date of submission: Actual	Date of submission: Fore-seen	Reasons for deviation and recu-perative measures	Indicative person-months: Estim.	Indicative person-months: Used	Lead contractor(s)
D31	Enduser evaluation	**5**	21	May 15, 2009		The main evaluation will be done not until the last reporting period (D46). However, a preliminary evaluation has been performed based on the experience collected until now.	2	2	THL (FSAI)
D37	Internet update	**5**	27	Aug 6, 2009		The Internet update has been a continuously ongoing process without a clear finalisation date. The deliverable was written after some larger updates.	3	3	Lendac
D42	VOI analysis of fish	**5**	37	15 Dec, 2009		Could only be done after the fish case study was ready.	0.5	0.5	THL
D43	Consumer reactions	**5**	38	15 Dec, 2009		FSAI was scheduled to play a role in this, using a test population of Irish consumers, and has undertaken a preliminary scoping exercise on methodology in 2007, a similar exercise has been carried out within Qalibra in 2007. In order not to duplicate activities, any further work will be undertaken as part of the Qalibra:Beneris cluster activities under the leadership of the lead contractors for both projects. Deliverable was based on a questionnaire performed by THL.	3	2	FSAI
D46	End-user evaluation	**5**	40	15 Dec, 2009		The evaluation by an end-user has been undertaken, together wih an appraisal of the method (WP1). The work has been delayed due to the slow development of the method (WP1)	3.5	0.5	FSAI

Milestones

Name	WP no.	Due (project month)	Actual achiev. date	Foreseen achiev. date	Reasons for deviation and recuperative measures	Lead contractor(s)
Decision on how the interface will be updated after the project. (Third project meeting)	**5**	38	15 Dec, 2009		Was depentend on D5.	

WP6: "Cluster activities"

WP leader	KTL/THL / Anna Karjalainen
Partners involved	KTL/THL, TUDelft, FSAI
Workpackage objectives	The objective is to establish a platform for cluster activities between Qalibra and Beneris projects and report about them to the Commission. (THL; D17, D5; year 4 M40)

Starting point at beginning of reporting period

Main achievements of the 1st reporting period:

- Beneris kick-off meeting on May 2006.
- The first Cluster meeting and a report containing the output from the Cluster meeting (deliverable D3)
- Joint web page opened.
- Collaboration with TU Delft and CSL about modeling.
- Cluster coordination.
- Joint project meetings planned/organized.
- Gordon conference in preparation.
- Scientific advisory panel appointed.

Main achievements of the 2nd reporting period:

- Roger Cooke visited Central Science Laboratory (CSL) on November 26-27, 2007.
- Visit by Alistair Murray to Delft on December, 2007.
- Patrycja Gradowska presented the Bayesian Belief Network approach in the "Valamo conference" on environmental health risk assessment
- Expert elicitation activities with Dr. W. Aspinall.
- Recognized the need for more collaborative work in order to develop of an integrated dissemination strategy for Qalibra and Beneris
- Open website for BRA (http://en.opasnet.org)

Main achievements of the 3rd reporting period:

- Beneris developed a Glossary of benefit-risk assessment terms and provided that to Qalibra.
- Beneris developed Opasnet Base that can be used also by Qalibra to store data.
- Beneris joined a Qalibra meeting to explain the use of Opasnet Base. Possible ways to utilise it in Qalibra were discussed.
- Beneris participated in the planning of the joint meeting in June 2009 (Qalibra was responsible for organising the meeting).
- Beneris has developed the first draft of a cluster dissemination plan

Main achievements of the 4th reporting period

- The final Beneris and Qalibra cluster meeting was organised and planned in cooperation

between Matis, THL, Altagra and FERA. The meeting was held in Budapest 10-11 June 2009. The objective of the final meeting was dissemination of activities and sharing of information between the two projects as well as the consultation with the Scientific Advisory Panel (SAP).

