
Fraunhofer Institute
Systems and
Innovation Research

# Impact evaluation of the Control of Infectious Diseases Key Action in the Fifth Framework Programme of Research

Final Report

Final version, July 2004

– Public version with pseudonymized references to evaluated projects –

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# 0 Executive Summary

Throughout the world, infectious diseases kill about 17 million people a year. For a large number of them still no satisfactory prevention or treatment exists. Thirty new epidemics have entered the floor in the last 20 years, and more **emerging or re-emerging diseases** have to be expected.

However, in recent years, the **number of approved anti-infective agents is declining**, and a large number of pharmaceutical and biotech companies have left the field or reduced their efforts. The potentially large markets are not attractive enough for the industry to take the risks of high R&D investments alone.

In Key Action 2 (KA2) of the Specific Programme 'Quality of Life and Management of Living Resources' under the Fifth Framework Programme of Research, approximately 200 projects are carried out.

The aim of the present study was to evaluate those of the projects in KA 2 dealing with human health according to their quality and impact.

The evaluation has **covered a broad range of aspects of the projects** under scrutiny, but could only be designed as a **"snap-shot" of the Key Action** for several reasons: The main data collection had to be closed by mid of 2003, a point where many of the KA2 projects had not delivered their final report yet or were even still ongoing. In addition, because of restricted resources some interesting aspects could not be investigated in detail.

The analysis was orientated only onto the human-health part of KA2, therefore projects on animal diseases and on prion diseases were excluded. In the end, the **evaluation comprised 145 projects**. The evaluation was based mainly on the periodic and final reports of the projects, on the mid-term reviews by external experts as well as on telephone interviews. Additional information was retrieved from different data files provided by the Commission.

## 0.1 Overview of the projects

The largest part of the projects are R&D projects (111 out of 145), followed by Concerted actions and Demonstration projects (Table 0.1). Only few projects were of the other types (CRAFT, TN, CM, NAS-Extension).

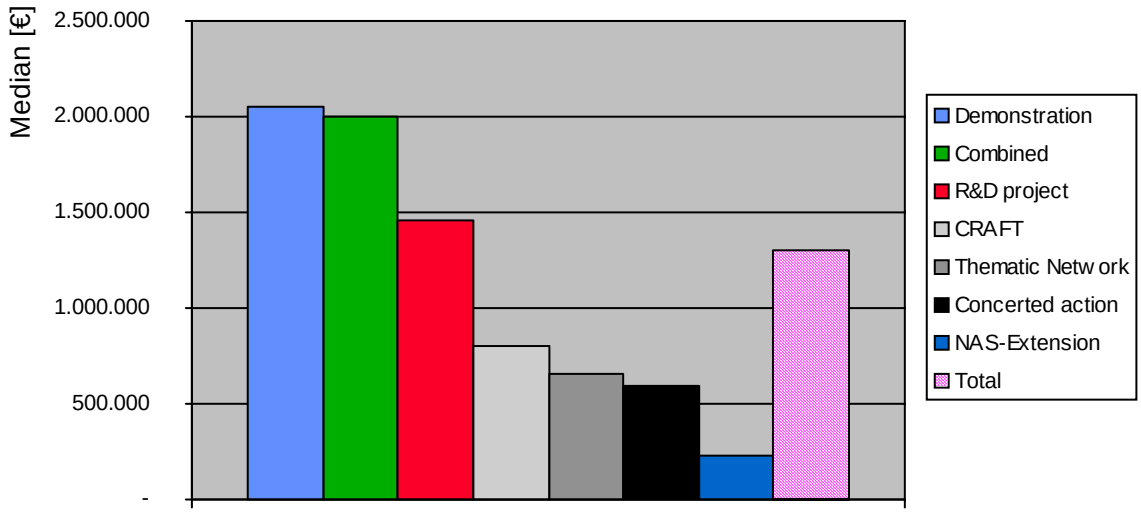
Table 0.1: Type of projects

| Type of project | | n of projects |
|---|---|---|
| RS | Research and technological development (R&D) project | 111 |
| CA | Concerted Action | 15 |
| DM | Demonstration Project | 7 |
| CRAFT | SME Co-operative Research | 6 |
| CM | Combined R&D and demonstration project | 3 |
| TN | Thematic Network | 2 |
| NAS-Extension | Extension for Newly Associated States | 1 |
| Sum | | 145 |

Source: Fraunhofer ISI

The average **financial contribution** per project as given in the data from the Commission is shown in Figure 0.1.

Figure 0.1: Budget by type of project




Source: Fraunhofer ISI

## 0.2 Implementation of the research

Many points have been learned on the implementation of the projects under KA2. They relate to the planning, selection of partners and industry involvement, and the implementation phase itself.

### 0.2.1 Planning

**Contract negotiations** were sometimes lengthy and problematic in part because of time-consuming processes within the Commission linked to the necessary procedures in place.

Very **clear plans, concrete formulation of objectives, milestones and deliverables** with specific performance criteria are necessary as a starting point for the work and were achieved sufficiently in most of the projects.

In some cases, the **severity of some problems was underestimated** by the project managers, e.g. technical problems with database development or patient recruitment.

For many projects that aimed at the development of drug or vaccine candidates, 3 years of funding were too short. **More flexible funding** schemes are suggested.

A **deficit** has to be noted in the **interaction with patients and other stakeholders** that should be tackled in future project planning and dissemination.

### 0.2.2 Implementation phase

Of overwhelming importance in the view of the researchers and mid-term reviewers is the **communication between the participants** and a **strong coordination**. To assure the quality and standardisation of project methods, the exchange of lab personnel was practised.

The **interaction and coordination of the projects with other EU-funded projects**, with national and international research programmes could still be improved. Within the EU-funded research it should be assured that the different projects and initiatives work closely together.

In the development of drugs or vaccines, it is normal that most candidates have to be dropped during preclinical or clinical development. **Projects need enough leeway** to overcome this and redirect their ongoing work if temporarily unfavourable results are encountered.

The researchers felt overcharged by **administrative tasks** to meet with procedures of the Commission that were sometimes perceived as unnecessarily rigid. Some of the participants expressed hope that the 6$^{th}$ framework programme made these things easier. However, in many cases, the feedback and control by the Commission was appreciated by the projects.

**Delayed payments** by the Commission sometimes even lead to delays in the start of projects or parts thereof. All possible measures should be taken not to slow down the projects for unnecessary administrative reasons.

# 0.3 Impacts

## 0.3.1 Coverage of the research field

74 of the projects primarily work on procedures for **diagnosis and therapy**, 51 projects work in the field of **vaccines** and 20 consider **public health interventions or monitoring** (Table 3.1).

Table 0.2: Thematic area of the projects

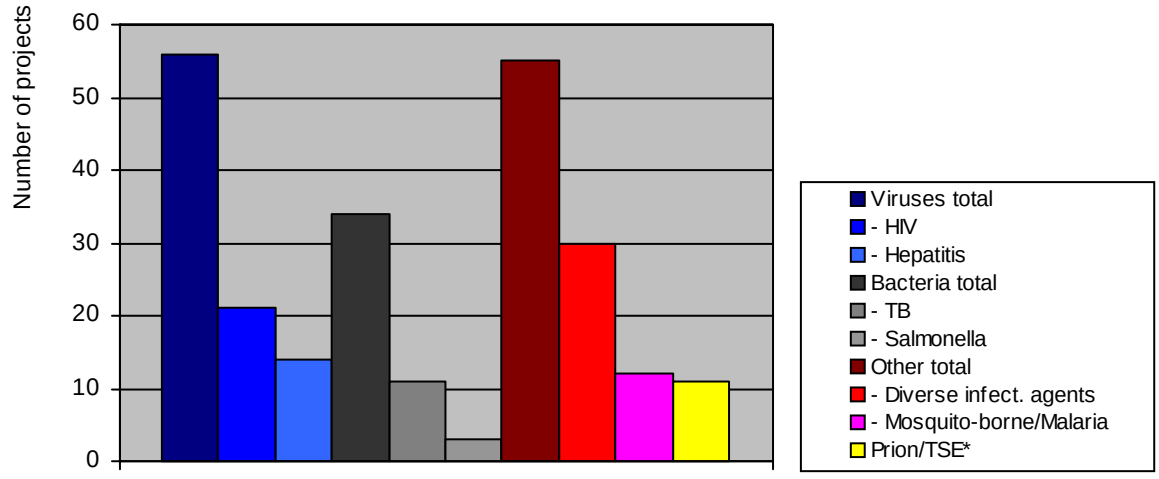
| Thematic area | n of projects |
|---|---|
| Diagnosis and therapy | 74 |
| Vaccines | 51 |
| Public health interventions/monitoring | 20 |

Source: Fraunhofer ISI

The range of agents and diseases under study in KA 2 is very broad. Many of the agents or diseases focussed in the KA2 projects are especially prevalent in developing countries, indicating a high **relevance of the research in an international context**.

In Annex 1 of **Commission Decision 2000/96/EC, a list of communicable** diseases is specified which are to be placed progressively under EU-wide surveillance because of their relevance for public health. Many of the infectious agents that deserve special surveillance in the EU are investigated under KA2, although the Commission Decision 2000/96/EC had not been a criterion for the selection of KA2 projects for funding (Figure 0.2).

Figure 0.2: Infectious agents (large groups)




Source: Fraunhofer ISI

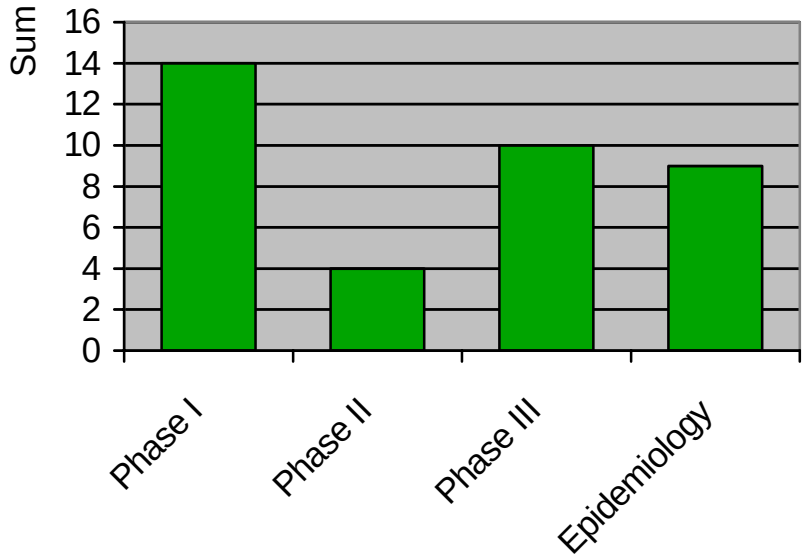
### 0.3.2 Exploitation and dissemination

Many contributions to scientific conferences were made by the KA2 projects. Dissemination to the scientific community was also ascertained by the generally large numbers of publications. However, there are only **few conferences that were organised by the projects themselves** directed to their **specific target groups including policy-making as well as the general public**.

Although some projects report **meetings with other research groups** or organised additional EC-funded conferences, this aspect is **not mentioned for most of the projects**, even not for collaboration with other KA2 projects that are working in the same field.

By far the largest number of studies was preclinical in character. In projects that aimed at the development of a new drug or vaccine, 14 were in clinical phase I, 4 in phase II, and 10 in phase III (the large **clinical trials**). 9 epidemiological studies (including the evaluation of already marketed treatments, treatment plans and monitoring systems) were carried out.

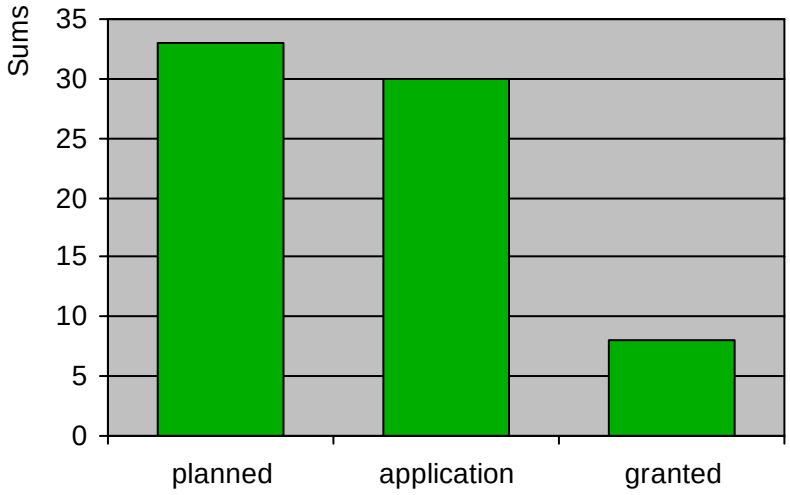
Figure 0.3: Number of clinical and epidemiological studies




Source: Fraunhofer ISI

A total number of **33 patents were planned**, another 30 patents were filed, and 8 patents have already been granted. **One enterprise was founded** as a spin-off from one of the projects.

Figure 0.4: Number of patents




Source: Fraunhofer ISI

### 0.3.3 'Non-thematic' goals

Besides responding to the “thematic” goals, European research funding has objectives that are unspecific to the field of application, e.g. to contribute to the European integration, to generate European added value, or to support the use of obtained evidence in policy-making.

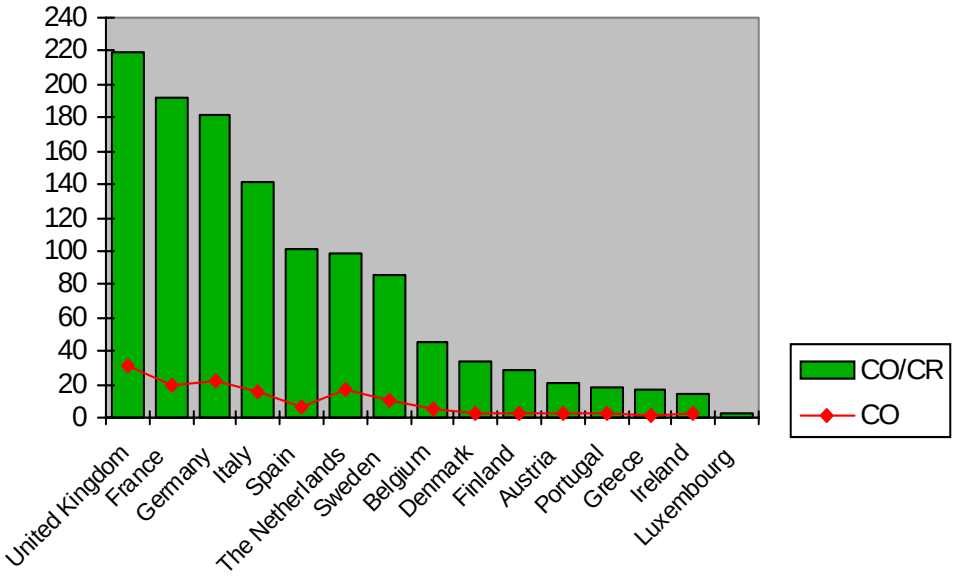
Especially the public health projects with their emphasis on harmonisation of research and laboratory methods as well as treatment standards, but also the other projects with participants from smaller or larger numbers of Member States had an impact on the policy goal of **European integration**. EU and national research was partially combined, including additional funding from national grants.

The transnational character of the projects combined with the fact that in most cases the EU was the only possible source of funding for this kind of projects, as well as the collaboration of experts from the Member States and the standardisation of methods and communication of results across borders show a **clear EU added value**.

An intrinsic goal of EU research funding is the **collaboration of public research and industry**. 45 of the funded projects have at least one industry partner, in total 122 industry partners are involved. The public-private partnership approach seems to be both especially necessary as well as successful for the field of infectious diseases. The integration of industry partners has worked very well in such projects where a market for the products of a project is in sight. However, the **number of industry partners was still low**.

The largest number of participants in total as well as in the role of the coordinator comes from the **UK, followed by France and Germany** (Figure 3.5).

Figure 0.5: Participating countries

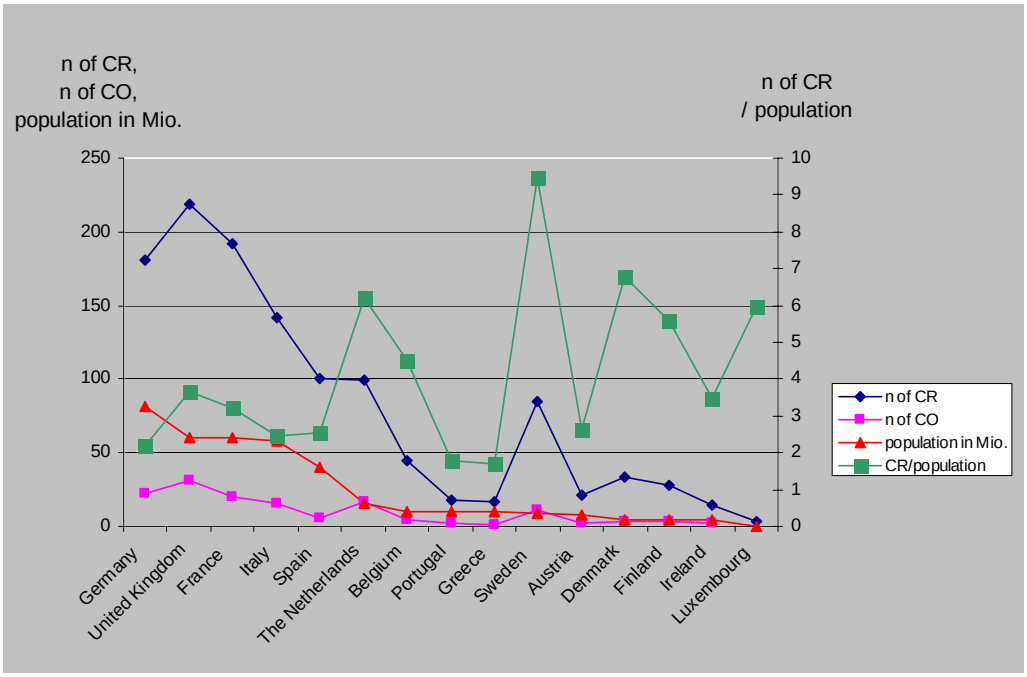



CO/CR: Participant from certain country is contractor (including coordinator); CO: participant is coordinator

Source: Fraunhofer ISI

The number of partners for the Member States roughly follows the size of their population with about 2 to 4 contractors per million inhabitants, with higher relative numbers for The Netherlands, Belgium, Sweden, Denmark, Finland and Luxembourg (Figure 3.4, line "CR/population").

Figure 0.6: Number of contractors and size of population

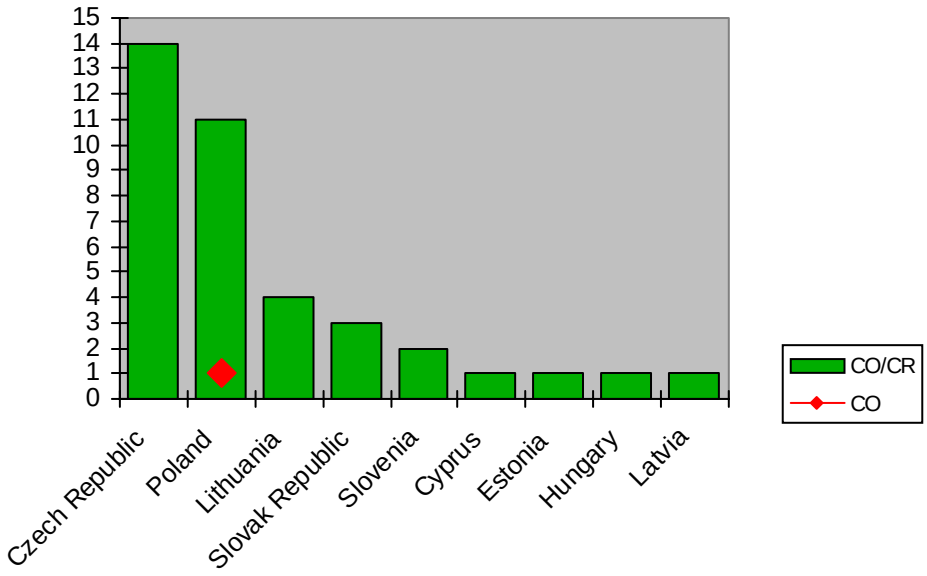



n of CR: number of contractors incl. coordinators; n of CO: number of coordinators;
n of CR/population: number of contractors per country divided by size of the population [in Mio.]

Source: Fraunhofer ISI

From the **Accession Countries**, the Czech Republic and Poland are represented the best (Figure 3.6). Although additional funding was available for these countries through the NAS-instrument, the other Accession Countries were included only very rarely.

Figure 0.7: Participation of Accession countries




CO/CR: Participant from certain country is contractor (including coordinator); CO: participant is coordinator

Source: Fraunhofer ISI

## 0.3.4 Employment and qualification

The impact on the science arena is firstly a direct via the employment of staff. Figures for this interesting aspect are not regularly presented in the periodic report. For 13 projects, which offered the figures in the closer evaluation, the total number of people employed was 293 (Md=14). The number of PhDs degrees acquired by students working within these 13 projects was 60 (Md=4).

## 0.3.5 Selection of partners

Especially for public health and surveillance programmes, it was **best to include as many partners as possible**. On the other hand, a **consortium should not be too large** to assure efficient communication between the contractors.

There were relatively few partners and coordinators from the smaller Member States. The **integration of the Accession Countries** was attempted in many projects, partly supported by NAS extension grants, and especially for the public health projects this was seen as especially rewarding.

## 0.4 Lessons learnt

Many conclusions for further similar research programmes can be drawn from the present impact evaluation. On this basis, **four main lessons** learnt are presented here.

### 0.4.1 Project implementation

The **selection of highly motivated and methodologically skilled participants** is of central importance for the success of a consortium as is a **strong and experienced coordinator** as well as **good communication between the partners**. More emphasis should be given to the **involvement of industry and SMEs** as partners because this is an adequate means to bring products onto the market quickly. Academic researchers can learn about the needs of the industry by direct interaction with industry partners and by exchange of personnel within the consortium. Interaction with related EU and international research should be strengthened.

### 0.4.2 Exploitation and dissemination

Whereas dissemination to the scientific community was very extensive, **more emphasis should be given to inform the public and the political level** on the practical consequences of a project e.g. by press releases, information events dedicated to policy-makers or even TV broadcastings. Although a number industry partners were attached to the projects, **more could be done to exploit the results with the industry**, e.g. in the form of information events. Other examples in KA2 projects are publications not only in scientific but also in business journals.

### 0.4.3 EU as research area

A **strong science base has been developed** in the KA2 projects. Resulting from the limited budgets and funding periods, a danger was seen by many projects to lose the elaborated knowledge after the finalisation of the project. Measures should be implemented like mailing lists or thematic expert networks, probably in the framework of the new European Centre for Disease Prevention and Control (ECDC), in order to **preserve the contacts of the Commission to successful coordinators and contractors** and to keep track of the well-functioning networks. As the development of new drugs and vaccines bears many risks, **more flexible funding schemes** should be allowed to assure that probable drawbacks can be coped with.

#### 0.4.3.1 Evaluation of EU-funded research programmes

The experiences with the present **impact evaluation** show that such projects are possible in principle and can **lead to useful and applicable conclusions**. It should be considered for similar projects in the future to draw more on the project leaders as a source of information that is not systematically given in the periodic reports. For future similar impact evaluations, a two-step approach is suggested:

(1) A more systematical internal registration and assessment of routine data which are already available yet dispersed at different Commission services. The methodology of the actual project could support this.

(2) A more comprehensive external evaluation to assess more in-depth the impacts of the programme with additional instruments and research questions specifically targeted to the requirements of further research policy making. The respective experiences of the present project should be used.

# Table of Contents

**Notice on confidentiality:**

In the present public version of the final report, all links to individual projects as contract numbers or acronyms have been replaced by a pseudonymized project number (e.g. "Proj_1")[1]. In addition, one part of the annex has been deleted which links the reports of the KA2 projects to their assessment. This has only been done to ensure the confidentiality of the source of the respective information. In all other respects, the present version of the report is totally identical with the full version of the report which is available only for the Commission's internal use.

[1] Based on the total number of projects in KA2, of which 145 could be included in the present study, these project numbers range from "Proj_1" to "Proj_205".

# List of tables

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# 1 Introduction

In Key Action 2 (KA2) of the Specific Programme ‘Quality of Life and Management of Living Resources‘ under the Fifth Framework Programme of Research, approximately 200 projects are carried out, about 150 of them dealing with human health. The projects cover three areas of activities:

1. Development of improved or novel vaccines
2. Strategies to identify and control infectious diseases
3. Aspects of public health and care delivery systems

The aim of the present study was to evaluate these projects according to their quality and impact in their respective research field.

The evaluation project began its work with the signature of the project contract on January 14, 2003 and was finalised in January 2004. It has covered a broad range of aspects of the projects under scrutiny, but at the same time could only be designed as a "snap-shot" of the Key Action for several reasons: As the main data collection for the present evaluation had to be closed mid of 2003, a point where many of the KA2 projects had not delivered their final report or were even still ongoing. In addition, because of restricted resources some interesting aspects could not be investigated in detail.

The present report covers the work and final results achieved by the project. According to the tender, the project dealt with the following work-packages (WP) and milestones (MS; see Table 1.1).

Table 1.1 Work steps according to tender

| | Workstep | scheduled for month |
|---|---|---|
| MS1 | Discussion of methodological approach with Commission | 1 |
| WP1 | Document searches and analysis | 1-6 |
| WP2 | Classification of projects | 2 |
| WP3 | Descriptive overview of all projects | 2-4 |
| | Development of projects database, data entry, validation | 2-3 |
| MS2 | Presentation of projects database | 3 |
| WP4 | Development of set of indicators | 2-3 |
| WP5 | Preparation of interim report | 3 |
| | Presentation of provisional interim report, revision if required | 3-4 |
| MS3 | Presentation of interim report final version | 5 |
| WP6 | Evaluation of all projects, selection of ‘most promising’ projects | 5-8 |
| WP7 | Closer evaluation of sample projects | 7-11 |
| | Supplementary interviews | 7-8 |
| MS4 | Interviews finished | 8 |
| WP8 | Recommendations | 10-11 |
| WP9 | Preparation of provisional final report | 11-12 |
| | Presentation of provisional final report, revision if required | 12 |
| MS5 | Presentation final report | 12 |

Source: Fraunhofer ISI

The kick-off meeting took place on February 13, 2003 in Brussels. Some modifications of the work plan were agreed upon:

Important additional goals of the evaluation were to determine how the projects cover their work programme and research field and the dissemination of their results especially beyond the scientific community in other target groups.

The proposed criteria for the selection of projects for the in-depth evaluation were also confirmed. Additional aspects were

– clusters (especially relevant because of high budget),
– budget,
– projects with industry partners,
– disease.

The final selection was discussed with the European Commission at the 2nd interim meeting. "Accompanying measures" were left out of the evaluation, as well as projects on prion disease.

Concerning the access to the data for the evaluation it was stated at the kick-off meeting that no common projects database was available, but some data from CORDIS or other electronic sources could be used by the evaluation. The primary source were the periodic project reports, in addition the mid-term review reports. Printed copies were sent to Fraunhofer ISI.

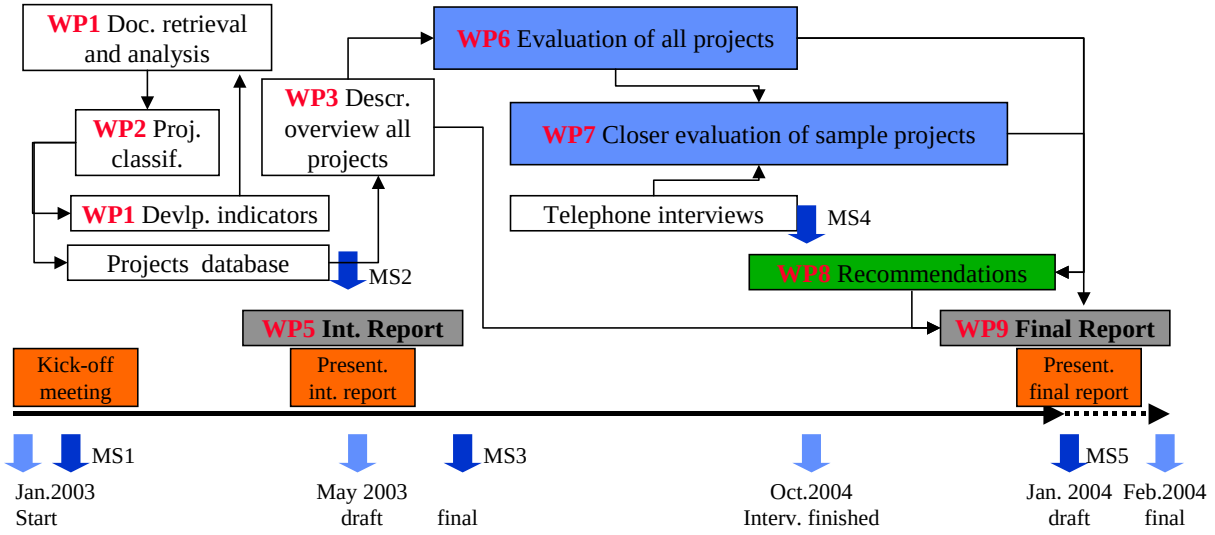
The importance of confidentiality concerning the evaluation itself and the data on the projects was highlighted. The project managers should not be involved unless urgently necessary. This was another modification of the initial plans which included a short questionnaire survey of the project managers if necessary.

An interim report was submitted to the Commission. It was modified to comply with suggestions by the Commission that arouse at the first interim meeting (Brussels, May 6, 2003) and accepted in final version in August 2003.

The present report gives an overview of the work in the whole course of the project.

The work programme and interlinked workpackages (WPs) are presented in the following figure.

Figure 1.1 Work programme




Source: Fraunhofer ISI

The milestones of the project have been achieved. Because of the unexpectedly small number of reports available for the evaluation, the descriptive overview of the research does not give a complete inventory of all activities (as arrivals at milestones or publications, e.g.) carried out in all KA2 projects. To overcome the problem of missing reports at least partially, technical annexes of 50 projects were additionally analysed. However, with a relatively small number of final reports the impact indicators that can be evaluated had to remain incomplete to some extent.

# 2 Methods

## 2.1 Document, literature and internet searches

As mentioned above it was agreed upon that the reports prepared by the projects should be the main source of information for the evaluation. At the kick-off meeting the Commission pointed out that the evaluation should not survey the project managers except the interviews with a smaller number of coordinators in the course of the closer evaluation.

The commission made available several electronic files with mainly administrative information on the projects and partners involved. These files include data from the reviewing process, mostly originating from the contractors themselves, and parts of the "CONTNEGFU"-database stemming from contract negotiations. Because of the heterogeneity of these data which covered different subsets of projects it was not in every case easy to decide which project should be included in the present evaluation. Different contract-numbers which had to serve as the identifiers to link different subsets of data, and which had in many cases changed over time made extensive security checks necessary.

These files were assembled to a MS-ACCESS database in a common format; the resulting projects database builds the basis for the further steps of the data collection and analysis.

The project reports available to the Commission were sent to the evaluation team at Fraunhofer ISI in hardcopy, 223 documents in total. Information missing in the projects database was extracted from the written reports, in cases without other sources also from the CORDIS database or the projects' WWW-sites. The project documents included periodic and final reports written by the contractors (in the following abbreviated by "PR1" for 1st periodic report etc.), mid-term reviews ("MTR") written by external experts, and technical annexes ("TA") where no reports were available.

Reports were available for a much smaller number of projects than expected (see below). Therefore it was agreed upon with the Commission to add the technical annexes to the database of those projects for which no later information (reports etc.) was available. Although the technical annexes were not sufficient for all planned analyses, they describe the aims of the projects and the research fields covered and therefore add valuable information on the coverage of the research fields by the KA2 projects.

The reports which could be analysed in the present project cannot be assessed as comprehensive in the way that for all projects the very last report was available. This is due to the fact that the collection of reports had to be finished in August 2003 and that not all reports which were due at this moment had already been sent to the Commission. Especially missing final reports lead to the fact that important results might be neglected by the present evaluation.

In addition to the collection of documents handed over by the Commission, the internet homepages of the projects were analysed. Since many projects present themselves in the internet but neglected to mention the internet address in their reports, many addresses had to be retrieved by the evaluation. The information presented there is quite heterogeneous but helped in some cases to find information on projects which had not yet delivered any report.

For the review of the relevant research fields as background for the KA2 projects, a systematic literature search was undertaken in MEDLINE for reviews from 2002 and 2003 in the field ("infectious disease" as search term in the Medical Subject Headings). In addition, the journals *Nature*, *Nature Medicine*, *Nature Reviews Drug Discovery*, *Nature Biotechnology*, *The Lancet Infectious Diseases*, and *Social Science and Medicine* were screened.

## 2.2 Classification of projects

The projects were classified with the aim of a descriptive overview on their main characteristics. Both information originating from the Commission's computerized files as well as extracted from the reports were used. The main characteristics to describe the projects were

- Infectious Agent,
- Thematic areas,
- Main goals,
- Project type,
- Types and number of partners,
- Budget,
- Target groups.

More information on the respective categories is given in Table 2.1.

## 2.3 Telephone interviews

In addition to the descriptive material collected for all projects telephone interviews with the project managers were carried out (WP7). The interviews aimed at the identification of factors and processes that led to the favourable or unfavourable state of the project and what could be learned from the specific project for other programmes. They included the following aspects:

- Process of implementation,
- Interlinking of the project activities with other national or Community activities and projects,
- Methodological quality of the study and validity of results,
- Project outcomes relative to its objectives and the set of indicators,
- Impact of the results on national and Community practice and policy making,
- Factors that influence utilisation of the results in a positive or negative way,
- Measures taken to promote the use of the results,
- Specific in-sights into the research field.

The documentation sheet for the telephone interviews can be found in Annex 2.

17 telephone interviews were carried out between 16th of October and 24th of November 2003. A list of the respective projects and interview partners can be found in Annex 3. To encourage frank evaluations of their own work it was assured to them that their personal views in the form of the interview protocols were not handed over to the Commission. All interviewees were very helpful for the evaluation and provided requested information on all topics, no restraint could be felt against this form of research.

The interviewees' explanations were entered into the projects database and analysed together with the material from the reports.

## 2.4 Development of projects database

The following section describes the structure, development and final status of the projects database.

### 2.4.1 Structure

The database was designed to make available all information which is needed to describe the funded projects and to evaluate the projects. The general structure of the database is presented in Table 2.1.

Table 2.1 Structure of projects database

| Issue | Operationalisation |
|---|---|
| Identification | • ID-Number (=Contract Number)<br>• Project title; Acronym<br>• Co-ordinator name, address etc.<br>• WWW-address |
| Excluded from evaluation | Yes/No |
| Infectious Agent | (as mentioned in project title or report) |
| Thematic area | Select one of three<br>1. Vaccines<br>2. Diagnosis and therapy<br>3. Public health interventions/monitoring |
| Main goal | Select one of seven<br>1. Advance of scientific knowledge (surveys, virology, epidemiology...)<br>2. Development of products or technologies<br>3. Development of interventions<br>4. Technology transfer (e.g. development of strategies or guidelines for monitoring/diagnosis)<br>5. Communication between experts (Networks, conferences...)<br>6. Education of health professionals<br>7. Other projects/Combination of goals |
| Start Date | Date |
| Duration | in months |
| State | Select one of three (determined from start date and duration):<br>1. not started; 2. ongoing; 3. finalised |
| Project type | Select one out of (CA; CM; DM; RS; TN; CRAFT, NAS-Extension) |
| Partners | |
| • Types of partners | One out of (HES; IND; REC; RPU; RPN; OTH) |
| • Number of partners | Total and in types |
| • Countries involved | Origin of partners |
| Budget | • Cost per partner<br>• EU final contribution for whole project |
| Target groups | Multiple choice, one or more out of<br>• Public<br>• Patients<br>• Scientists<br>• Health carer<br>• Policy-maker<br>• Administration |
| Documents available | • Periodic report 1 to 4<br>• Mid-term review report<br>• Techn. Annex<br>incl. date of respective document |
| Comments | Text field |

Source: Fraunhofer ISI

The data structure used to evaluate the quality of the projects is described in the respective chapter below.

### 2.4.2 Organisation of the content

The content of the database is organised by means of tables, forms and queries. The data sets are identified in the forms and tables by a variable "ID_NR" which is based on the contract number.

#### 2.4.2.1 Tables

In total there are 11 tables in the data base with only 4 of them holding static content. These are:

- "Projects_final": This is where the main data concerning the projects such as their financial budgets, goals, IDs and coordinators are located. Projects are classified into three thematic areas and each project is associated with one of 7 different main goals. Data in here originate from several sources, mainly from two data files received from the Commission and the analysis of the project documents.
- "Projects_final_COA": Made to contain data relating to the criteria of the outcome-assessment, this table holds ratings, comments and figures concerning the evaluation of progress made by specific projects.
- "publications": Publications originating from the projects, their titles, authors and classifications are listed here. Information is based on statements in periodic reports.
- "TJ_ALL_KA2_partners_mit_ID": Stores information about the partners involved in the projects such as an organisation's name, type, role, size, location, contact person. Size is distinguished between 7 magnitudes, type varies in 6 and role in 4 categories. These data are based on a file provided by the Commission and were corrected and complemented on the basis of the project documents.

Remaining 7 tables are used to hold temporal data, e.g. on the institutions or publications related to a specific project, which are used in one of the forms.

#### 2.4.2.2 Forms

Of the 11 existing forms 5 are used within other forms thus the remaining 6 are:

- "Projects_final": The main form, used for modification of the table "Projects_final". Also used to illustrate project specific information concerning publications and the partners involved, these data are shown in pop-up forms hence cannot be modified here. Use "Input_Partners" instead and add publications directly to the table "publications".
- "Input_Partners": Allows to add new partners and view or change already existing data. Input here will be stored to table "TJ_ALL_KA2_partners_mit_ID".
- "Project_Coordinator: The analogue to the above, for modification of the projects' coordinators this time. Note that this form is included entirely in "Projects_final". Modifications affect the table "Projects_final".
- "Projects_final_COA_x": Three forms for input and illustration of the outcome-assessment, all of them direct-linked to each other.

#### 2.4.2.3 Queries

There is a greater number (40) of queries included in the data base easening statistical analysis of data. Query-names beginning with "E_" or "N_of_" contain descriptive data on the numbers of projects, often cross-tabulated with different categorical variables. Queries beginning with "OA_" contain information for the outcomes assessment.

Some of the most remarkable queries are:

- "E_Country_of_Partners": Gives total numbers of partners per country and broken down to the role within the project.
- "E_Status_of_Projects": Gives numbers of finalised versus ongoing projects and broken down to the planned duration of the project.
- "N_of_documents": Overview on received documents such as periodic, mid-term and final reports broken down to the thematic areas.
- "OA_Interlinking-projects": Overview on projects' interlinking with other national or community activities or projects as stated by the criteria outcome-assessment

### 2.4.3 Development and final content of the database

The database was built on the basis of the two MS-Excel-files which were kindly handed over to Fraunhofer ISI by the Commission. The two files included data on 181 and 127 projects, respectively. The contract numbers were used as a key variable to merge the data from the different sources. However, in some cases, projects with the same title had different contract numbers and vice versa, which had to be resolved with great care to avoid far-reaching mistakes.

After deleting double datasets and adding some new from the reports and technical annexes sent to us, the database finally contains datasets on 205 projects, thereof 48 that investigate only animal diseases. Another 11 projects should not be analysed because they are dealing

with prion diseases (BSE or TSE), one other project in the database was not funded finally. The remaining 145 projects on human diseases were to be analysed in our project.

Periodic or final reports for 90 projects were received by the evaluation, as well as 43 mid-term reports. 50 technical annexes are available for those projects for which no report was received yet. In total, 225 documents build the basis for the evaluation actually. For most of the projects only the first periodic report is available (Table 2.2).

Table 2.2 Number of documents available for evaluation

| Type of document | | n |
|---|---|---|
| Technical Annex | | 50 |
| Periodic report | #1 | 90 |
| | #2 | 38 |
| | #3 | 3 |
| | #4 | 1 |
| Mid-term report | | 43 |
| Total | | 225 |

(total 145 projects)

Source: Fraunhofer ISI

As proposed in the tender, to reach the highest possible completeness of the database "late" information on additional projects has been included into the evaluation until the database had to be closed for the final analyses in August 2003.