- At the final Beneris and Qalibra cluster meeting the draft cluster dissemination plan was discussed and a revised final version accepted.
- The final report on the cluster activities was written and submitted to the European Commission by QALIBRA in September 2009
- Beneris participated in a final end-user workshop held by QALIBRA 9-10th September 2009 in Budapest. This end-user workshop included practical hands-on training with the risk-benefit software produced by QALIBRA, using case studies developed in the project.
- In order to promote post-project activities of the two consortia Beneris and QALIBRA aim to publish several scientific articles together in a special issue. The tentative journal for this joint dissemination is Food and Chemical Toxicology.

Progress towards objectives

FSAI:
FSAI has not contributed to the objective of this WP, as the main responsibility was taken by THL.

THL:
Beneris has participated in the QALIBRA end-user workshop in September 2009. Planning of the workshops for using Opasnet base and Opasnet has been initiated.

Beneris and Qalibra agreed on a dissemination strategy at the Final cluster meeting in Budapest in June 2009. The practical actions in the plan relate mostly to Opasnet, and therefore this mostly guides Beneris - and especially THL after the project has ended. The dissemination strategy has been sent to the Commission previously, and it is also available on Opasnet: http://en.opasnet.org/w/Dissemination_plan_for_benefit-risk_assessment_of_food .

Beneris and Qalibra also aim to submit together several scientific papers to Food and Chemical Toxicology and suggest a special issue or a sub-issue about the results of the projects. A revised deadline of February 28, 2010 has been agreed by the consortia to manuscripts. A list of manuscripts that are being planned and could fit into the journal have been listed by both Beneris and Qalibra.

Planned articles from Beneris:

Anna Karjalainen et al.: *Contaminant exposure from fish consumption in children*

Hannu Kiviranta et al: *Correlation between intakes of contaminants and concentration in placenta.*

Olli Leino et al: *Health effects of methylmercury and docosahexaenoic acid from fish on child's cognitive health.*

Planned articles from the QALIBRA project:

Bas Bokkers et al:*The application of animal toxicity data in risk-benefit analysis: 2,3,7,8-TCDD as an example*

Marco J. Zeilmaker et al: *Fish consumption during child bearing age: A quantitative risk-benefit analysis on neurodevelopment*

Andy Hart et al: *Risk-benefit analyses of fish including multiple risks and benefits and quantitative and qualitative approaches*

Deviations from the project workprogramme, and corrective actions taken/suggested

None.

Deliverables

No.	Name	WP no.	Due (project month)	Date of submission Actual	Fore-seen	Reasons for deviation and re-cuperative measures	Indicative person-months Estim.	Used	Lead contractor(s)
D5	Beneris&Qalibra dissemination strategy	**6**	4	Aug 6, 2009		The deliverable was approved at the final cluster meeting in June 2009	1	1	THL
D44	Third project meeting	**6**	39	15 Dec, 2009		Meeting arranged in due time, documentation delayed until the final report.	1	1	THL
D47	Scientific advisory panel	**6**	42	15 Dec, 2009			1	0.5	THL

Milestones

Name	WP no.	Due (project month)	Actual achiev. date	Foreseen achiev. date	Reasons for deviation and recuperative measures	Lead contractor(s)
Scientific Advisory Panel Meetings	**6**	19 and 39	8 Nov, 2007 and 11 June, 2009			
Sharing data on concentrations (exposure assessment) for different fish species (Salmon & herring from BENERIS and other oily fish from QALIBRA)	**6**	12	15 Dec, 2009		Postponed due to changes in the development of data repository.	THL
Planned cluster meetings of the partners, month 19 (midterm) where results from riskbenefit analysis of salmon & herring (BENERIS) and other oily fish (QALIBRA) will be compared, integrated and discussed and month 39 (final cluster meeting) where final results of salmon & herring (BENERIS) and other oily fish (QALIBRA) will be integrated	**6**	19 and 39	7-9 Nov, 2007 and 10-11 June, 2009			THL

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The work undertaken in WP7 is described below under Section 3 (Consortium management).