The numbers and types of partners involved in the projects are a main target of the evaluation. To make best use of the available data, features to count the number of partners of different types and to store this information in separate variables were included in the database. Similar procedures were implemented for the products and publications. Various forms and queries were constructed to retrieve the information necessary for the present report. These data were automatically updated as new entries were added to the database or existing datasets were modified.

Table 2.3 Number of 1st periodic reports per year

| Year (Start of Project) | n of 1st periodic reports | n of projects |
|---|---|---|
| 1999 | 25 | 26 |
| 2000 | 34 | 34 |
| 2001 | 31 | 41 |
| 2002 | 0 | 44 |
| Sum | 90 | 145 |

(Year as given in the Contract-Number)

Source: Fraunhofer ISI

As Table 2.3 shows, most of the 1st periodic reports available are from year-2000-projects, none from 2002. For one project from 1999 even the first periodic report is missing. The

delivery dates of the reports begin with 01.01.2001, with 35 dated from 2002 and only 8 from 2003.

The compilation of the information on the KA2 projects was more time-consuming than expected because of the heterogeneity of the data sources and the missing opportunity to survey all coordinators. Information from the different sources on some of the projects was diverging to a considerable extend, and especially as far as the contract numbers and starting dates were affected this made demanding cross-checks necessary. Building on these experiences, suggestions will be made in the last section of this report to enhance the 'evaluability' of similar research programmes in the future.

## 2.5 Data analysis

After exclusion of projects on animal and prion diseases (on advice of the Commission), 145 projects were left that build the basis for all analyses. If it is not explicitly mentioned that results are based on another sample, these 145 projects are the background for all presented results.

The projects database was analysed descriptively by means of the therein implemented queries etc. Ratings are made on a five-point Likert-scale ranging from 1 ("very unfavourable") to 5 ("very favourable").

For some statistical purposes, a part of the data was exported to the statistical software package SPSS version 10.0.

A large amount of qualitative data on the implementation process and goal attainment of the projects was extracted from the project documents and equally entered into the database (Forms "Projects_final_COA_x"). The data were extracted from the database into issue-specific tables[2], and qualitatively summarised for chapters 4 and 5 of this report. As a reference to the original source, the ID-numbers of the respective projects are indicated in the text (e.g. "Proj_37").

If available, the mid-term review report was used as a source of assessments of the relevance, methodological quality, coordination and internal communication, and impacts of the projects.

# 3 Descriptive overview of all projects

This chapter contains results on the projects. In accordance with the tender of the present project, the descriptive overview consists of three parts:

(1) a description of the three thematic areas of KA2,

(2) a description of the non-thematic goals of the Key Action,

(3) an overview of relevant statistical data of formal aspects of the funded projects.

The overview will begin with the description of the research fields and the integration of the funded projects into them.

[2] see Annex 4.

## 3.1 Integration of the projects in the research fields

In the following chapters, international trends and challenges in the research fields of KA2 as well as on the agendas of the relevant international bodies and associations are presented. It is pointed out in the text how the projects of KA2 have responded to these challenges. A synopsis of diseases/pathogens and respective numbers of projects that deal with them can be found in Table 3.2.

### 3.1.1 Research fields

#### 3.1.1.1 General developments

Throughout the world, infectious diseases kill about 17 million people a year. For a large number of them still no satisfactory treatment exists. Thirty new epidemics have entered the floor in the last 20 years, and as the example of SARS shows, new emerging or re-emerging diseases have to be expected (European Commission 2003b).

However, in recent years, the number of approved anti-infective agents is declining, and a large number of pharmaceutical and biotech companies have exited the field or reduced their efforts. The reason might be that antibiotics represent a complex market which is perceived as presenting too little incentives compared to medicines for chronic diseases (Clarke 2003a; Fox 2003). Other factors that might in fact lead to a vaccine (or drug) shortage are the high cost and complexity of developing, manufacturing, and distribution of vaccines, few manufacturers, and the lack of continuous investment among manufacturers (Nelson 2004). The development of resistance makes antibiotics less profitable over time, new drugs are often kept only as reserve, and – unlike drugs for chronic illnesses – antibiotics cure the patients, thereby eliminating their customers (Clarke 2003a). On the other hand, antibiotic resistance allows to market new drugs that replace older ones (Fox 2003).

Market-related problems with the development of vaccines and medicines for poor countries are reduced prices with the danger of illegal diversion of discounted products to high-price countries, international patent rights and insufficient funding, the latter being targeted in the light of the threats to stability and growth of the poorer countries which are most affected by these diseases (Wechsler 2003).

*Many of the KA2 projects are directed to poverty-related diseases or other fields which are of minor interest for the pharmaceutical industry, e.g. the treatment of children.*

The OECD underlines the necessity to develop adequate, cost-effective measures against the spread of infectious diseases and overcome hindrances to their practical implementation. Means to improve research and to reach this goal are seen in the evaluation of research programmes, identification of gaps and double work, new assessments of corporate structures and strategies in public and private biomedical institutions as well as the implementation of early warning systems (Infektionskrankheiten 2003). Companies can be supported in the development of anti-infective by lighter regulation and increased public research funding (Clarke 2003a).

Solutions to improve vaccine development are seen in increased public demand, more support for regulatory agencies, stronger liability protections, public information, and financial incentives to manufacturers (Nelson 2004).

Despite the rising public awareness of infectious diseases, it is argued that – at least in the USA – this concentrates to a large extent on biodefence while it distorts the research priorities of the US NIAID, and funds are cut in other fields and redirected to fund for example anthrax vaccines (Check 2003).

In 2003, large funds were allocated to control of and research in malaria, TB and AIDS. Efforts to control diseases do also increase the demand for research, and public-private partnerships (PPPs) have emerged and resulted in newly developed drug and vaccine candidates (Butler 2003). PPPs make the market of neglected diseases attractive for biotech companies and helps them to develop technologies that can later be applied to other areas (Louet 2003). A public-private partnership in the UK has lead to the development of a new malaria drug that will soon enter the market, and a number of other antimalarial drugs in the pipeline are equally resulting from this collaborative form of research funding (Schubert 2003). Yet, such efforts will need to be sustained for many years to make a significant impact (Butler 2003).

*An intrinsic goal of EU research funding is the collaboration of public research and industry. 45 of the funded projects have at least one IND partner, in total 122 IND partners are involved.*

A stronger partnership with developing countries in the clinical development of treatments for poverty-related diseases is the aim of the Europe-Developing Countries Clinical Trials Partnership (Clarke 2003b). This initiative by the European Commission aims at overcoming earlier failures which resulted from inadequate follow-up of trial participants, poor clinical practice and data collection, and ethical issues. Furthermore it is recognised as essential that drugs and vaccines are developed in the target countries themselves rather than shipped in.

*KA2 projects which support this initiative are under way like the participation of project Proj_98 in the WHO collaborative study on artesunate.*

### 3.1.1.2 Thematic areas of KA2

The three thematic areas of the Key Action 2 of the QoL-programme in the 5$^{th}$ European Framework Programme for research are (1) vaccines, (2) diagnosis and therapy, and (3) public health interventions and epidemiology/monitoring.

#### *3.1.1.2.1 Vaccines*

The world market for vaccines is 3.5 billion EUR worth each year, other estimations go up to 6 billion US$ for 2002, and expected to grow by 10 to 15% each year (Smith and Renaud 2003; The European Commission 2003). The European industry has traditionally a large share on this market of around one third of the world production, more than a half of it for developing countries (The European Commission 2003).

Recent outbreaks of West Nile Virus (WNV), severe acute respiratory syndrome (SARS), avian influenza or monkeypox, as well as threats from bioterrorism have increased the interest in developing new vaccines, but also for HIV feasible vaccination would be a great achievement because of the missing definitive eradication of HIV by antiretrovirals, their financial burden, and the high degree of antigenic variability among HIV strains (Smith and Renaud 2003).

More than 20 therapeutic vaccines to stimulate T-cell responses of persons with HIV are currently under development, most of them in the USA, but some also in Europe (McMichael and Hanke 2003). At present, more than 15 phase I, II or III trials are ongoing involving a variety of different strategies, including more complex subunit vaccines, recombinant viral vectors, prime-boost strategies and DNA vaccines, as well as new delivery mechanisms like intranasal application (Smith and Renaud 2003).

*Proj_40 is an example for KA2 projects that use these new approaches to HIV vaccination.*

There are a number of main challenges ahead to developing an effective HIV vaccine. These lie in protein engineering, the optimisation of T-cell inducing vaccines, to increase the capacity to carry out phase-III trials, and to manufacture them in sufficient quantities (McMichael and Hanke 2003).

Recently, an AIDS vaccine candidate has failed in clinical trial, new tests are carried out with combination of two vaccine candidates ('Money down the drain' fears for AIDS vaccine trials 2003). The challenges that are faced in this field highlight the need for international collaborative efforts, as Autran, Debré, Walker and Katlama (2003) state[3]. Despite clear successes in the development of treatments, the drugs are not able to eradicate HIV from the body. The costs for lifelong therapies are so high that they are only accessible for less than 2% of the infected people. Patient adherence is a problem due to negative side effects and resistant strains of HIV are further challenges, as well as treatment schemes that reduce adverse effects and therapeutic vaccines to boost the immune reaction (Autran et al. 2003). Interdisciplinary teams which consist of immunologists, vaccinologists, virologists, experts for clinical trials and clinicians are necessary to tackle these tasks.

*Internationally coordinated research programmes have begun, one of which is the EU-funded Proj_69.*

Another new approach are vaccines based on the carbohydrates on parasite surfaces instead of proteins. Some pathogens like Trypanosoma brucei, a protozoan that causes sleeping sickness, can change their protein coat every two weeks which makes it very difficult for the immune system to develop a sufficient immune response. Carbohydrates e.g. in the cell walls are not or less fast changed and therefore present a much more stable target. An Australian group is currently working on vaccines based on these substances against Plasmodium falciparum (Dennis 2003).

Research in vaccine adjuvants has gained growing attention in the last years and resulted in promising approaches. The field is moving rapidly. Mucosal vaccine delivery systems are specifically designed to allow vaccines to enter the body through mucosal surfaces via nasal or oral application and thereby avoid invasive forms of application. Additional components are necessary to protect antigens from degradation and promote their interaction with the host tissue (O'Hagan and Valiante 2003).

*Many of the KA2 projects are explicitly directed to this emerging field, e.g. Proj_132, CRAFT-project Proj_31, Proj_169, Proj_149, Proj_38, the cluster Proj_172, Proj_203, or Proj_3, most of them working with adjuvants.*

[3] B. Autran and C. Katlama are coordinator and partner in KA2 projects, respectively.

#### *3.1.1.2.2 Diagnosis and therapy*

Promising immunological approaches to identify molecular and cellular targets, and to potentially break antigen-specific resistance, are to enhance the function of antigen-presenting cells, e.g. dendritic cells (DC), to enhance T-cell activation, to use genetically engineered viruses and bacteria as vaccine vectors, and to block immunological "checkpoints" or signalling pathways (Pardoll 2002).

*For example, the project Proj_90 analyses the interaction of DC with pathogens, Proj_97 works on cell signalling to improve treatment for Leishmaniasis.*

Therapeutic *antibodies* offer new treatment options. They are now genetically engineered molecules with high functionality and specificity. The treatment strategy has developed out of the passive antibody serum therapy and is now applied mostly to patients with immune disorders, for post-exposure prophylaxis against several viruses (e.g. rabies, measles, hepatitis A and B, varicella and respiratory syncitial virus (RSV)) as well as for toxin neutralisation in diphtheria, botulism and tetanus. Advantages compared to antimicrobial agents and vaccines are the low toxicity, high specific activity and immediate effects. Limitations to the approach are the still high production costs, which is approached by producing blocking antibody fragments in E. coli or even in plants (Brekke and Sandlie 2003).

*Antibodies for HBV are developed in the KA2 project Proj_111, Proj_44 prepares mono-clonal antibodies as well as Proj_203, Proj_17 and others.*

*Antibiotics*

In the development of antibiotics, *antimicrobial resistance* has become a dramatic problem. Antimicrobial resistance arises by two mechanism: Under direct antibiotic pressure, bacteria can acquire mutations or pick resistance genes from other bacteria that reduce antibiotic susceptibility. Alternatively, resistance can spread in a population by introducing a resistant clone from another population (McGeer and Low 2003). The frequency of strains as oxacillin-resistant Staphylococcus aureus is strongly related to the amount of antibiotics used in a country. Much higher levels of resistance are observed in Southern European countries (but also in Ireland), where consumption is high, than in Scandinavian countries (Schröder et al. 2003). One approach to remedy this situation is to reduce the consumption of antibiotics by improved treatment strategies or with the help of vaccines, but also improved hygiene can reduce the need for antibiotic treatment (McGeer and Low 2003).

Enhanced methods of clinical diagnosis to rapidly identify the causative pathogens help to develop and apply narrow-spectrum antibiotics that reduce the danger of antibiotic resistance (Senior 2003). Molecular "theranostics", the combination of the terms "therapeutics" and "diagnostics" is an emerging concept in which molecular biology tools are used to provide diagnostic assays to enable better initial management of patients and more efficient use of antimicrobials. These tests are based on rapid and sensitive nucleic acid testing assays for infectious diseases and reduce the need for standard culture-based microbiological methods that take at least two days (Picard and Bergeron 2002).

*Diagnostic tools like specific assays are developed or optimised in a large number of projects. Several projects aim at the EU-wide or international standardisation of testing methods to obtain internationally comparable results.*

New targets for antibiotic therapy emerge, e.g. the cell membrane of the pathogen (Xiao-Quing et al. 2003). Another example are inhibitors of bacterial RNA polymerase, the most important enzyme of gene expression, which have been newly discovered in the USA and could lead to a new class of antibiotics (Senior 2003).

Tuberculosis is a disease which claims two million lives per year worldwide, its infectious agent, Mycobacterium tuberculosis, is present in one third of the global population. The risk of developing the disease after being infected is highly dependent on the immune status of the person being affected. Persistence of the bacterium in the body even after antibiotic treatment is a wide-spread problem because the bacterium can develop a phenotypic state which renders it tolerant to treatment and allows it to remain even in a immunologically educated individuum for decades and to be reactivated to develop a new period of the disease. Therefore, besides the "normal" questions of diagnosis and interruption of transmission, adherence to long-term treatment and emanating drug-resistant strains of M. tuberculosis, specific challenges lie in the metabolism of the persistent form, progression from latent infection to active TB, and in targeting the persistent form of the bacterium by drugs or by post-exposure vaccination (Stewart et al. 2003).

Another cause of concern, for example, especially for poorer countries is Leishmaniasis, which is currently affecting some 12 million people, mostly in the tropics and subtropics (Dennis 2003).

*The projects Proj_4, Proj_101, Proj_132 and Proj_169 investigate in the role of RNA as target for drugs or vaccines.*

*11 of the 145 projects consider TB, and 2 Leishmaniasis.*

*Antivirals*

The elimination of viruses requires a number of events, including the inhibition of cell infection, mediation of killing infected cells, inhibition of virus replication, of virus release and of cell-cell-transmission (Brekke and Sandlie 2003). Large progress has been made in recent years in the development of antiviral medicines, especially for the treatment of AIDS. The antiviral market has an annual volume of almost US$ 8 billion, thereof over US$ 5 billion alone for HIV (Milroy and Featherstone 2002). However, companies in this area face a strong competition, which is much lower for other fields like hepatitis C virus (HCV), cytomegalovirus (CMV), herpes simplex virus (HSV) and respiratory syncytial virus (RSV), which rewarded companies in these areas with strong sales (Milroy and Featherstone 2002).

Other virus diseases are of rising interest to research and public health: West Nile virus, a mosquito-born disease, has recently been found in wild birds in the UK (West Nile virus invades UK 2003), a first human case was detected in France in October 2003, as well as a number of equine cases (Das 2003). Although no human cases have yet been found in the UK (unlike the USA), the situation could change with the emergence of types of more contagious mosquitoes in an environment changed by global warming (West Nile virus invades UK 2003). Human metapneumovirus (hMPV) could be the second leading cause of hospital visits among infants in the developed world (Wechsler 2003), and regularly outbreaks of virus influenza are reported (as recently in the UK), or of polio in Nigeria (Das 2003).

*HIV/AIDS*

HIV infection and AIDS are one of the diseases that became important only in the last about 20 years. In 2002, 570,000 persons were infected with HIV in Europe, nearly 42 million

worldwide (Werber 2003). Still many questions are open with regard to HIV infection. They relate to (Rowland-Jones 2003):

- the origin of HIV,
- the mechanisms responsible for the decline in $CD4^+$-T-cell function and number,
- the development of AIDS in infected persons, and
- the development of resistance against treatment.

The standard for treatment in Europe and Northern America consists of a protease inhibitor (PI) or a non-nucleoside reverse transcriptase-inhibitor (NNRTI) and two nucleoside reverse transcriptase-inhibitors (NRTI). In the United States, 335,000 patients receive this kind of treatment, of which 270,000 display resistance to at least one class of therapeutics, and 52,000 patients are considered triple-class failures. Around 50% of all patients can be expected to experience treatment failure within 12 months (Werber 2003).

The field is very dynamical with almost 100 investigational drug applications (INDs) submitted to the US FDA to conduct clinical trials up to now. To tackle growing resistance against older drugs, new principles are developed, e.g. the new entry inhibitors (Milroy and Featherstone 2002). Fusion inhibition is another strategy that is investigated at the moment, as well as the disruption of the integration of HIV DNA into the host genome (Werber 2003). To simplify drug administration and encourage patient compliance, combinations of active substances or long-acting drugs are developed (Milroy and Featherstone 2002).

The largest challenge in the field of HIV is the translation and dissemination of therapeutic advances in the developed world to the millions of people affected in the developing world. This is not only a economic challenge, other problems are the lack of medical expertise and infrastructure required to administer the complex regimens. As mentioned, drug resistance makes new types of drugs as well as new treatment schemes necessary. Therapeutic vaccination and new targets derived from HIV's proteome and genome are promising approaches to reach the ultimate goals of eradication of HIV from infected people and protection from infection through vaccination (Pomerantz and Horn 2003).

*Seroconversion and AIDS pathogenesis are treated in a large number of KA2 projects, e.g. in Proj_110.*

*Hepatitis*

Major gaps exist in the diagnosis and treatment of hepatitis. Persistent diseases and treatment-related toxicity remain problems in the treatment, but progress is being made in the tailoring of the treatment to the type of infection and novel antiviral agents (Nierengarten 2003). In the UK alone, around 200,000 persons are thought to be infected with HCV, but only 35,000 have been diagnosed and less than 1500 have been treated. The absence of a patient voice, knowledge gaps among general practitioners and shortage of trained other staff, and little access to treatment (which could be highly cost-effective) especially in the UK are the hurdles that impair adequate treatment (Breaking the silence 2004).

#### *3.1.1.2.3 Public health interventions/monitoring*

As mentioned above, the problem of resistant strains of infectious agents which are resistant to one or more anti-infective drugs is strongly related to the prescription and consumption behaviour towards antibiotics or antivirals. Patients are lacking information to assess their contribution to health outcomes and improve their behaviour (e.g. Bonn 2003). These results

are supported by a Eurobarometer public opinion poll in 2002 (European Opinion Research Group EEIG 2003). 93% of the consumed antibiotics were obtained through prescription of a physician which hints that there are strong possibilities to optimise their prescription behaviour.

Studies in consumption patterns and patients' adherence to treatment are necessary to understand the relevant factors to be able to design effective interventions.

*Antibiotic resistance is the issue of a large number of KA2 projects. Proj_105 e.g. tests interventions to reduce the rate of carriage of antibiotic-resistant Streptococcus pneumoniae in children. Proj_119 aims at the development of strategies for control and prevention of antibiotic resistance in European hospitals.*

Epidemiological surveillance of infectious pathogens build the basis for effective prevention strategies. A good example for this is again HIV. While no cure exists and most of the infected persons have no access to treatment, prevention is the best way to minimize human suffering and to prevent the future cost of unchecked HIV transmission. As substantial advances have been made in HIV prevention, the biggest challenge now is the full implementation of existing preventive interventions worldwide (Valdiserri et al. 2003).

*Proj_77, e.g., harmonises the serological surveillance of immunity to a variety of vaccine preventable infections, Proj_103 studies the impact of meningococcal epidemiology and population biology on public health in Europe.*

### 3.1.2 International agendas

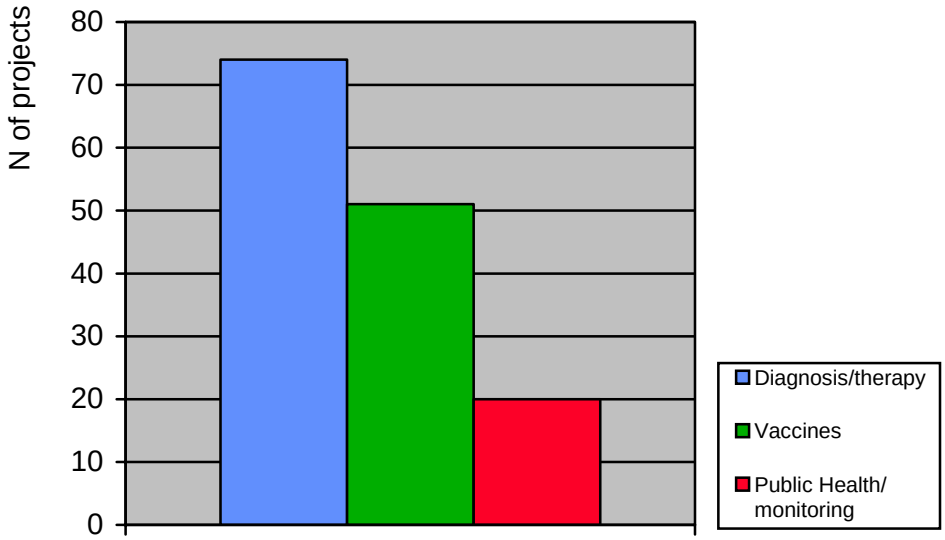
At the moment, the database contains 74 projects which primarily work on procedures for diagnosis and therapy (area of activity "Strategies to identify and control infectious diseases"), 51 projects work in the field of vaccines ("Development of improved or novel vaccines") and 20 consider public health interventions or monitoring (KA2 area "Aspects of public health and care delivery systems"; see Table 3.1 and Figure 3.1).

Table 3.1 Thematic area of the projects

| **Thematic area** | **n of projects** |
|---|---|
| Diagnosis and therapy | 74 |
| Vaccines | 51 |
| Public health interventions/monitoring | 20 |

Source: Fraunhofer ISI

Figure 3.1 Thematic area of the projects




Source: Fraunhofer ISI

The infectious agents which the projects are aimed at were in part already available in the electronic files, in other cases they were derived from the reports. The largest number of projects in one category of Table 3.2 (30 projects) target diverse or unspecified infectious agents, most of them consider issues of antimicrobial resistance or general vaccine strategies. The second most projects (21) care about HIV. 14 projects are targeted to Hepatitis (incl. HBV and HCV), nearly the same number to tuberculosis (TB, 11 projects) and mosquito-borne diseases (incl. malaria, 12 projects). Prions as the supposed vectors of TSE are considered with several projects, these projects were excluded from the further analysis on suggestion of the Commission. Overall, viruses are the most prominent research objects (in 56 projects), followed by bacteria (34 projects) and smaller groups of other infectious agents.

*The range of agents and diseases under study in KA 2 is very broad. Some of the projects are dedicated to zoonoses, e.g. by viruses or by Mycobacterium avium paratuberculosis. Many of the agents or diseases focussed in the KA2 projects are especially prevalent in developing countries (HIV, Malaria, TB, Meningococcus, Leishmaniasis), a fact which shows a high relevance of the research in an international context.*

Table 3.2 Projects on infectious agents

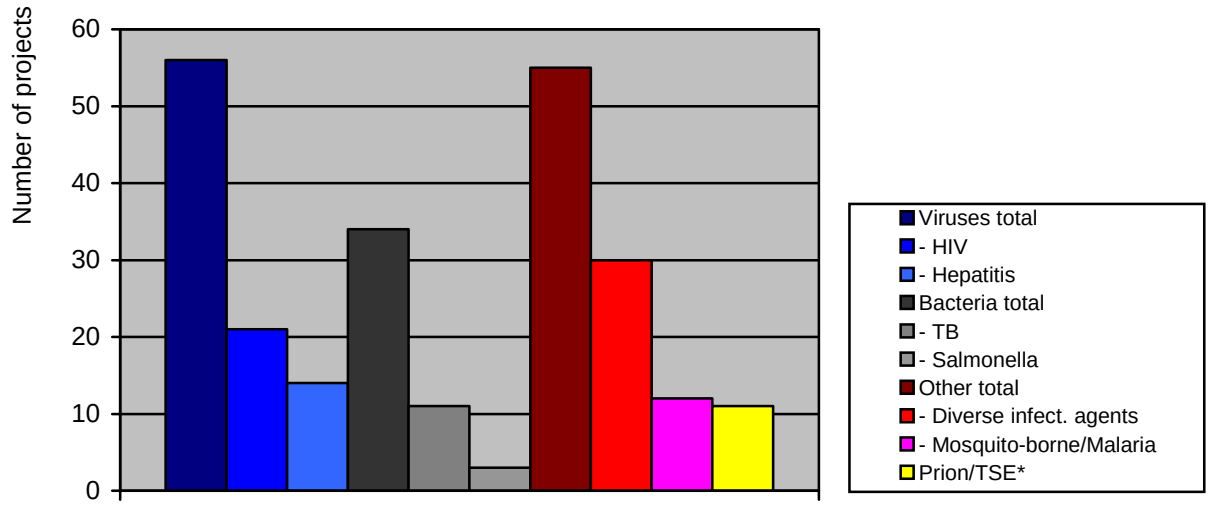
| Infectious Agent | n of projects | Infectious Agent | n of projects | Infectious Agent | n of projects |
|---|---|---|---|---|---|
| **Viruses** | | **Bacteria** | | **Miscellaneous** | |
| – Adenovirus (ADV) | 1 | – E.coli | 1 | – Alveolar echinococcosis | 1 |
| – CMV | 2 | – Meningococcus B | 2 | – Fungi | 2 |
| – Enterovirus | 1 | – Mycobacteria | 1 | – Pneumonia or other lung infections | 3 |
| – Hantavirus | 1 | – TB | 11 | – Pneumocystis carinii | 1 |
| – Hepatitis | 1 | – Paratuberculosis | 1 | – Yeast | 1 |
| – HBV | 3 | – Pertussis | 1 | – Leishmaniasis | 2 |
| – HCV | 10 | – Pseudomonas aeruginosa | 1 | – Mosquito-borne diseases | 1 |
| – HIV | 21 | – Salmonella | 3 | – Malaria | 11 |
| – HPV | 2 | – Shigella | 1 | – Tick-borne diseases | 1 |
| – HSV-1 | 1 | – Staphylococcus | 1 | – Zoonoses | 1 |
| – Influenza | 3 | – Streptococcus | 1 | – Diverse or unspecified infect. agents | 30 |
| – Measles | 1 | – Bacteria, gram-positive | 2 | – Intracellular pathogens[1)] | 1 |
| – Metapneumovirus | 1 | – Bacteria and fungi | 1 | **Total other agents** | **55** |
| – Paramyxovirus (e.g. Mumps) | 1 | – Diverse or unspecified bacteria | **7** | – Prion/TSE[2)] | |
| – Reoviridae | 1 | **Total bacteria** | **34** | | |
| – Respiratory syn-cytical virus (RSV) | 2 | | | | |
| – Rotavirus | 1 | | | | |
| – Viral zoonoses | 1 | | | | |
| – Diverse or unspecified viruses | 2 | | | | |
| **Total viruses** | **56** | | | | |

[1)] i.e. Chlamydia, Mycobacterium and Rotavirus

[2)] Projects on prion-diseases/TSE are carried out under KA2 but were excluded from the evaluation based on a request by the European Commission.

Source: Fraunhofer ISI

Figure 3.2 Infectious agents (large groups)




Source: Fraunhofer ISI

To give an impression of the actual research topics in the field of infectious diseases, in addition to the above mentioned review articles, the agendas of relevant institutions and scientific conferences have been analysed.

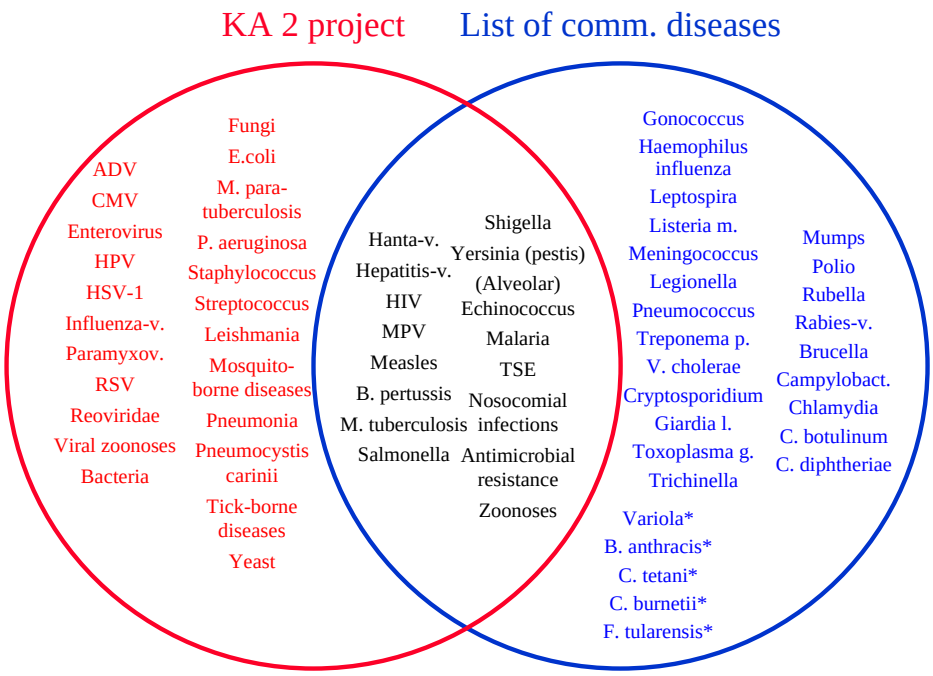
In Annex 1 of **Commission Decision 2000/96/EC**, a list of communicable diseases is specified which are to be placed progressively under EU-wide surveillance because of their relevance for public health and therefore can be understood as an agenda for research in the field of infectious diseases[4].

Recently, five diseases (Anthrax, Smallpox, Tetanus, Q-fever, Tularaemia) have been added to the list mainly for bioterrorism reasons which were not on the agenda when the Commission had to decide which projects to fund in KA2. The main body of the list contains 39 diseases and two special health issues (Nosocomial infections and Antimicrobial resistance).

The projects funded under KA2 had not been selected with the aim to cover some or all the diseases in this list, but the comparison, which is shown in Figure 3.3, might nevertheless be informative.

[4] http://europa.eu.int/comm/health/ph_threats/com/comm_diseases_annexe1.pdf

Figure 3.3 Coverage of EU Communicable Diseases List[5]




*) 5 diseases (Anthrax, Smallpox, Tetanus, Q-fever, Tularaemia) have been added to the list only recently (mainly for Bioterorrism reasons).

Source: Fraunhofer ISI

A more detailed comparison of the coverage of KA2 projects and the List of Communicable Diseases can be found in Annex 4.

*The preceding figure shows that – among others – many of the infectious agents that deserve special surveillance in the EU are investigated under KA2, although around one half of them only in a general way, e.g. under the issue of "zoonoses". Yet it has to be noticed that the Commission Decision 2000/96/EC had not been a criterion for the selection of KA2 projects for funding.*

In its Fact Sheet No. 97 (last revised August 1998; http://www.who.int/inf-fs/en/fact097.html) "Emerging and Re-emerging Infectious Diseases", **WHO** names several infectious agents and diseases as priority research targets because of their status as emerging or re-emerging diseases:

- Viruses: Ebola; HIV; Hepatitis C; Sin nombre; Influenza A(H5N1).
- Bacteria: Legionella pneumophilia; Escherichia coli O157:H7; Borrelia burgdorferi; Vibrio cholerae O139.
- Antimicrobial resistance: Escherichia coli, Neisseria gonorrhoea, Pneumococcus, Shigella, Staphylococcus aureus.

[5] Annex I of Commission Decision 2000/96/EC, cf. European Commission 2000. For more details on the projects and infectious agents see Annex 4.

- Re-emerging infectious diseases: Cholera; Dengue fever; Diphtheria; Meningococcal meningitis; Rift Valley fever; Yellow fever.

Many of these infectious agents and diseases are studied by one or more of the KA2 projects.

The **US National Institute of Allergy and Infectious Diseases** (US NIAID) Global Health Research Plan for HIV/AIDS, Malaria, and Tuberculosis (http://www.niaid.nih.gov/publications/globalhealth/global.pdf) lists the following goals for NIAID's global health research:

- Reduce the number of HIV/AIDS-infected young people by 25 percent by 2010 (UN Secretary-General Report to the General Assembly on March 27, 2000).
- Reduce the burden of disease associated with malaria by 50 percent by 2010 (WHO Roll Back Malaria).
- Reduce TB deaths and prevalence of the disease by 50 percent by 2010 (WHO Stop TB Initiative).

In July 2003, a whole Symposium was held on antimicrobial resistance (**4th International Symposium on Antimicrobial Agents and Resistance**, ISAAR 2003), in Seoul, which highlights the relevance of this research topic which is under study in many KA2 projects.

The Programme of the **Sixth Annual Conference on Vaccine Research**, which calls itself the "largest scientific meeting devoted exclusively to research on vaccines and associated technologies for disease prevention and treatment through immunization" (http://www.nfid.org/conferences/vaccine03/vaccineconf.pdf) contains among others

- Impact of Vaccination Strategies on Disease Epidemiology,
- Vaccines for Zoonotic Diseases,
- Vaccine Supply: Global Crisis,
- Regulatory/Suppressor T Cells: Implications for Vaccinology,
- Vaccines Against Nosocomial Infections,
- Vaccines and Biodefense,
- Malaria Vaccines.

*Again, many of these research fields are covered by at least one KA2 project, e.g. the zoonoses, nosocomial infections and malaria. Research is carried out under KA2 in vaccines for the following infectious agents: Diverse/unspecified agents, intracellular pathogens and viruses; HIV; Malaria; TB; Influenza; HCV; RSV; CMV; Fungi; Hantavirus; HBV; Meningococcus B; Salmonella; Rotavirus; Shigella.*

And finally, at the **13th European Congress of Clinical Microbiology & Infectious Diseases**, May 10 to 13, 2003 in Glasgow, Scotland, keynote lectures are held concerning the "Genetic basis of susceptibility to infectious diseases", "Modelling in infectious diseases: achievements and shortcomings", and "Emerging techniques for the rapid diagnosis of infectious diseases".

*Other programmes and articles show a similar picture. The high correspondence between international goals for research and scientific discourse on the one hand and the topics of the KA2 projects on the other hand give the (preliminary) impression that the projects cover many relevant and actual research areas.*

*Some of the most recent issues like especially agents which might be used in bio-terrorism are scientifically discussed but could not be included in the FP5 projects because the high priority of these issues emerged only after the considered projects had already started.*

## 3.2 Non-thematic goals of the Key Action

The main objectives of KA2 are (European Commission 2001b):

- to improve the prevention and treatment of important infectious diseases through the development of new and improved preventive and/or therapeutic vaccines and vaccination strategies,
- to identify and exploit new targets for anti-infective interventions,
- to develop new diagnostic tests,
- to develop tools for epidemiological monitoring and forecasting, and
- to develop the research base for rational public health practices related to infectious diseases.

Important contributing factors are seen in a deeper understanding of pathogen genomes and in the exploitation of new technologies based on genomics and proteomics, in the integration of human and animal health research. Expected outcomes are control tools against major human and animal infectious diseases and contributions to the major poverty related diseases (European Commission 2001b).

Besides responding to these "thematic" goals, European research funding has objectives that are unspecific to the field of application. The Fifth Framework Programme as a whole was conceived to help solve problems and respond to major socio-economic challenges. Its general objectives lie in the combined areas of technology, industry, economy, as well as social and cultural aspects (European Commission 2003c).

The Key Actions are targeted at enhancing the quality of life of European citizens and improving the competitiveness of European industry. The projects are expected to actively contribute to the policy objectives. An important mean to do this is to use the potential synergies between different projects.

Intrinsic to the programme are activities such as support for research infrastructures, dissemination and exploitation of results, and training opportunities. Entrepreneurship and participation of small and medium enterprises shall be supported, as well as the consideration of relevant gender specificities in all of the activities, as well as contributions to the European Research Area initiative (European Commission 2001b).

To achieve the goals, the links between discovery, production and end-use must be consolidated. The needs of society and the requirements of the consumer have to be recognised and research must lead to future wealth and job creation, while respecting the principles of sustainable development (European Commission 2001a).

Other goals to be kept in mind are the European integration and international collaboration, the complementation of national initiatives (subsidiarity principle) and generation of European added value, the development of products and processes for the benefit of the

European consumers, the generation of knowledge and development of a European Research Area[6], the application of this knowledge in practice and technology transfer, the use of obtained evidence in policy-making, and education and the development of labour force.

Summarising these considerations, the non-thematic objectives of the QoL-programme and KA2 are the following:

- contribute to the European policy objectives,
- respond to major socio-economic challenges,
- improve future wealth and help create jobs,
- contribute to the European integration, complement national initiatives, generate European added value,
- recognise the needs of society and of the consumers, develop products and processes for the benefit of the European consumers,
- enhance the quality of life of European citizens,
- improve the competitiveness of the European industry,
- support entrepreneurship and the participation of small and medium enterprises,
- strengthen links between discovery, production and end-use, combine aspects of technology, industry, economy, society and culture,
- use potential synergies between different projects,
- support research infrastructures, contribute to the European Research Area initiative,
- develop training opportunities, enhance education and encourage the development of labour force,
- consider relevant gender specificities,
- respect the principles of sustainable development,
- support the application of the generated knowledge in practice, technology transfer,
- support the use of obtained evidence in policy-making.

The present reports not only summarises the field-specific research results, but also reviews the outcomes of the Key Action on these non-thematic goals. Consequently and as far as possible, data were collected for indicators that allow the assessment of how the projects managed to achieve these more general objectives. Numbers of countries involved, collaboration with industry partners, patent applications and measures taken to disseminate the results into science and policy-making are examples for this.

The more descriptive indicators are statistically analysed in the following chapter 3.3. Results on the implementation process and impacts of the funded projects are later presented in chapters 4 and 5.

[6] The purpose of the European Research Area is to establish a border-free zone for research, in which scientific resources will be better deployed to create more jobs and to improve Europe's competitiveness (European Commission 2002).

## 3.3 Statistical characterisation of projects

### 3.3.1 Type of projects

The largest part of the projects are R&D projects (111 out of 145), followed by Concerted actions and Demonstration projects (Table 3.3). Only few projects of the other types (CRAFT, TN, CM, NAS-Extension) are in the database.

Table 3.3 Type of projects

| Type of project | | n of projects |
|---|---|---|
| RS | Research and technological development (R&D) project | 111 |
| CA | Concerted Action | 15 |
| DM | Demonstration Project | 7 |
| CRAFT | SME Co-operative Research | 6 |
| CM | Combined R&D and demonstration project | 3 |
| TN | Thematic Network | 2 |
| NAS-Extension | Extension for Newly Associated States | 1 |
| Sum | | 145 |

Source: Fraunhofer ISI

According to their start date and duration, 49 of the 145 projects should already be finalised.

### 3.3.2 Partners

#### 3.3.2.1 Number and type of partners

As Table 3.4 shows, the projects under evaluation have 1370 partners in total, including the coordinators themselves. Most of the partners are Higher Education (i.e. organisations only or mainly established for higher education/training, e. g. universities and colleges) or research institutes (i.e. organisations only or mainly established for research purposes). Three of the research partners are categorised as "Research Public University" and might be added to the HES category. One belongs to the RPN category. These small numbers for RPU and RPN might result from the fact that the categorisation was done by the authors of the research applications themselves who possibly found it easier to select the HES or REC category instead of the more differentiated RPU or RPN category.

122 industry partners are involved, an information that will have to be verified from the project reports because of its outstanding relevance. 104 partners were given the "Other" category, most of them are hospitals, public health services or public authorities. In one case a group of n=49 clinical centres participating in a thematic network are summed up as one "other" partner. For 2 partners no information on the main activity is available yet.