Section 3 - Consortium management

WP leader	KTL/THL / Jouni Tuomisto
Partners involved	KTL/THL, TUDelft, FFiles, FSAI, DTU, FVST, Lendac, FIN
Workpackage objectives	The objective of this activity is to guarantee a smooth and effective collaboration between partners, and an organised processing of different activities so that all partners are working in concert, and at the end of each year and at the end to take lead in reporting activities. (THL+all; D13, D24, D34, D41, D48; Year 4 M43)

Starting point at beginning of reporting period

Main achievements of the 1st reporting period:

- Kick-off meeting organised.
- Steering committee elected.
- Framework development agreed upon.
- Project deliverables prepared.
- Upcoming Gordon conference and 2nd project meeting prepared.
- Partners informed via email on relevant issues.

Main achievements of the 2nd reporting period:

- Tasks reorganized and redistributed (due to sick leaves of key researchers) by the coordinator for improving project coordination and management.
- Updateing the project timetable.

Main achievements of the 3rd reporting period:

- Project was managed according to the new timeline.
- Ethical reports were updated as requested.
- Opasnet was utilised in managing the case studies.
- Adjustments to the timeline were made as a response to delays (these were explained in detail under the Workpackages in question).

Main achievements of the 4th reporting period

- The finalisation of the case studies and other remaining deliverables was organised.
- The final meeting was held (see WP6 cluster activities)
- Funding was reallocated to some new tasks (see WP2.2 and WP5)
- Fourth project report and the final report were written.

Progress towards objectives

FSAI:
FSAI has responded to the project leader as required and has contributed to all necessary reports. Specifically, during the period, FSAI has prepared responses to the European

Commission and project leader on questions arising in response to the P3 report, and has undertaken a re-evaluation of FSAI's role in the project.

THL:
Contact has been kept with other Beneris partners in D40 (Full benefit-risk analysis: vegetables) in order to find out which data would best suit the needs to obtain answers for the questions in the deliverable. Methodological assistance has been provided by the Finnish members of Beneris to other partners involved in the deliverable.

Changes in personnel. Consortium management problems and corrective actions.

THL:
Deliverable 40 (Full benefit-risk analysis: vegetables) was originally under the responsibility of the Spanish partner. However, the statistical and nutritional knowhow of analyses needed for the deliverable has been the strength of the Finnish members of Beneris. Due to this situation, the factual responsibility of the deliverable has been in Finland.

Some deliverables were deliberately postponed to the last reporting period due to reasons described in previous reports. All deliverables have now been finalised.

Due to the shifts in responsibilities, the role of FSAI had diminished from the original plan; this has been reported also in the previous reports. On the other hand, the responsibilities of THL and TU Delft have increased. The impact of this shift is 80 912.82 € during the whole project period. A part of this funding was redistributed for the last reporting period to the partners with new tasks. The decision was made in the project meeting in June, 2009.

Adjustments to the costs from previous periods

Several Adjustments in the P4 Forms C were made, as follows:

- in the Form C of **THL**, an adjustment of -25.70 € to RTD costs was made due to VAT corrections affecting the costs from year 2006. Detailled calculations kindly provided by Mrs. Sirkku Blomberg of THL (tel. +358-20-610 8233, sirkku.blomberg@thl.fi) are available from the coordinator.
- in the Form C of **TU Delft**, adjustments to RTD costs and Management costs of previous periods were made. Detailled calculations kindly provided by Mr. Nils Meijer of TU Delft (tel. +31-15-278 83 76, n.meijer@tudelft.nl) to justify the adjustments have been forwarded to the EC and are available via the coordinator.
- in the Form C of **Foodfiles**, two adjustments to previous periods were made due to minor technical errors in Foodfiles' accounting. Adjustment to RTD costs (297.50 €): due to a missing formula in an Excel file. Adjustment to Management costs (487.73 €): due to a missing project number from the accounting entry. (E-mail information kindly provided 22-Oct-2009 by Mrs. Anne Toroi, Foodfiles Ltd, tel. +358-17-288 1270, anne.toroi@foodfiles.com.)
- in the Form C of **FSAI**, the adjustment relates to items discovered in FSAI when preparing their data for the Audit certificate: "The main item relates to what Irish civil/public servants are required to charge for their time when involved on projects both within the EU and in other locations. This had not been accounted for when the original returns had been prepared and submitted. There were also hours worked, particularly in the finance area which had not been accounted for or charged to the project." (E-mail information kindly provided 6-Nov-2009 by Ms. Margaret Campbell, FSAI, tel. + 00-353-1817 1312, mcampbell@fsai.ie)

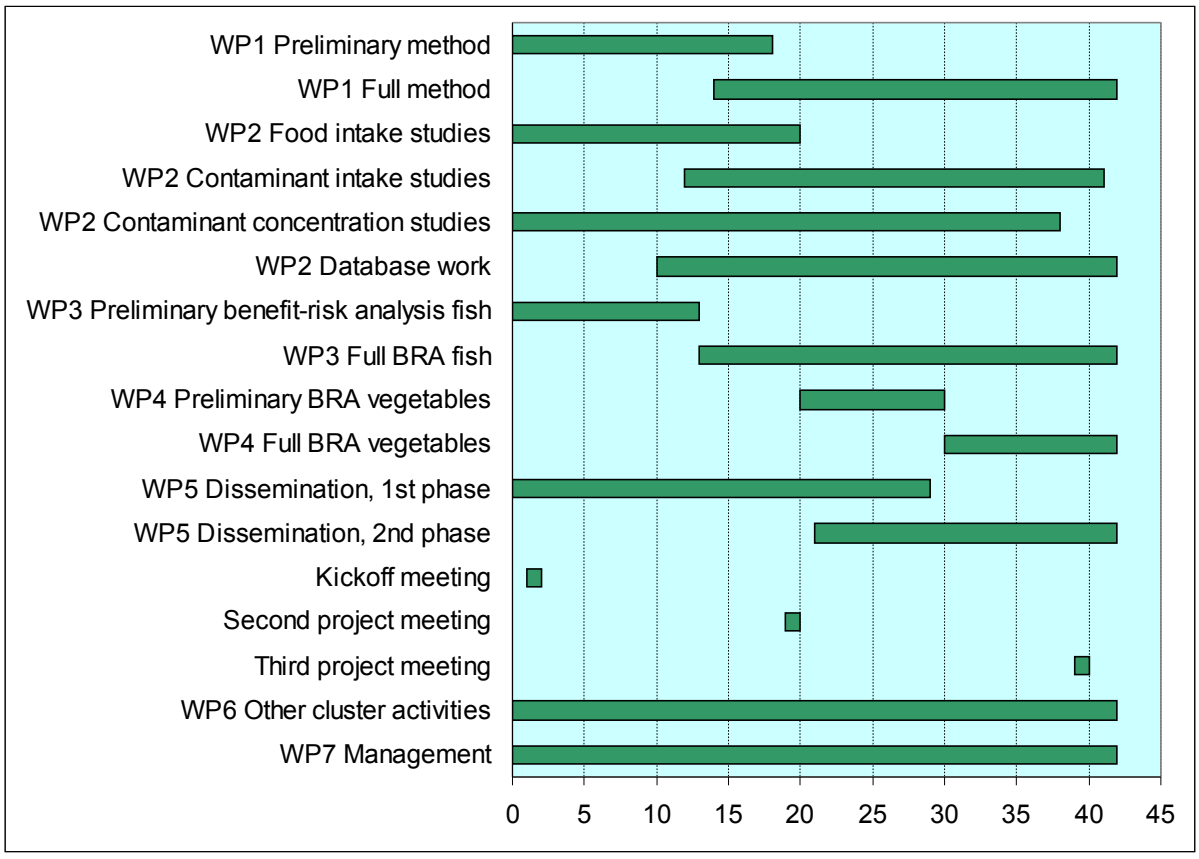
- in the Form C of **DTU**, a final adjustment (-8946.48 €) to RTD costs of previous periods was made: "The claim in period 2 was incorrectly high, and thus we claimed nothing in period 3. This did however not entirely make up for the first mistake, and thus we claim a negative amount in period 4, to pay back excess funding." (E-mail information 17-Nov-2009 from Mrs. Carina Hilligsøe Grølsted, DTU, tel. +45-35-886 142, cah@adm.dtu.dk.) Detailled calculations kindly provided by Mrs. Hilligsøe Grølsted are available from the coordinator.