Table 3.4 Type of project partners

| Type of partners | Category | n of partners |
|---|---|---|
| Higher Education | HES | 649 |
| Research | REC | 489 |
| Research Public University | RPU | 3 |
| Research Private National | RPN | 1 |
| Industry | IND | 122 |
| Other | OTH | 104 |
| Unknown | | 2 |
| Sum | | 1370 |

Source: Fraunhofer ISI

The projects have a median of 7 partners altogether (Table 3.5). Because the distribution of the numbers is very skewed, the median is more reliable in this case to describe the central tendency of the distribution than the arithmetic mean but can be interpreted in the same way. The number goes up to 80 partners in one project, the projects with the highest numbers of partners are CAs or research clusters. Knowing the absolute numbers, it is not astonishing that HES and REC partners are most prevalent in the projects (on average 41 and 31 partners of either type per project, respectively).

Table 3.5 Statistics on partners

| Statistic | | n of partners total | n of HES partners | n of IND partners | n of REC partners | n of RPN partners | n of RPU partners | n of other partners |
|---|---|---|---|---|---|---|---|---|
| **Median** | per project | 7 | 3 | 0 | 3 | 0 | 0 | 0 |
| **Minimum** | per project | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Maximum** | per project | 80 | 41 | 5 | 31 | 1 | 2 | 32 |
| **Sum** | all projects | 1370 | 649 | 122 | 489 | 1 | 3 | 104 |

n=145 projects, data from July 2003

Source: Fraunhofer ISI

45 projects have at least one industry partner, most of them (n=27) only one, 7 projects have two industry partners, 7 projects have three industry partners each, and 3 have four IND partners, one has five. The size of the industry partners – as far as it is known – is nearly equally dispersed over all categories from 1 to 9 employees (S2) up to more than 2000 employees (see Table 3.6). At least 41 of the partners have less than 250 employees and therefore can be regarded as SMEs.

Table 3.6 Size of industry partners

| Size category | n of employees | n of IND partners |
|---|---|---|
| S1 | 0 | – |
| S2 | 1 – 9 | 12 |
| S3 | 10 – 49 | 20 |
| S4 | 50 – 249 | 9 |
| S5 | 250 – 499 | 8 |
| S6 | 500 – 1999 | 14 |
| S7 | > 2000 | 24 |
| Size unknown | | 35 |
| Sum | | 122 |

Source: Fraunhofer ISI

*The numbers and types of partners show that the projects meet the goal of bridging the gap between academic and industry research.*

### 3.3.2.2 Country of origin of coordinators

Table 3.7 Representation of countries as CR and CO

| Country | Country long | absolute numbers | | percentages | | |
|---|---|---|---|---|---|---|
| | | CR[7] | CO[8] | % CR of total CR | % of CO of total CO | % of CO in country |
| EU-15 | | | | | | |
| UK | United Kingdom | 219 | 31 | 16,0 | 20,9 | 14,2 |
| FR | France | 192 | 20 | 14,0 | 13,5 | 10,4 |
| DE | Germany | 181 | 22 | 13,2 | 14,9 | 12,2 |
| IT | Italy | 142 | 16 | 10,4 | 10,8 | 11,3 |
| ES | Spain | 101 | 6 | 7,4 | 4,1 | 5,9 |
| NL | The Netherlands | 99 | 17 | 7,2 | 11,5 | 17,2 |
| SE | Sweden | 85 | 11 | 6,2 | 7,4 | 12,9 |
| BE | Belgium | 45 | 5 | 3,3 | 3,4 | 11,1 |
| DK | Denmark | 34 | 3 | 2,5 | 2,0 | 8,8 |
| FI | Finland | 28 | 3 | 2,0 | 2,0 | 10,7 |
| AT | Austria | 21 | 2 | 1,5 | 1,4 | 9,5 |
| PT | Portugal | 18 | 2 | 1,3 | 1,4 | 11,1 |
| EL | Greece | 17 | 1 | 1,2 | 0,7 | 5,9 |
| IE | Ireland | 14 | 2 | 1,0 | 1,4 | 14,3 |
| LU | Luxembourg | 3 | | 0,2 | 0,0 | 0,0 |

[7] CR: Contractor incl. coordinator

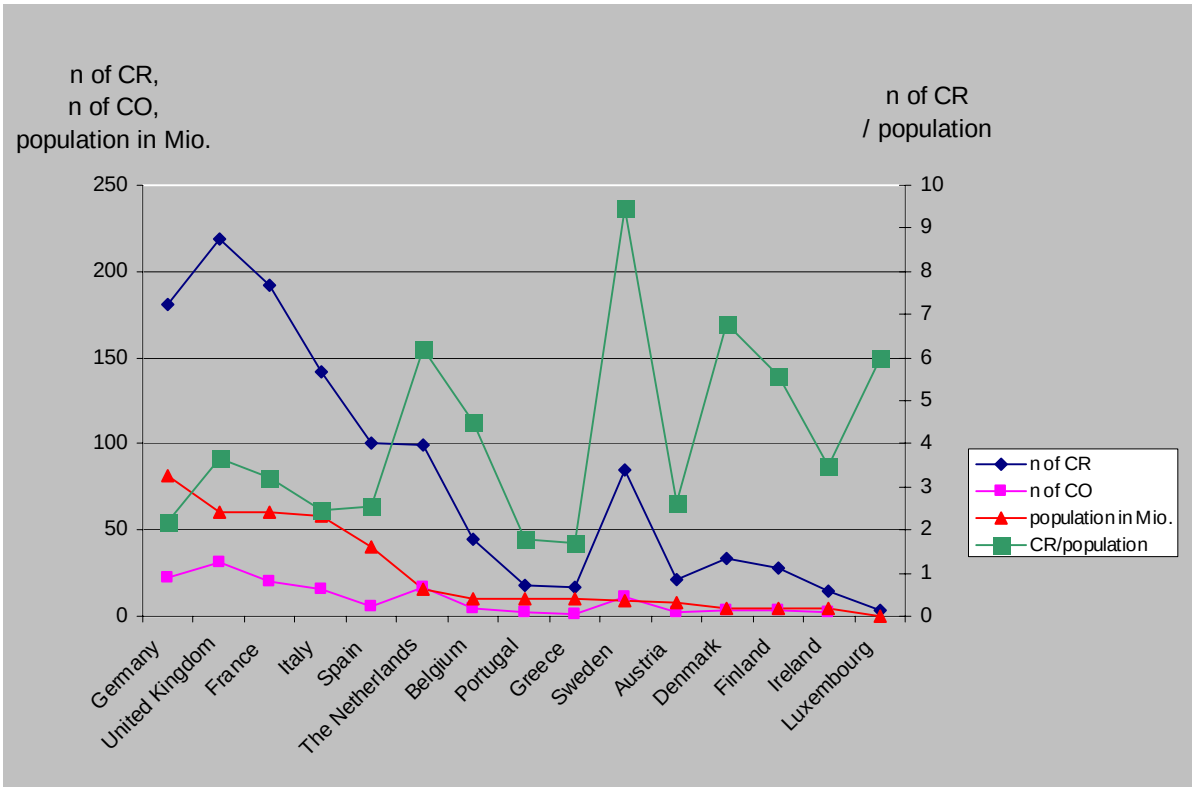
[8] CO: Coordinator

| Country | Country long | absolute numbers | | percentages | | |
|---|---|---|---|---|---|---|
| | | CR[7] | CO[8] | % CR of total CR | % of CO of total CO | % of CO in country |
| Accession Countries | | | | | | |
| CZ | Czech Republic | 14 | | 1,0 | 0,0 | 0,0 |
| PL | Poland | 11 | 1 | 0,8 | 0,7 | 9,1 |
| LT | Lithuania | 4 | | 0,3 | 0,0 | 0,0 |
| SK | Slovak Republic | 3 | | 0,2 | 0,0 | 0,0 |
| SL | Slovenia | 2 | | 0,1 | 0,0 | 0,0 |
| CY | Cyprus | 1 | | 0,1 | 0,0 | 0,0 |
| EE | Estonia | 1 | | 0,1 | 0,0 | 0,0 |
| HU | Hungary | 1 | | 0,1 | 0,0 | 0,0 |
| LV | Latvia | 1 | | 0,1 | 0,0 | 0,0 |
| Other Europe | | | | | | |
| CH | Switzerland | 50 | | 3,7 | 0,0 | 0,0 |
| NO | Norway | 24 | 2 | 1,8 | 1,4 | 8,3 |
| RO | Romania | 7 | | 0,5 | 0,0 | 0,0 |
| IS | Iceland | 6 | | 0,4 | 0,0 | 0,0 |
| BG | Bulgaria | 3 | | 0,2 | 0,0 | 0,0 |
| RU | Russian Federation | 1 | | 0,1 | 0,0 | 0,0 |
| Africa | | | | | | |
| ZA | South Africa | 3 | | 0,2 | 0,0 | 0,0 |
| GA | Gabon | 1 | | 0,1 | 0,0 | 0,0 |
| GH | Ghana | 1 | | 0,1 | 0,0 | 0,0 |
| GM | Gambia | 1 | | 0,1 | 0,0 | 0,0 |
| LR | Liberia | 1 | | 0,1 | 0,0 | 0,0 |
| SN | Senegal | 1 | | 0,1 | 0,0 | 0,0 |
| Asia | | | | | | |
| IL | Israel | 15 | 4 | 1,1 | 2,7 | 26,7 |
| IN | India | 1 | | 0,1 | 0,0 | 0,0 |
| TH | Thailand | 1 | | 0,1 | 0,0 | 0,0 |
| Americas | | | | | | |
| US | United States of America | 9 | | 0,7 | 0,0 | 0,0 |
| CO | Colombia | 3 | | 0,2 | 0,0 | 0,0 |
| AR | Argentina | 1 | | 0,1 | 0,0 | 0,0 |
| BR | Brazil | 1 | | 0,1 | 0,0 | 0,0 |
| Other | | | | | | |
| AU | Australia | 2 | | 0,1 | 0,0 | 0,0 |
| **Totals** | | **1369** | **148** | **100,0** | **100,0** | **10,8** |

Source: Fraunhofer ISI

The participation of contractors and coordinators from the different countries is presented in Figure 3.5. The largest number of participants in total as well as in the role of the coordinator comes from the UK, followed by France and Germany. Also Italy has by far more than 100 participants in KA2 projects, but the relative number of coordinators is larger in the Netherlands than in Italy. The number of partners for the EU Member States (MS) follows in general the size of the respective population with an approximate value of 2 to 4 contractors per million inhabitants, with higher relative numbers from The Netherlands, Belgium, Sweden, Denmark, Finland and Luxembourg (Figure 3.4, cf. line "CR/population").

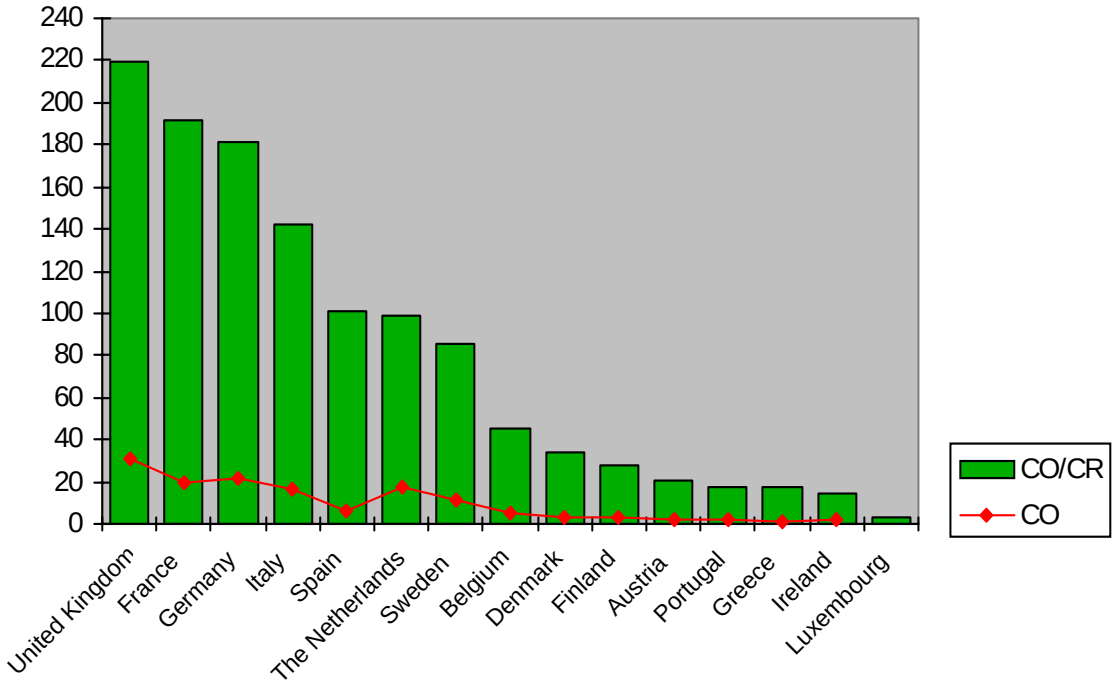
Figure 3.4 Number of contractors and size of population




n of CR: number of contractors incl. coordinators;
n of CO: number of coordinators;
n of CR/population: number of contractors per country divided by size of the population [in Mio.]

Source: Fraunhofer ISI

Figure 3.5 Participating countries



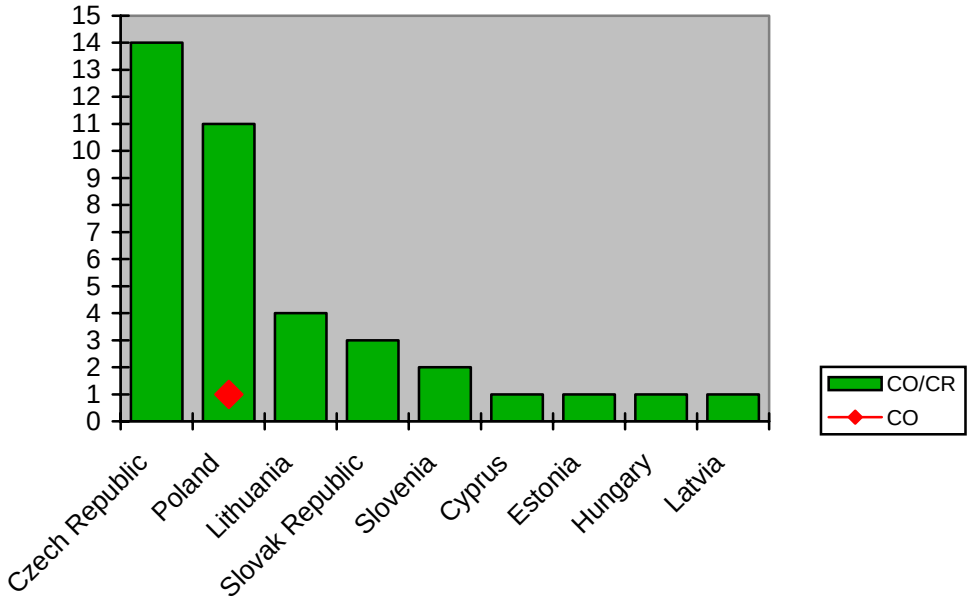

CO/CR: Participant from certain country is contractor (including coordinator)
CO: participant is coordinator

Source: Fraunhofer ISI

In the light of the EU enlargement, the participation of Accession countries is of special interest. The participation of partners from these countries is shown in Figure 3.6. From the Accession Countries, the Czech Republic and Poland are the best represented, from Poland comes even one coordinator. Although additional funding was available for these countries through the NAS-instrument, the other Accession Countries were only very infrequently included.

Partners from outside the EU come mainly from Switzerland, followed by Norway, Israel and the USA. A number of developing countries from Africa and Asia have also at least one representative included.

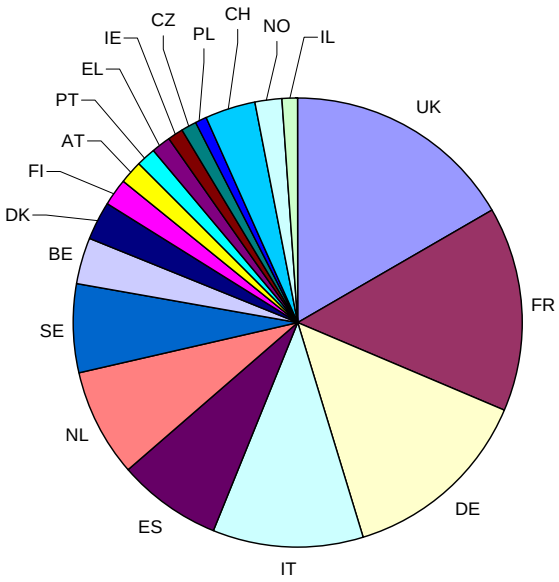
Figure 3.6 Participation of Accession countries




CO/CR: Participant from certain country is contractor (including coordinator)
CO: participant is coordinator

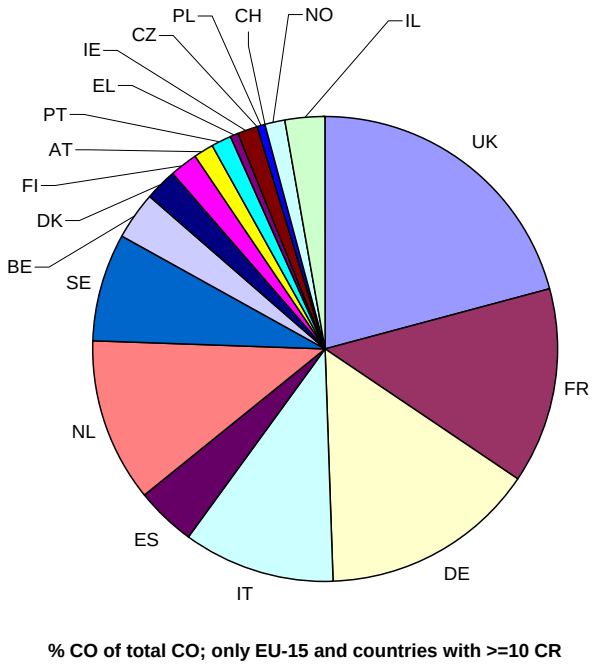
Source: Fraunhofer ISI

Figure 3.7 Percentage of contractors by countries




Source: Fraunhofer ISI

Figure 3.8 Percentage of coordinators by countries




Source: Fraunhofer ISI

*Participants from a large number of EU Member States are involved in the KA2 projects, which is a sign for a contribution to European integration. However, only a few participants come from the smaller Member States, and also the Accession Countries are only weakly represented.*

### 3.3.3 EC financial contribution

The financial contribution as given in the data from the Commission in the different types of projects is shown in Table 3.8. Again, the analysis is possibly not representative of all projects funded under KA2 because some for a number of projects no reports or contractual data were available to the evaluation. In addition, for some of the project types the case numbers are small what makes the statistics vulnerable to the influence of outlier values.