In addition, to correct the zero requests of FSAI for reporting periods 2-3, FSAI submitted **revised Forms C for reporting periods 2-3** (as suggested by the EC financial secretary for BENERIS), declaring the same eligible costs as originally, but now requesting the maximum EC contribution.

Project timetable and status

There are no major changes in the project timetable. The completion of the full benefit-risk analysis of fish has been postponed by six months.

The current timetable is shown below.



Deliverables

No.	Name	WP	Date of submission: Due (project month)	Date of submission: Actual	Date of submission: Fore-seen	Reasons for deviation and re-cuperative measures	Indicative person-months: Estim.	Indicative person-months: Used	Lead contractor(s)
D41	Third project report	**7**	36	15 May, 2009			0.2	1	THL
D48a	Fourth period-ic report	**7**	44	15 Dec, 2009		Delayed due to the extra time needed for obtaining audit certi-ficates and for the completion of the final deliverables.	0.3	1.5	THL
D48b	Final report								

Milestones

Name	WP no.	Due (project month)	Actual achiev. date	Foreseen achiev. date	Reasons for devi-ation and recu-perative meas-ures	Lead contractor(s)
The third project meeting (month 38), reporting and fur-ther planning	**7**	38	10-11 June, 2009			THL

Section 4 - Other issues

None.

Appendix I - Plan for using and disseminating the knowledge

Section 1 – Exploitable knowledge and its use

Beneris, with others, has produced a website for working on and disseminating benefit-risk analyses of food. The website is a collaborative effort between several research projects, especially Beneris, Intarese, Heimtsa, Erac, and Hiwate. New projects that will start using the website include Tapas, Bepraribean, and Plantlibra. The results of the analyses have potentially high economic interest and hopefully will result also in commercial use. However, the website itself and its contents are open and distributed freely on a non-profit basis. The website is open (http://en.opasnet.org; previously heande.pyrkilo.fi), and it already contains several benefit-risk and other analyses on food and other topics.

Table 1. Exploitable Knowledge and its Use

Exploitable Knowledge (Description)	Exploitable Product(s) or Measure(s)	Sector(s) of Application	Timetable for Commercial Use	Patents or Other IPR Protection	Owner & Other Partner(s) Involved
Benefit-risk assessments (BRA) of food issues. The content is open and freely available to all.	A website to collect, organise, and distribute BRA information. http://en.opasnet.org	Food safety. Environmental health.	Products are available for commercial use as soon as they appear on Opasnet website.	Based on Creative Commons license: Attribution – Share alike.	Owner: KTL/THL and all partners involved in developing the website and/or producing information.
Background information for assessments, such as population, mortality, morbidity, and food intake data..	Data available on Opasnet Base. (http://base.opasnet.org)	As above	As above	As above	As above
Method descriptions for making benefit-risk assessments. E.g models to compute health summary measures such as DALYs.	Descriptions available on Opasnet (http://en.opasnet.org), possibly accompanied by actual models to apply the methods. E.g. http://en.opasnet.org/w/Value_of_information , http://en.opasnet.org/w/Life_table	As above.	As above.	As above.	As above.

Section 2 – Dissemination of knowledge

Table 2. Dissemination of Knowledge - Overview.

Planned/Actual Dates	Type +	Type of Audience ++	Countries Addressed	Size of Audience	Partner Responsible
1 April, 2009	Press conference about Baltic fish consumption and health. Presentation of risks and benefits of fish by Jouni Tuomisto.	Journalists, authorities from food administration, researchers.	Finland	ca. 50	Hannu Kiviranta, Jouni Tuomisto (THL)
11-12 September, 2009	Brafo meeting, Budapest	Food authorities and researchers	Several EU countries	ca. 15	Jouni Tuomisto / THL (participants)
10-11 September, 2009	QALIBRA workshop	Researchers from several EU-funded projects, authorities	Several EU countries	25	THL, Jouni Tuomisto; Olli Leino
9-11 November, 2009	TAPAS project meeting	Researchers from several fields	Several EU countries	20	THL, Jouni Tuomisto
June 16-17, 2009	Bepraribean project meeting, Bilthoven NL	Researchers from several fields incl. food.	Several EU countries	10	THL, Jouni Tuomisto
Fall 2009	Plantlibra project kickoff	Researchers from several fields incl. food.	Several EU countries.	ca. 20?	THL, Jouni Tuomisto
June 12-13, 2009	AGORA project meeting, Cambridge, UK	Researchers civil engineering, geology, earthquake sciences	Several EU countries, US	30	THL, Jouni Tuomisto
5-6 November, 2009	OPEN 2009 symposium	Researchers	Several EU countries		THL, Mikko Pohjola, Juha Villman
28 September - 2 October, 2009	Philosophy for Science in Use -conference in Linköping, Sweden	Philosophers, scientists	Several EU countries		THL, Mikko Pohjola
17-19 November, 2009	Intarese annual meeting	Researchers	Several EU countries	Ca .70	THL, Jouni Tuomisto

+ Includes press releases (press/radio/TV), media briefings, conferences, exhibitions, publications, project website, posters, flyers, direct e-mailing, film and video

++ General public, higher education, research, industry (sector x)

Section 3 – Publishable results

Table 3. Publishable Results.

Result Description	Possible Market Applications	Stage of Development	Collaboration Sought or Offered	Collaborator Details	IPR Granted or Published	Contact Details
Opasnet: A website to collect, organise, and distribute information on issues relevant for benefit-risk analyses (BRA) of food. http://en.opasnet.org Current size: 980 web pages, 450 files, 176 users, 270000 page views.	The content is open and freely available to all.	The website has been intensively utilised. Several assessments are being worked on at the website.	Interested parties are welcome to contribute to the case studies with their own information, as long as it is offered under IPR rules.	Main developer: THL	Based on Creative Commons Attribute – Share alike copyright license	Jouni Tuomisto, THL, P.O.Box 95, FI-70701 Kuopio, Finland. email: jouni.tuomisto @thl.fi
Opasnet Base: A database to collect, organise, and distribute quantitative model results and input data http://base.opasnet.org Current size: 66 data tables, 2 million rows.	The content is open and freely available to all.	The website was recently opened. Data from several assessments are being uploaded to the database.	As above.	Main developer: THL	As above.	Jouni Tuomisto, THL, P.O.Box 95, FI-70701 Kuopio, Finland. email: jouni.tuomisto @thl.fi
D33 Consumer info about benefits and risks of fish.	As above.	To be published in November 2009; draft available now	The product has a feedback and discussion functionality to facilitate contribution.	THL	As above	As above
D46 End-user evaluation.	As above.	Published in November 2009.	As above.	FSAI, THL	As above	As above
D38 Final fish benefit-risk assessment.	As above.	As above	As above	TUDelft, THL	As above	As above