Table 3.8 EC final contribution to documented projects

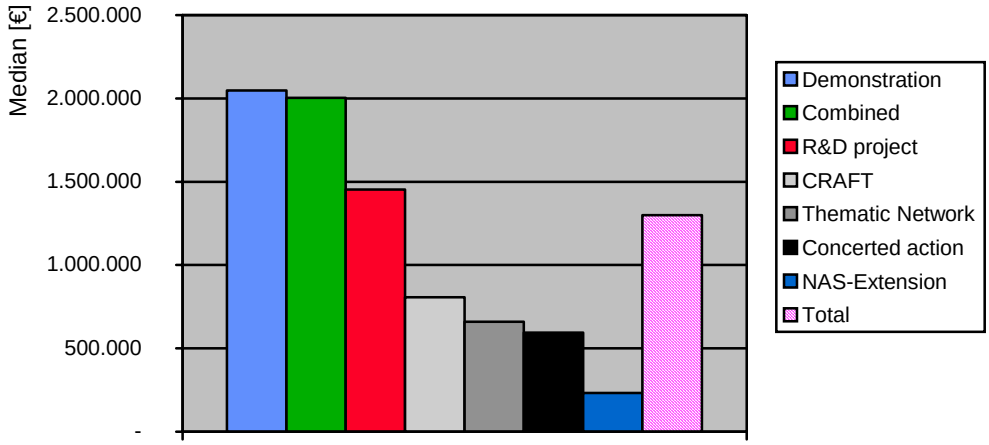
| Type of project | n | Median (one project) | Minimum (one project) | Maximum (one project) | Sum (all projects) |
|---|---|---|---|---|---|
| **Concerted action** | 14 | 595,611 | 19,580 | 957,000 | 7,958,757 |
| **Combined** | 2 | 2,003,183 | 506,365 | 3,500,000 | 4,006,365 |
| **Demonstration** | 6 | 2,046,995 | 1,003,359 | 2,999,997 | 12,060,080 |
| **R&D project** | 108 | 1,453,756 | 499,959 | 8,845,000 | 175,943,162 |
| **Thematic Network** | 2 | 660,854 | 171,708 | 1,150,000 | 1,321,708 |
| **CRAFT** | 6 | 806,200 | 262,000 | 945,844 | 4,400,249 |
| **NAS-Extension** | 1 | 233,400 | 233,400 | 233,400 | 233,400 |
| **Total** | 139 | 1,300,000 | 19,580 | 8,845,000 | 205,923,721 |

Source: Fraunhofer ISI

According to the median values, RS, DM and Combined projects are nearly equally expensive, whereas CAs, TNs, and CRAFT projects lie below the average. The one NAS-Extension projects has a duration of only three months and was also relatively cheap. Because the number of R&D projects is by far the highest, the gross median over all categories lies very near to the value of R&D projects, and for these type of projects the highest amount of money is spent. Because of the restricted database, these figures have to be interpreted with great care and should be checked with other sources.

The following diagram visualises the budgets.

Figure 3.9 Budget by type of project




Source: Fraunhofer ISI

# 4 Implementation

The implementation of the projects was extensively described in the interviews as well as in the periodic reports and to some extent also in the mid-term reviews. In the present chapter, these results are presented in terms of the process itself, the number of preclinical and clinical studies undertaken, the comprehensiveness of the projects according to the target populations, the methodological quality and the interlinking with other national or Community activities. The statements from the projects on which the following analyses are built can be found in in a confidential Annex.

## 4.1 Implementation process

The quality of the implementation is seen as being strongly influenced by the collaboration of the participants as well as the work of the coordinator. A high morale and commitment of the participants was very often described (Proj_148; Proj_90; …), in some cases the initial enthusiasm was seen as a bit hindering because it had lead in the proposal to too ambitioned work plans (Proj_101), e.g. the aim of reaching clinical trials was too ambitious in only 3 years (Proj_50).

Exchange of lab personnel is one form of intensive collaboration which was assessed as helpful if carried out (Proj_60; Proj_123), other forms were frequent meetings (Proj_6), monthly internal reports of the partners to the coordinator (Proj_100), centralised management of blood samples (Proj_149); a laboratory manual complied to coordinate individual technologies and the standardisation of assays (Proj_58).

Only in a few projects a too weak collaboration had to be diagnosed, e.g. in one project where the mid-term review came to the conclusion that the partners went too strongly for their individual goals and scientific coordination was lacking (Proj_62).

These measures are also related to a strong management by an experienced coordinator, which very often helped to cope with sometimes complicated research issues and complex structures (Proj_172; Proj_51; Proj_52) and allowed to react positively on new developments in the field (Proj_54; Proj_56).

Problems in a number of projects arose with the recruitment of the staff, because after the signature of the contract by the Commission (which followed sometimes long contract negotiations) the projects normally start in the following month, and in such a short "warning period" it was sometimes not easy to find the appropriate staff (e.g. Proj_53), in some cases this lead to the necessity of an extension).

For the evaluation it was not always easy to determine if upcoming problems could not have been expected in advance, e.g. safety or ethical issues (Proj_135; Proj_108) or problems of database development (Proj_113).

In the development of new procedures and drug or vaccine candidates, some delays are unavoidable, because of several approaches it is normal that some do not work and that the focus has to be changed to another procedure or substance (e.g. Proj_2; Proj_83; Proj_106).

In some cases, problems arose that were clearly unforeseeable, e.g. the acquisition of one partner by another company (Proj_114), bankruptcy or other economic problems of an IND partner (Proj_205; Proj_111; Proj_123), which mostly made lengthy contract amendments necessary, or a fire in a lab (Proj_107).

Specifically targeted measures were taken to overcome delays (extra meeting, leasing of staff from one partner to the other, additional staff in 2 groups) were taken in especially well managed projects (Proj_17; Proj_4; Proj_97).

Some projects found it helpful to have external administrative or management support separated from the scientific management (Proj_4; Proj_45)

The interaction of the projects with the Commission was sometimes hampered by delays in the payments (Proj_115; Proj_82; Proj_104) or complicated administrative procedures (Proj_99).

## 4.2 Number of preclinical and clinical studies planned or underway

The development of new drugs or vaccines is subdivided in preclinical and four phases of clinical studies. By far the largest number of studies carried out in such projects of KA2 was preclinical in character, e.g. in vitro tests to prove the principle, or in vivo toxicological studies in tissues or animals. The number of preclinical studies could not be counted reliably because not every single study was reported separately in the projects' documents.

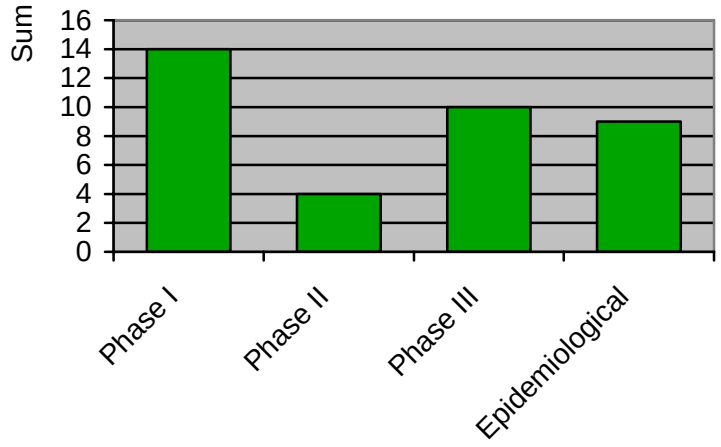
Of the studies, 14 were phase I clinical trials, 4 in phase II, 10 in phase III (the large clinical trials in patients) and 9 epidemiological studies (including clinical evaluation of already marketed treatments, treatment plans and monitoring systems). The medians for all phases were 1 or 2 studies in those projects which reported such studies at all. The figures together with minima and maxima are presented in the following table and figure.

Table 4.1 Clinical studies

| | Phase I | Phase II | Phase III | Epidemiological |
|---|---|---|---|---|
| N | 9 | 2 | 3 | 7 |
| Median | 2,00 | 2,00 | 1,00 | 1,00 |
| Minimum | 1 | 2 | 1 | 1 |
| Maximum | 2 | 2 | 8 | 3 |
| Sum | 14 | 4 | 10 | 9 |

Source: Fraunhofer ISI

Figure 4.1 Number of clinical studies




Source: Fraunhofer ISI

For the projects, also the number of target persons included was recorded; most of them were participants in clinical or epidemiological studies. As Table 4.2 shows, around 50,000 persons from the target groups were included in the projects for which such figures were reported.

Table 4.2 Number of target persons/patients included in the projects

| Statistic | Value |
|---|---|
| N | 11 |
| Median | 3500 |
| Minimum | 42 |
| Maximum | 10,000 |
| Sum | 47,813 |

Source: Fraunhofer ISI

## 4.3 Comprehensiveness according to target population and member states

As presented above (chapter 3.3.2.2), most projects have participants from a larger number of EU Member States. This is especially relevant when the aim is to harmonise procedures or to get an overview e.g. on the epidemiological situation related to a specific pathogen. In these cases (e.g. in the projects Proj_80; Proj_60; …) up to 49 countries were included, mainly in concerted actions and cluster projects.

## 4.4 Methodological quality

The methodological quality of the projects was assessed by the mid-term evaluators in general as good or very good. However, if no MTR was available, it was sometimes not assessable only from the projects reports.

Many projects were assessed as scientifically excellent and carried out with high professional skills (Proj_37; Proj_172; Proj_49, very often associated with faster progress than expected (Proj_51; Proj_57) and the work published in 1st quality journals (Proj_56; Proj_47). Some projects met all criteria (e.g. deliverables, milestones) well, but no special excellence was mentioned (e.g. Proj_205; Proj_39).

A tight focus on major objectives seems to be important (Proj_47; Proj_79), as well as a clear work plan and measurable objectives (Proj_81)

The methodological quality was rated according to the commentaries which were made in the mid-term reports from the external experts or from the project managers themselves. The results are shown in Table 4.3. The median is 5 and therefore lies in the best possible category, no project had to be rated with less than the middle value 3.

Table 4.3 Rating methodological quality

| Value | Frequency | Percent |
|---|---|---|
| 1 | – | |
| 2 | – | |
| 3 | 1 | .7 |
| 4 | 33 | 22.8 |
| 5 | 38 | 26.2 |
| total | 72 | 50.3 |

Source: Fraunhofer ISI

To enhance or assure the methodological quality of the study, many projects used quality assurance protocols, e.g. the standardisation of protocols (Proj_59; Proj_49; Proj_172). Only rarely a need for more standardisation, more exchange, more focusing was noted by an evaluator (Proj_50).

## 4.5 Interlinking with other national or Community activities

An important factor to assure the methodological quality of research is the tight contact to other research groups or other stakeholders. Although some projects report meetings with other research groups (e.g. Proj_51; Proj_53; Proj_57) or organised additional EC-funded conferences (Proj_175; Proj_83) this aspect is not mentioned for most of the projects, even not for other KA2 projects that are working in the same field. For some projects, this was directly assessed as a problem by the mid-term review or advice was given to strengthen this kind of collaboration (Proj_56; Proj_102). An interesting approach was the development of a PhD programme in project Proj_46.

# 5 Impacts

## 5.1 General outcomes

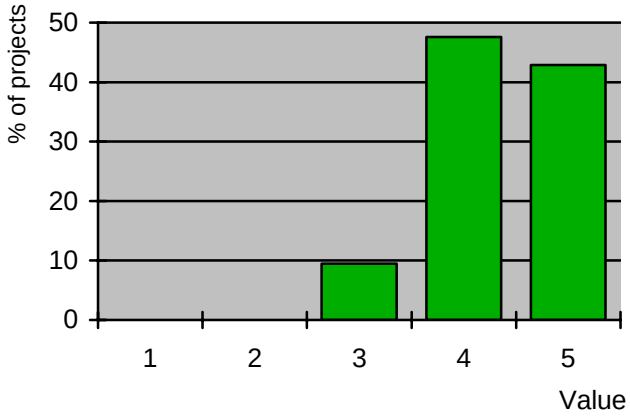
The rating of the attainment of the specific project goals by the evaluation team and evaluation of programme by participants and staff had both a median of MD=4,0 and minima and

maxima of Min=3 and Max=5 (i.e. "very favourable") on the five-point rating scale, respectively.

### 5.1.1 Attainment of specific project goals

In the reports strong emphasis was given to the description of the attainment of the specific project goals. This point was analysed in general regarding the achievement of relevant milestones (MS) and deliverables. The details can be found in a confidential annex. In general, the projects met their aims very well, often achieved more than expected (Proj_37) or proceeding ahead of their schedule (Proj_53; Proj_86; Proj_82). Only in very few of them specific goals could not be reached. The distribution of the values, which resulted from an assessment by Fraunhofer ISI, is shown in Figure 5.2.

Figure 5.1 Attainment of specific goals




Source: Fraunhofer ISI

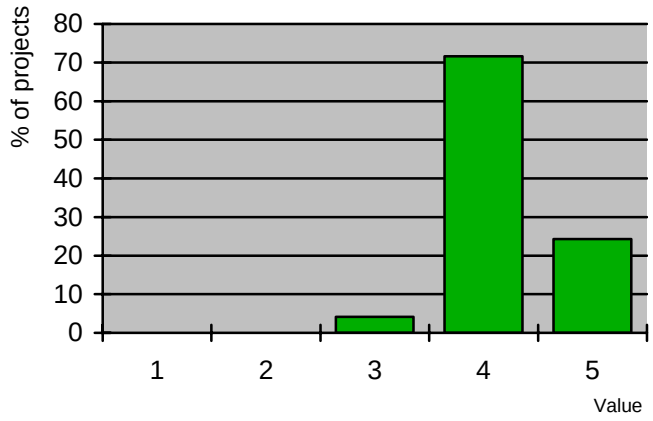
As mentioned above, some goals are more difficult to reach, especially the development of new drugs until the clinical phase, or the development of new constructs by genetical modification (Proj_37; Proj_49; Proj_106). It is normal that some candidates are lost in the process of development (Proj_56; Proj_204).

A number of projects found that the regular funding period of three years was too short to bring new drugs into clinical trials (Proj_49; Proj_58; Proj_45; Proj_101)

### 5.1.2 Evaluation of programme by participants and staff

The evaluation of the project by its participants was generally good, sometimes more critical than the external evaluations by the MTR. The distribution of the values is shown in Figure 5.2 (assessment by Fraunhofer ISI).

Figure 5.2 Evaluation of project by staff




Source: Fraunhofer ISI

In some cases the participants themselves were surprised by the good advance of the progress (e.g. Proj_172; Proj_51; Proj_34)

Sometimes, the evaluation of the project was not explicitly given by the staff because the report only reported factual information but neglected to compare this with the initial planning (e.g. Proj_52). In these cases it would have been helpful to directly ask the project managers in interviews or by means of a written questionnaire.

Some reports include a specific part on obstacles and highlight the problems (Proj_101), other reports did not really explain why they failed to meet a milestone (Proj_102).

## 5.2 Science impact

### 5.2.1 Employment and qualification

The impact on the science arena is firstly a direct via the employment of staff. Figures for this interesting aspect are not regularly presented in the periodic report. For 13 projects, which offered the figures in the closer evaluation, the total number of people employed was 293 (Md=14). The number of PhDs degrees acquired by students working within these 13 projects was 60 (Md=4).

### 5.2.2 Publications

The second important impact on the scientific level is the production of publications. In the 145 projects analysed, in total 995 publications have been counted, which is a mean of $\bar{x}$ = 6.8 publications per project.

### 5.2.3 Specific in-sights into the research field

A large amount of specific in-sights into their respective research field has been reported. Here, just a few can be mentioned.

Among these results, which were mentioned by the reports as especially interesting, are proofs of concept e.g. for mucosal vaccination (Proj_38), "revolutionary" technical developments (Proj_37), e.g. new mouse models (Proj_54), or new vaccination strategies (Proj_205).

A lot of new vaccine or drug candidates have been developed for clinical testing, partially called as "breakthrough" (Proj_52; Proj_54; Proj_57, for HIV: Proj_42), proteins and DNA as immunogens (Proj_175), monoclonal antibodies (Proj_44), small RNA inhibitors and peptides with chemotherapeutic potential (Proj_132). In part for these candidates clinical trials have already started (e.g. Proj_62).

On the side of basic research, advances have been made e.g. on the pathogeneity of Shigella (Proj_59), RSV (Proj_204), host-parasite interactions for malaria (Proj_47) and malaria metabolism (Proj_107), dormancy of M. tb. (Proj_99), as well as in innate immunity (Proj_45), the basic biology of dendritic cells (Proj_76) or triggered apoptosis (Proj_97).

Advances in diagnostics have been made, e.g. markers for monitoring (Proj_175), and a lot of improved or novel assays (Proj_43, Proj_77, for TB e.g. Proj_80, Proj_81).

These and other results are also relevant for public health and prevention, e.g. new knowledge on the vertical transmission of HIV or the increasing importance of heterosexual transmission (Proj_46), cross-resistance and adherence to treatment, HIV and cardiovascular risk (Proj_82), and the treatment of children with HIV and AIDS.

Many results are applicable also in other diseases (Proj_51), e.g. new platform technologies for infections, cancer, and autoimmune disease (Proj_39).

## 5.3 Practice impact and technology transfer

The following chapter on the impact of KA2 projects for research and health care practice are described in terms of applicable methods and patented knowledge, methods that are applied to improve the use of the results, practice guidelines, use of the developed methods in day-to-day life and the impact of the results on national and Community practice.

### 5.3.1 Methods developed, patents, enterprises funded

Important results from research according to the general aims are the generation of new methods and knowledge including the protection of this intellectual property. In addition, this could result in the development of a economic basis for new enterprises which work with the knowledge generated in the research project. As described above, a large number of technologies from new platform technologies to new or improved assays. However, as these methods represent a broad continuum from project-specific tools to generally applicable devices and as they are not systematically described in the reports, no comprehensive figures on new technologies can be presented.

Table 5.1 and Figure 5.3 show that in 15 projects a total number of 33 patents were planned, in 19 projects another 30 patents were filed, and in 4 projects in total 8 patents were granted.

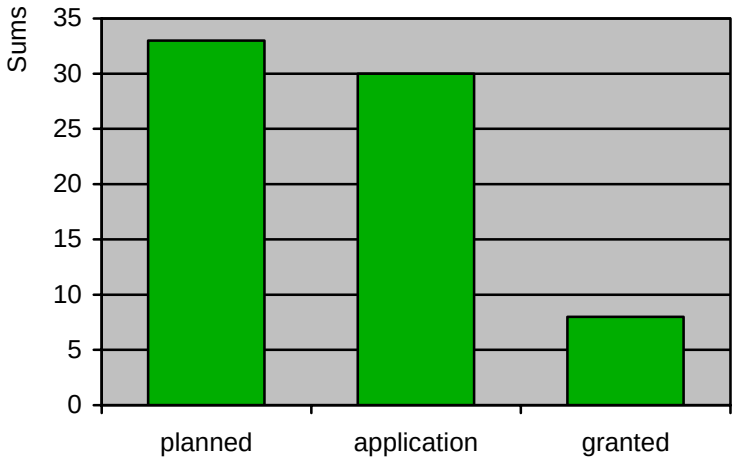
One enterprise was founded as a spin-off from one of the projects.

Table 5.1 Number of patents

| | Nr of patents planned | Nr of patent applications | Nr of patents granted |
|---|---|---|---|
| N | 15 | 19 | 4 |
| Median | 2,00 | 1,00 | 2,00 |
| Minimum | 1 | 1 | 1 |
| Maximum | 11 | 3 | 3 |
| Sum | 33 | 30 | 8 |

Source: Fraunhofer ISI

Figure 5.3 Number of patents




Source: Fraunhofer ISI

A specific question to the interview partners in the closer evaluation was whether they had applied for additional funding for the protection of IPRs, because for the Commission astonishingly few had used this opportunity. Of the 17 coordinators interviewed, 5 have applied for additional funding from the Union (Proj_123; Proj_150; Proj_57; Proj_205; Proj_45). In two cases, however, they added that the sum was very low or that this task had to be partly covered by the industry partners.

The other projects had not applied for additional IPR funding because – in most of the cases – they had nothing to patent or were at least not sure if their results would be patentable. Two projects felt that patenting is industry partners' task or the fees would be paid from the SMEs' contribution, and one project found the Commission's funding scheme for this purpose too inflexible while having another source available.

### 5.3.2 Measures taken to promote the use of the results

To encourage the use of the results in practice outside the research project, the teams are requested to carry out promotional activities. These are dependent of the type of the project,

because the results of more basic research are merely directed to other scientists, while treatment studies can be already very useful for practical care or day-to-day laboratory work.

Most of the projects do only mention *scientific publications* and the participation in scientific conferences as means to inform about their results; partly the results were published in excellent journals (Proj_57; Proj_47). Many others have also made available at least some information on specific internet sites (e.g. Proj_37; Proj_203; Proj_205; Proj_56). A *scientific workshop* was planned or carried out by projects Proj_172; Proj_176; Proj_107; Proj_109; Proj_115), some projects made their results available to the scientific community in the form of a database (Proj_105; Proj_83; Proj_113).

Only few projects have used press releases or a poster directed to the *general public* (Proj_49; Proj_61; Proj_77; Proj_118), and articles for business journals (Proj_35). In one project (Proj_100) even a short TV documentary on the project was produced for the general public.

One form to inform the economic sector is via existing *industry collaborations* (Proj_62), the presentation in industrial platforms (Proj_52; Proj_34) or other meetings with potential commercial partners (Proj_175).

To collaboratively exploit the results, in one project a foundation was built to use infectious material by private companies (Proj_49), another to use combined licences from industry partners and carry out trials (Proj_45). Follow-up projects can also be funded by the industry, e.g. to work towards clinical trials (Proj_59; Proj_76) or further research with some of the partners can be funded in a new public project (Proj_113).

A very direct means to bring the scientific results into practice is the *inclusion of an industry partner* in the project consortium, which was done regularly (see above, e.g. Proj_38; Proj_50; Proj_51). These partners often can directly exploit the techniques developed in the projects.

Only a few projects worked together with an NGO (Proj_48), potential users (Proj_102) or other unspecified stakeholders (Proj_177)

In many projects, besides scientific publication and a web-page, no specifically designed activities were mentioned to disseminate and exploit the results (e.g. Proj_43; Proj_101; Proj_136; Proj_135; Proj_99), in some cases the reason for this can be that the data were still too preliminary to inform the relevant stakeholders (Proj_79) or for commercial exploitation (Proj_90).

Besides neglecting this aspect, in some projects the exploitation strategy was called "uncertain" by the MTRs (Proj_106; Proj_112). In one case, the MTR suggested a specialist consultant for the exploitation (Proj_112), in other projects consultants (Proj_5) or a responsible Exploitation manager (Proj_35) were already in charge for the business plan.

#### 5.3.2.1 Information events

There were too few specific information events (not: scientific conventions) reported for statistical analysis, nearly no information is available on conferences that were organised to inform the public or the scientific community. Only one project (Proj_57) reports on an "excellent public meeting."

### 5.3.3 Practice guidelines

The results of certain projects which might be directly applicable for the *clinical practice* were partly disseminated via local clinicians who took part in the study, or in treatment guidelines (Proj_46; Proj_48; Proj_82; Proj_119; Proj_16). Where the development of practice guidelines was mentioned, they were regularly based on the newest scientific insights (Proj_38; Proj_58; Proj_59), and international consensus (Proj_46) or best Community practice (Proj_77).

### 5.3.4 Impact of the results on national and Community practice

This paragraph summarises the practical impacts of the research results including the use of developed methods in day-to-day life.

In the view of the mid-term reviews as well as of the coordinators, the projects contribute to diagnosis and control of diseases (Proj_175) and make a significant contribution to the QoL programme (Proj_61).

Many of the developed methods can (possibly, when the development was successfully finished) be used in day-to-day life, e.g. enhanced and internationally standardised *diagnostic and lab methods* (Proj_205; Proj_60; Proj_45; Proj_176; Proj_43; Proj_118; Proj_141) and new or more economic *assays and DNA chips* (Proj_56; Proj_83; Proj_5; Proj_123), proteins (Proj_49) and other *reagents* (Proj_55), as well as standardised *research methods* (Proj_51), methods for *prevalence assessment* (Proj_148) or *quality assurance* schemes for biobanks (Proj_142).

Having a vaccine where no precursor has existed could have a strong impact on *prevention strategies and public health policies* (Proj_38). This is also true for new forms of application, e.g. mucosal vaccines, which could result in great social benefit (Proj_172), e.g. by a reduced number of doses needed for immunisation (Proj_149) or less invasive immunisation.

The findings from epidemiological studies might have high impact on prevention strategies (Proj_135) because they allow to identify immunisation gaps (Proj_77), enable harmonised and improved *immunisation* practice (Proj_77) and control of disease in Europe (Proj_136; Proj_119), e.g. preventive regimens and treatment strategies of vertically infected children are implemented (Proj_46), *treatment* of HIV infection (Proj_82), TB control (Proj_80; Proj_81), make a contribution to the policy goal of measles elimination from Europe (Proj_133), and in general to evidence-based clinical practice (Proj_16).

The projects help to prepare the Community for epidemiologically relevant diseases with rising importance as pertussis (Proj_137), Salmonella outbreaks (Proj_141). Surveillance programmes and improved vaccination policies are hoped to be sustainable (Proj_77).

The developed arrays and other products can be used by other companies (Proj_50; Proj_51) and thus can have an impact on the *market and employment* (Proj_52; Proj_118). Hospitals that participate in EU funded studies can experience a competitive advantage (Proj_119).

New *research opportunities* are fostered by the provision of reagents and tools (Proj_55), collaborative activities persist even after the EU funding has finished in the form of exchanged lab personnel, common projects on national level, ongoing product development, or proposals for new projects (Proj_57; Proj_60; Proj_107; Proj_148) also from other sources of funding (Proj_123).

On the other hand, not all activities can be maintained, without further funding for a working group the projects might suffer from a brain-drain (Proj_176).

## 5.4 Policy impact

The information on potential policy impacts is rare, in most reports this issue is even not implicitly touched, which is in accordance with the few information events that were directed to policy makers.

A direct impact of the research that affects the policy goal of European integration is the collaboration of project members from different EU Member States. This feature is presented in chapter 3.3.2.2). Additionally, many projects carried out their data collection together with external institutions, e.g. hospitals. This information is only available from four projects, which collaborated with 329 partners (Md=27). One project worked with partners from up to 33 countries.

### 5.4.1.1 Transfer into policy making

To make the research results available to policy making is an objective which is normally not in the central focus of scientists. This is also true for the KA2 projects, where most projects had no concrete plans for the dissemination of their results to policy makers (Proj_150; Proj_46; Proj_107; Proj_113; Proj_90). One argument for this was that the results were too far from application because the projects belonged more to basic research (Proj_205; Proj_57), another that it was too early to say something about the usefulness of the results for policymaking (Proj_45; Proj_150). In many cases the transfer is a workpackage only in the last year (Proj_148). The above mentioned press releases might also find the attention of policy makers.

Some stated a potential relevance of their results for policy making, but without taking measures to promote their results (at least in the reports that could be analysed). One MTR stated that the availability of epidemiological data in many EU countries was important (Proj_175), potentially the policy on antibiotics could be changed and an EU campaign on the use of antibiotics initiated in the light of results on antibiotic resistance (Proj_123).

One project has "attracted the interest of regulatory bodies" (Proj_82).

Only few activities are explicitly mentioned to inform policy makers, e.g. workshops or meetings with policy makers (Proj_176; Proj_77; Proj_119; Proj_100) or a brochure directed to policy makers (Proj_148).

One project reports on contacts with a large number of patients organisations, lobbying in the EP and national parliaments, ministries, WHO, and the European Commission to discuss the relevance of their research. Policy contacts were also used to get access to primates for their research (Proj_49).

### 5.4.1.2 Impact of the results on national and Community policy making

The impact of the results on national and Community policy making is not easy to determine because normally only little feed-back is given from the political level back to the researchers. So in the reports it must stay somewhat diffuse and speculative, e.g. in just stating that the impact was "potentially high" (Proj_46; Proj_150). Some argued, that their results might

possibly change vaccination strategies (Proj_38; Proj_60; Proj_77; Proj_80), change the policy to antibiotics (Proj_123), contribute to the control of pathogens (Proj_176) or that their new products could exert an influence on Public Health (Proj_57). Other projects directly respond to policy goals while they make a contribution to the measles elimination from Europe (Proj_77; Proj_133), or to the WHO Roll back Malaria strategy (Proj_98).

One project expected no impact on policy making (Proj_36).

### 5.4.1.3 EU added value

The EU added value, i.e. the idea that activities carried out on a European level brings about specific advances, can be seen in different areas.

#### *5.4.1.3.1 Responding to EU policy goals*

The first is that the projects respond to EU policy goals: Many examples exist, e.g. a general contribution to QoL programme (Proj_61), research in neglected areas (children: Proj_48) and the participation in efforts for (poverty-related) diseases which affect Asia/Africa (Proj_97; Proj_98), and the preparation for health threats, e.g. diseases due to global warming and risk of emergence and re-emergence of mosquito-born diseases in Europe (Proj_100).

The QoL programme intended to combine research in human and animal diseases (Proj_135), gender aspects are subject of project Proj_16. Education is strengthened by training courses (e.g. Proj_133), exchange of scientists or lab personnel (e.g. Proj_60) and knowledge transfer into Accession countries (Proj_77).

The competitiveness of the European economy is supported by the strong involvement of IND partners (e.g. in the in DM-project Proj_149) and the combination of high-level expertise from IND and REC partners (CRAFT-project Proj_35 and many others).

#### *5.4.1.3.2 Funding*

All interview partners stated that their projects would not have found other than the EU funding, because they were too complex and only EU funding offered the opportunity to include strong partners from several countries (Proj_38; Proj_50; Proj_51; Proj_57; Proj_45; Proj_176; Proj_148; Proj_150). This is especially true for large networks (Proj_77).

For other projects the EC funding was critical, because a large consortium was necessary but wouldn't have received funding from the industry as the science base was too weak to be relevant for the industry (Proj_51), so that the project is economically not interesting for the industry, as for research in TB or other poverty-related diseases (Proj_59).

Another argument for the necessity of EU (as opposed to private) funding was that a database to be developed needed to be public to be of most use for other research and therefore shouldn't be under private proprietorship (Proj_113).

Small companies often have no possibility to fund projects because the research questions are not close enough to market (Proj_36).

Many projects have integrated additional funding from national sources, e.g. from the Swiss Science Board for Swiss partners, FR, NL, BE, and NO (Proj_46; Proj_176; Proj_48; Proj_123; Proj_132; Proj_148; Proj_123; Proj_133; Proj_135).

#### *5.4.1.3.3 European integration*

The added value of such consortia can only emerge if there is excellent collaboration within the consortia, as found e.g. in projects Proj_58; Proj_59; Proj_56.

The partners should contribute specific expertise in complementary fields (Proj_204; Proj_55; Proj_81) which can increase the efficiency of the total work (Proj_205).

Especially where national policies are compared, one can learn from other countries (Proj_119; Proj_137). International collaboration can lead to

- *harmonisation of methods*, e.g. via the exchange of lab personnel or guidelines for standardisation of assays (Proj_60; Proj_62; Proj_77; Proj_79; Proj_80; Proj_105; Proj_148),
- a *unified picture of outbreaks* (Proj_77), embedded in national or international surveillance networks and programmes (Proj_141; Proj_77),
- *harmonisation of national clinical monitoring systems* (e.g. Inclusion of 243 hospitals from the EU and 23 from abroad, 33 European countries in Proj_119; Proj_16),
- standardisation of treatment across EU MS, transfer of knowledge to many clinical centres (Proj_46).

The number of partners in the project ranges from 3 in project Proj_34 (DK, NL, DE, thereof one only subcontractor) or Proj_59 (FR, IT, BE) to 80 (Concerted action Proj_48).

A special emphasis is given to *Accession countries* in a number of projects (Proj_82; Proj_77). Partners are involved from:

- Lithuania (Proj_175; Proj_111; Proj_133),
- Estonia (Proj_104),
- Latvia (Proj_111),
- Czech Republic (Proj_109; Proj_151),
- Poland (Proj_5; Proj_6).

*Other participating European countries* are

- Bulgaria (Proj_131),
- Switzerland (Proj_60; Proj_75; Proj_101; Proj_108; Proj_109; projects with Swiss coordinator: Proj_99; Proj_133),
- Norway (Proj_60; Proj_75; Proj_133; Proj_90),
- Russia (Proj_99).

*Other countries outside Europe* include:

- Israel (Proj_75, with coordinator from Israel: Proj_79; Proj_101),
- USA (collaboration with US NIH: Proj_55), US FDA and CDC: Proj_137, US university: Proj_177),
- South Africa (Proj_109; Proj_98),
- Ghana (Proj_98),
- Australia (Proj_110),
- patients from Argentine (Proj_82),
- subcontractor from Thailand (Proj_100; Proj_98).

#### *5.4.1.3.4 Effective use of resources*

An added value arises from work that integrates resources from different origin. This may come from the fact that the participating institutes have other related projects (e.g. Proj_113).

The integration of additional funding from national or other resources was already mentioned above. This is especially needed for clinical testing as this was normally not covered by the EU contribution, as done in projects Proj_62 and Proj_76.

The collaboration with IND partners brings about additional funding from the industry (e.g. Proj_48) and gives access to non-financial resources of IND partners (e.g. Proj_1).

Some projects are extensions of pre-existing collaborations (Proj_57; Proj_83), or benefit from the continuation of earlier EU or national projects (Proj_77; Proj_137; Proj_142). EU projects can build on complementary support by the Member States, e.g. for malaria research (Proj_47), and create or use links with other European disease specific networks (Proj_77; Proj_86) and pharmaceutical companies (Proj_86).

#### *5.4.1.3.5 Results*

Also the results can represent a specific added value, especially if they make a great contribution to scientific community (Proj_56) or support many other EU projects (Proj_55). The MTR of Proj_60 confirms very significant results which are good value-for-money for this project, in another project the development was faster than it would have been possible for the industry (Proj_45).

An outcome that exceeds the project itself is that it makes the EU a leading force in one field (for neonatal immunity: Proj_51, for a novel aspect of epidemiology: Proj_108; characterisation of a new TB strain: concerted action Proj_80: strengthening European impact on bioinformatics: Proj_83), and enhances the reputation of EU research (Proj_107), e.g. by a review on the project in high-level scientific journals ("Nature Medicine" for Proj_109).

Results should persist and be of use for later research after the finalisation of a project. This is possible for example for developed databases e.g. for assessment of resistance (Proj_42; Proj_80; Proj_83; Proj_105; Proj_113; Proj_141), the developed technologies and contacts between industry and contractors (Proj_50) or the establishment of a centre for clinical malaria studies in Nijmegen (Proj_62).

# 6 Influencing factors for impacts

Factors which influence the strength and the utilisation of the projects' impacts were mainly derived from the interviews and the mid-term review reports.

## 6.1 Factors influencing utilisation in a positive way

Factors which supported the generation of the intended results can be found in the areas of funding, starting points of the project, selection of partners, project management, internal collaboration within the consortium, external support by the Commission and other institutions, as well as in the dissemination and exploitation of the results.

### 6.1.1 Funding

Not astonishingly, many projects recognised the funding itself as a supporting factor (e.g. Proj_38; Proj_205; Proj_119). For one project it was explicitly important that the funding came from the EU because it was a motivating factor for participating hospitals that they liked to be involved in an EU project (Proj_119). Extra sponsorship obtained for a US expert was positively mentioned in another project (Proj_59).

### 6.1.2 Starting points

Concrete, measurable objectives and a tight focus on them, as well as a clear work plan are important starting points already in the writing of the proposal (Proj_51; Proj_47; Proj_81; Proj_38), as is the concentration on a promising target (Proj_112). This target should have direct relevance for health (e.g. for drug and vaccine development: Proj_47, Proj_98, Proj_104, for patient management: Proj_82). The potential for exploitation should be high (Proj_104).

For the recruitment of patients it is helpful if the project has goals with which the patients can identify (Proj_101).

Other helpful factors from the beginning are seen in the integration in a WHO approach (Proj_98), the usability of the results for different purposes (virological, immunological, and genetic studies: Proj_16), to start with existing products (Proj_51) or directly build on existing knowledge of one partner (Proj_17) or other work which is carried out independently from project by one of the participants (Proj_204).

### 6.1.3 Partners

The selection of partners is of crucial importance in the view of the coordinators and mid-term evaluators. Well-fitting, complementary groups should be organised (Proj_150) including the best available partners (Proj_38; Proj_2; Proj_3; Proj_123; Proj_36), with high expertise (Proj_61; Proj_119). The partners should have access to high standard (animal) facilities (Proj_3) and be able to carry out excellent research (Proj_86).

Very often the consortia evolved from pre-existing networks (Proj_137) and built on traditional and successful earlier collaboration of the partners (Proj_175; Proj_42; Proj_77).

Industry partners make the researchers aware of industry's needs. (Proj_50; Proj_48) and therefore should be involved in steering committees (Proj_2).

For some purposes it was seen as important to include national bodies and reference labs (Proj_137) and that EU reference labs collaborate with labs in countries where the target disease is prevalent (Proj_176).

The size of the consortium was assessed somewhat unequivocally; it is self-evident that this depends on the project's aims. Some argued in favour of a large size (Proj_50), which can help shift tasks from a leaving partner to another, others find a small group more effective in the cooperation (Proj_81; Proj_34). One project found a size of 7 to 10 partners adequate (Proj_150).

More often than the size of the group, it was mentioned that the success depended on the involved people (Proj_51), who need a good motivation and commitment (Proj_107;

Proj_123; Proj_57), and should be dedicated to the projects aims (Proj_34). The group should be well-focussed (Proj_34), each partner should have a clear role (Proj_81).

The partners should bring in complementary expertise (Proj_34; Proj_47; Proj_42; Proj_81; Proj_60), also to avoid internal competition (Proj_50). To cover all necessary competencies including clinical testing, the inclusion of experts for clinical studies and vaccine manufacturers in the process was seen as important (Proj_60).

In one project it was seen as supportive that the subcontractors participated like full contractors (Proj_57).

Partners from NAS countries were also seen as helpful, (Proj_77), especially if the target diseases have a high prevalence there (e.g. M. tuberculosis: Proj_80).

### 6.1.4 Project management

A large number of mid-term review reports, interviews and periodic reports considered an excellent coordination (Proj_204; Proj_47; Proj_42) as very important factor for the attainment of the project goals. This includes the capability of the coordinator (Proj_57), an experienced central project management (Proj_77), with the steering committee supported by full-time project manager (Proj_49) or up to 2 full-time persons for the larger projects (Proj_45).

The scientific and logistical management should be strong and close (Proj_79; Proj_50) with meetings of the partners or the steering committee every 6 months (Proj_50; Proj_60, Proj_45; Proj_176; Proj_123)). Partially, a strong controlling of the progress is carried out by the CO with internal reports every 3 months (Proj_203). In other projects a database and specific system of administrative monitoring was applied that had already been used in earlier projects (Proj_81).

To foster the exploitation of the results a company-oriented management is highlighted (Proj_38), one project mentioned a special clinical trials committee (Proj_45).

### 6.1.5 Internal collaboration

Related to the management is the relevance of an excellent collaboration (Proj_61; Proj_47; Proj_113; Proj_4). It was stressed that it was helpful to create a momentum or a project "spirit" (e.g. "Proj_49").

Another factor in this field is excellent communication (e.g. Proj_36), supported by visits of the CO to participating centres (Proj_46; Proj_75). Internet web sites are helpful for the exchange of data and papers (Proj_176; Proj_48).

Methods should be internationally harmonised (Proj_141), e.g. by a manual (Proj_58), by bilateral visits and exchange of staff for up to several months (Proj_59; Proj_60; Proj_175; Proj_148; Proj_150).

### 6.1.6 External support

External support for a project can on the one hand come from the Commission: good communication and scientific contacts with the Commission, as well as support and counselling by Commission's scientific officer were explicitly appreciated by a number of projects

(Proj_38; Proj_57; Proj_61; Proj_45; Proj_148), also the careful watching and keeping pressure by the Commission (Proj_123).

On the other hand, other institutions were helpful for the projects, namely support for the CO by his home institution (Proj_205; Proj_123), a good interaction with stakeholder groups (Proj_49), and strong international cooperation also with external programmes (Proj_46).

To find collaborating clinical centres, a personal approach to hospitals and via scientific society, presentations on conferences, and personal feedback to hospitals were mentioned as supporting factor (Proj_119).

### 6.1.7 Dissemination and exploitation

The utilisation of the results is influenced by the appropriate dissemination of results (Proj_16). One MTR recognised a very straight-forward exploitation strategy (Proj_44). To be ahead of scientific competitors, results in the form of a genome database were early published. In some cases, no-cost extensions were used to increase the efforts in dissemination and exploitation (Proj_83).

Equally important as scientific publications can be to assure the maintenance of databases which include the project's results after the end of a project (Proj_109).

## 6.2 Factors influencing utilisation in a negative way

Among the factors, that hamper the production and utilisation of the results negatively are deficits in funding, in the planning of the project, in its implementation and unexpected results, dissemination and exploitation, the organisation within the Commission, and the framework conditions.

### 6.2.1 Funding

The researchers and sometimes also the MTRs perceived the funding in some cases as too small. This resulted in a duration of the projects for 2 years (Proj_113; Proj_36) or 3 years, which were especially too short to reach clinical trials (Proj_50; Proj_56; Proj_58; Proj_123).

Because of too narrow limitations in the funding of one CA, some hospitals could not participate which would have taken part if paid; in one case country representatives for the translation of deliverables were missing (Proj_119). In two other projects, a strong reduction of the budget implied that important aspects for policy making (economic evaluation) had to be dropped (Proj_77), or cost cuts reduced the usefulness for public health (Proj_148). One project had too little capacity for the information of the public (Proj_148).

Besides the planning and the contract negotiations, delays in the implementation process can lead to the need for additional funding (Proj_106), e.g. for additional meetings in a (possible) extension period even if other parts of the budget (staff) need no additional funding (Proj_106).

In many cases it was seen as important even by the MTRs to keep the study groups together in the post-contract period, e.g. to maintain a developed database (Proj_83; Proj_105). If there is no further funding after the project, products that need continuing maintenance and the contacts/knowledge of the consortia are feared to get lost (Proj_150; Proj_60).

Short funding periods and missing perspectives after the finalisation are seen as a problem of a general lack of continuity in the EC funding policy (Proj_52; Proj_51).

### 6.2.2 Planning

It is not easy to determine which problems emerged because of problems in the planning of the project (and might have avoided) and which ones were not foreseeable.

In a number of projects, the group was a bit too enthusiastic in the beginning and sometimes overlooked the severity of some problems (Proj_38) or made too tight time schedules, e.g. for the ethical reviewing of a clinical study or for patient recruitment (Proj_45; Proj_101).

In one project, the CO had no sufficient resources (due to a delay?; Proj_106), in another the group retrospectively had included a bit too little fundamental research (bioinformatics, immunology; Proj_60).

Sometimes, difficulties arouse from the large size or heterogeneity of a cluster which was not easy to manage (Proj_60; Proj_62). This was associated with roles of IND partners which were not well defined (Proj_106) or the danger of losing track of the final goals (Proj_112). More than one consortium had problems with the inclusion of unstable start-up companies (Proj_123; this project suggested to include SMEs instead).

### 6.2.3 Implementation

As mentioned, delays were caused by different factors, e.g. difficulties to agree on definitions, technical problems with data transmission via an internet site, liability problems with a clinical study, or the provision of a placebo drug (Proj_79).

Unexpected results were, for example, serious adverse events in an attached phase-III trial, which stopped the clinical development and further patenting plans (Proj_204), or the risk of toxicity of a candidate (Proj_107).

Other problems emerged from different database software and other standards within a consortium (Proj_113). In one project, the MTR found missing entrepreneur activities of the coordinator to elaborate solutions for emerging problems (Proj_62).

### 6.2.4 Dissemination and exploitation

Not much was said about problems with dissemination and exploitation. In one project, only a low intensity of dissemination activities was criticised (Proj_34), in another the MTR called for patenting and industrial exploitation of the results (Proj_105). An uncertain exploitation strategy due to the confidential nature of results was described for project Proj_106.

### 6.2.5 Organisation within the Commission

In some projects, the burden of administration was complained that is associated with the submission of a proposal and the implementation of the project (e.g. Proj_50; Proj_51; Proj_205). Especially the financial administration was seen as too detailed (Proj_148). The inflexibility, e.g. with respect to requests to shift money from one category to another, often makes contract amendments necessary (Proj_49), which – like other administrative processes – need a long time (Proj_205; Proj_34; Proj_45).

Delays of payments by the Commission were quite frequent (Proj_34; Proj_57; Proj_176; Proj_77; Proj_36), in at least one case this led to a delay in the start of the scientific work (Proj_131), in others the late information about the signature of the project led to problems with the recruitment of the necessary staff on time.

One MTR found that payments were refused due to minor administrative delays (Proj_83).

Another MTR mentioned that the communication between the Commission and the coordinator could have been improved (without saying by whom: Proj_131), insufficient support by or interaction with Commission was also a problem in other projects (Proj_150; Proj_49). In some projects, the feedback from Brussels was seen as not adequate (Proj_176), e.g. missing feedback on reports (Proj_205; Proj_77), and frequent change of the scientific officer in Brussels, who did not come to the MTR meeting (Proj_205).

The communication with the Commission about contract amendments was perceived as lengthy (Proj_36), the change of partners difficult (Proj_148), the obligation to find a new 3rd partner after the exit of an IND partner very time-consuming (Proj_36).

More flexibility in contract matters would be helpful (Proj_50), the CO should have more competence to make flexible decisions, combined with more control and feedback by the Commission (Proj_45). For example, one project found it had too much money for meetings and too little for consumables and would have liked to shift money from one to the other (Proj_113).

### 6.2.6 Framework conditions

A last group of hampering factors are framework conditions that cannot easily be influenced, as the public resistance to primate research (Proj_49), difficulties to get viruses even from Italy because of fears for bioterrorism (Proj_176), or the lack of an information ethics strategy for unaggregated DNA data (Proj_80).

# 7 Discussion and conclusions

In the present and final chapter, the results of the impact evaluation of the research carried out under KA2 are summarised and discussed. Conclusions are drawn for similar research programmes in the future. To be able to assess the validity and relevance of the findings, the methodological approach of the present evaluation has to be taken into account.

## 7.1 Methodology of the present project

The evaluation focussed on 145 KA2 projects for which at least one document was available. Of the total number of 205 projects in our database, 60 other projects funded in the same Key Action were excluded either on advice of the Commission (projects on prion-diseases or on animal diseases) or because no single document was available to us. It is possible that a small number of other projects has not found its way into our documentation system at all. Although the distribution of the projects over the years is not known, it can be seen that a larger number of those projects from the later calls for proposals are documented less completely and are therefore underrepresented in the present evaluation.

The evaluation was based mainly on the periodic and final reports written by the members of the projects themselves. Another important resource were the reports on the mid-term

reviews. A closer impression on the functioning of the projects and on some impacts which are less well documented in the reports was gained by 17 telephone interviews. Additional information was retrieved from different data files provided by the Commission and – where no other documents were available – from the technical annexes of the projects.

*Periodic reports*

The periodic reports were – in general – a good source for the necessary information on the projects. With few exceptions, they stick to the reporting format suggested by the Commission and (e.g. as derived from the comparison with the MTRs or interview data) report frankly even on the projects' weaker points.

*In some cases, the reports should have been written in a more systematic way to make it easier for the evaluation (and in the regular case also for the Commission's scientific officers) to find the relevant information.*

In many reports it was not easy to find out what were the achievements, publications etc. from the actual reporting period and what was only repeated from earlier periods.

*The periodic reports should clearly differentiate the results from different reporting periods and not repeat results from earlier periods.*

The information on the relevant milestones for a reporting period is generally very good and presented in a transparent tabular way. In some reports, however, it was difficult to determine the reasons for not achieving a milestone.

*The reporting format should force the participants to comment on every missed or delayed deliverable/milestone.*

Some interesting aspects like numbers of staff employed for the projects, numbers of PhD degrees acquired etc. are not systematically included in the reports. The same is true for other non-thematic goals like gender-aspects and contributions to other European policy objectives (cf. chapter 3.2).

*It should be considered to develop the reporting scheme in a way that makes this information more easily accessible for the evaluation of the projects. Desirable aspects for which no systematic information was available in the reports are*

- numbers of staff employed for the projects,
- numbers of PhD degrees acquired,
- number of publications which have been published in the reporting period, broken down in different categories (books, book chapters, articles in peer-reviewed vs. other journal, presentations/posters on scientific conferences),
- potential use of (lab) methods, databases etc. in research and practice outside the project,
- collaboration/meetings with other research groups,
- meetings with stakeholders/target groups for dissemination of the results,
- other indicators for contributions to other European policy objectives.

The regularly updated plans for using and disseminating the knowledge and new Technology Implementation Plans (TIP) including electronic tools like the eTIP will partly remedy this lack of information.

For a number of projects there were no final reports available, so that it was not possible to give a final evaluation of the attainment of the projects' objectives and milestones. Some

impacts, e.g. granted patents, licensing, publication of the results, establishment of companies, or meetings with policy-makers or other stakeholders to disseminate the results will only take place after the finalisation of a project and therefore will not be covered even by the final report.

*If possible it should be considered to implement a reporting system for such important longer-term impacts.*

*Mid-term reviews*

Although of different comprehensiveness, the mid-term review reports done by external experts in the field were especially helpful to assess the methodological quality of the projects. The MTR seems to be well-accepted by the project participants, its recommendations were most often implemented in the further course of the project. Sometimes, the reports restricted themselves to a very factual level, including too little evaluative statements by the external experts to allow the assessment of the project's quality.

Regular scientific reviews similar to the MTR are not foreseen in FP6. The reasons for this decision are unknown to us, but in general this instrument is made available by the standard contracts.

*From the view of the present evaluation external scientific reviews should be used if not generally but at least in cases of emerging questions of if and how a project should be continued.*

*Telephone interviews*

For 17 of the 145 projects, telephone interviews were carried out with the coordinators. They were necessary to obtain interesting information which cannot be found in the written reports and to get a deeper understanding of the impacts and factors which influenced the attainment of the project's goals. In advance, the Commission was concerned about the additional burden for the coordinators related with these interviews and a possibly poor willingness to support the evaluation. However, it turned out that such concerns were not shared by the coordinators: Many of the coordinators were very pleased to learn that the Commission made efforts to learn more about the implementation and impacts of the projects and therefore were very supportive to the evaluation, allowing timely appointments, dedicating more than one hour for the interviews and offering additional time and information if needed. The statements given were very sophisticated and self-critical, no one expressed his or her astonishment or concerns about information security.

*This experience indicates that future similar evaluations can hope for sufficient support by the respective project leaders and coordinators.*

*Data files from the Commission*

The data files which were provided by the Commission contained information from the proposal procedure (table with all partners, obviously provided by the participants themselves) and contract management (part of the 'CONTNEGFU'-database produced by the Commission). In part, the information on the projects from these sources was inconsistent and not available for all projects.

*It should be considered how the data management within the Commission can be optimised to be more comprehensive and useful also for evaluation purposes.*

### 7.1.1 Conclusions for the evaluation of EU-financed research

As no objections by project leaders were encountered, the experiences with the present impact evaluation show that such projects are possible in principle and can lead to – as we think – useful and applicable conclusions. However, with the relatively low budget available, the evaluation had to restrict itself to a relatively rough level of detail.

*It should be considered for similar projects in the future to draw more on the project leaders and coordinators as a source of information that is not systematically given in the periodic reports. This can be done by telephone interviews which have proven to be extremely helpful, but also by a short written questionnaire which would collect data on the projects in an economical way. This was suggested in the original tender for the impact evaluation but was dropped to keep the things as easy as possible for the project leaders. This seems not to be necessary in the future.*

*For a more comprehensive picture it would be desirable to broaden the empirical basis by*

- *a larger number of telephone interviews,*
- *a written questionnaire,*
- *a bibliometric analysis of the publication activities, and*
- *a final workshop to discuss the lessons learnt and their application to future funding programmes in the field.*

Another idea for the impact assessment was to combine the evaluation of the impact of finalised projects with aspects of counselling for those projects which are still ongoing. The latter could not be realised in a satisfying manner because of the sheer number of the projects. In addition, there were too many projects for which the most actual periodic report was missing. The only instrument which would have allowed a sufficiently close look at the momentary proceeding of a project were the telephone interviews, and even they had to be focussed mainly on the impacts.

*Therefore, for the future, the evaluation should concentrate on the impacts of finalised projects, leaving the counselling – if necessary – to mid-term reviews or similar instruments.*

In the present project strong efforts were undertaken to (in close collaboration with the Commission) define the relevant impacts and to collect data which allow to evaluate these impacts. Tradeoffs had to be made between the goal to include as many projects as possible (even if there was only few information available on them) and the aim to comprehensively assess all aspects of a project including its final outcomes. For the present project, both aspects have been included, leading to the fact that only poor information is available for some projects (which are still ongoing) and the quantity and quality of information on the different projects is quite heterogeneous.

The data provided by the commission and extracted from the reports were transferred to a database.

*With little efforts, this database could be adapted to similar evaluation projects in the future. Given that it could be connected to already available administrative data within the Commission services, a basic overview on the funded projects could be provided easily on the basis of routine data. Having the experiences of the present project in mind, it might be discussed how the efficiency and usefulness of such a data management system for the Commission services should be optimised.*

*For future similar impact evaluations of certain research programmes, a two-step approach is suggested:*

*(3) A (more systematical) internal registration and assessment of routine data which are already available, yet dispersed at different offices (e.g. administrative data, deadlines for deliverables, deliverables, extensions…), eventually also integrating some additional data provided by the project managers via internet tools like eTIP or a slightly supplemented reporting format for the periodic reports.*

*(4) A more comprehensive external evaluation to assess more in-depth the impacts of the programme*

- *based on these routine data, but also including telephone interviews, a questionnaire for all projects, TIPs, MTRs, and probably also the periodic reports,*
- *analysing them statistically, including a quality assessment, the integration of the research projects into their research field, etc.,*
- *with the possibility to focus on specific questions of high relevance for the Commission, e.g. for the preparation of future research programmes.*

For both approaches, the experiences and methodology (e.g. questionnaires, database structure and queries) of the present project should be exploited.

The assessment of how far especially the non-thematic goals have been reached is impaired by the fact that these goals are not associated with explicit and operational outcome criteria.

*For future evaluations it would be helpful to have more explicitly formulated objectives and exact a priori numerical standards against which the measured outcomes of the projects can be compared.*

Objectives and standards could resemble the following examples:

- Objective 1: Reduce gender inequalities in research:
  - Standard 1.1: At least 30% of the senior scientists who lead a working group are female.
  - Standard 1.2: At least 30% of the scientific coordinators are female.
  - Standard 1.3: Explicitly include specific work packages on gender differences in every project.
- Objective 2: European integration:
  - Standard 2.1: Participation of contractors of at least four EU Member States, whereof at least one comes from an Accession Country.
  - Standard 2.2: The relative number of coordinators from all EU Member States equals their countries' share in the European population.

...and so forth.

This kind of measurable standards for the non-thematic goals of the research programmes would possibly require additional efforts to clarify these goals, but would contribute to the general trend to sustainable policy-making and impact-assessment of EU policy also in the field of research.

## 7.2 KA2 projects in their research fields

As shown in the review of actual trends in research on infectious diseases and development of vaccines and anti-infective drugs (chapter 3.1.1), there is a rising need for research not only in countries where epidemics are actually prevalent but also in Europe in general for several reasons:

- world-wide mobility leads to rapid distribution of infective agents around the world,
- the enlargement brings countries into the EU where severe problems exist with infectious diseases,
- communicable diseases, especially poverty related like malaria, AIDS, and TB lead to public health disasters in developing countries which are not able to cope with these challenges alone but desperately need help from the richer countries,
- bioterrorism is an emerging threat,
- even in the EU a general lack of awareness of the problem of infectious diseases is found (e.g. concerning HIV protection, consumption of antibiotics…).

Despite these needs, the industry is at least partially withdrawing from anti-infective pharmaceuticals. The potentially large markets are not attractive enough for the industry to take the risks of high R&D investments alone. Therefore, to tackle the emerging and re-emerging threats to public health with the help of new drugs and vaccines, public-private partnerships are supported by public funding (as well as by charities as the Bill-and-Melinda-Gates-foundation) to alleviate the industry's risks and to support the (often sub-optimal) collaboration of academic and industry research.

*From the point of the actual research, the public-private partnership approach seems to be both especially necessary as well as successful for the field of infectious diseases.*

Many of the KA2 projects are directed to poverty-related diseases or other fields which are of minor interest for the pharmaceutical industry, e.g. the treatment of children. The issue of poverty-related diseases has left its formerly marginal place and now ranks very high on the international agendas, as e.g. recent policy initiatives in the USA, discussions in the WTO about the provision of anti-HIV medicines for poor countries etc. show.

*The relatively large number of projects in KA2 on malaria, AIDS, and TB shows that the Commission has responded early to this international trend.*

Novel and up-to-date approaches and methods are used in the projects, and are applied to relatively new research fields. The projects combine research groups from the Member States thus improving the chance to be successful and internationally competitive. Many of the projects have met their objectives very successfully, bringing candidates faster into clinical testing than the industry would have, making important contributions to their respective research field, and so on. Although the international literature – at least in selected journals – is still dominated by authors from the USA, and publications from third countries as e.g. China also important, the KA2 projects have resulted in a large number of international publications, partially also in top-level journals.

*These positive outcomes contributed to the visibility of EU-funded research and efforts in this direction should be continued or even increased.*

The review of the exploitation and dissemination activities showed that publications and contributions to congresses are broadly used by the scientists to inform the scientific community, that patents are filed where industry partners in the consortia push this, but that other activities are scarce. The exchange with other researchers seems to be quite informal, only a few information events were held to directly liase with other R&D initiatives working on similar questions. Some projects argued that the most important research groups in their field were already involved in the consortium, others mentioned the high competitiveness in their field as a hindering factor.

*These results indicate that the interaction and coordination of the projects with other EU-funded projects, with national and international research programmes could still be im-*

*proved. Within the EU-funded research it should be assured that the different projects and initiatives (e.g. projects funded by different DGs, European & Developing Countries Clinical Trials Partnership) work closely together wherever possible.*

Public health research on the EU level is of growing importance and – as the respective projects show – has its specific added value in the harmonisation of research and surveillance methods, transfer of knowledge, and European integration in general.

*With the exception of antibiotic resistance and the harmonisation of surveillance methods, public health issues seem to be underrepresented in the KA2 projects. It should be examined if they are sufficiently covered by other EU-funded research (e.g. by DG SANCO) and exchange of knowledge is assured between the different programmes.*

According to the political priorities set up for the QoL programme, the KA2 projects cover poverty related diseases, zoonoses, as well as most of the diseases on the EU "bug list" (European Commission 2000) and international agendas. In research that is strongly driven by the proposals the researchers submit, the Commission can only set the higher goals and the framework conditions, while it depends on the expertise of the applicants and the reviewers of the single projects to decide which projects are submitted and get a favourable assessment.

*Despite this, KA2 projects were able to meet the requirements of their research fields as well as the higher policy goals.*

It has been shown that a strong science base has been developed in the projects. Resulting from the limited budgets and funding periods, a danger was seen by many projects to lose the elaborated knowledge after the finalisation of the project ("brain drain"). Some groups tried to respond to this danger by common applications for new projects, but naturally the success thereof is not predictable.

*For tasks of real European dimension which need a longer perspective, as the maintenance of databases which result from a project and can build the basis for future research, structures are needed that keep track of past and present projects and make the methodological knowledge and final results accessible to future research.*

CORDIS is a technical solution that serves a lot of these purposes. However, the projects also show that the quality of research is strongly dependent on the persons who participate.

*Measures should be implemented like mailing lists or thematic expert networks, probably in the framework of the new European Centre for Disease Prevention and Control (ECDC)[9], in order to preserve the contacts of the Commission to successful coordinators and contractors.*

## 7.3 Project implementation

Many points have been learned on the implementation of the projects under KA2. They relate to the planning, selection of partners and industry involvement, the implementation phase itself, as well as to the exploitation and dissemination of the results. Combined with these aspects, the factors which influence the production and utilisation of the results in a positive or negative way are discussed.

[9] Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European centre for disease prevention and control. OJ L142/1 of 30.4.2004

### 7.3.1 Planning

Contract negotiations were sometimes lengthy and problematic not only because of time-consuming processes within the Commission but also because extensive verifications were necessary by the legal departments of the participants, e.g. with respect to IPR protection. In one project it was suggested that the Commission should establish guidelines or terms to facilitate and speed up the contract negotiations and even to establish a legal-aid department to assist the coordinator in managing the different interests of the other contractors. More information would be helpful how long the contract negotiations will take because the contractors have to plan the recruitment of the staff in this period, but often cannot employ people without having the signed project contract in their hands.

*Very clear plans, concrete formulation of objectives, milestones and deliverables with specific performance criteria are necessary as a starting point for the work and were reached sufficiently in most of the projects.*

In some cases, the severity of some problems was underestimated by the project managers, e.g. technical problems with database development or patient recruitment.

*If results shall be disseminated in the form of a database, sufficient expertise and funding has to be invested, and the product should clearly be oriented at the needs of its end-users.*

For many projects that aimed at the development of drug or vaccine candidates, 3 years of funding were too short. As one interview partner put it, the pace in the field is 5 years to bring a new candidate vaccine etc. into clinical trials.

*More flexible funding schemes were suggested, e.g. an initial funding for 2 years with automatic prolongation after having successfully passed a review.*

As mentioned above, in general a tight supervision of the projects by the Commission was welcomed, and successful projects were able to redirect their work when they faced unexpected results and to include recommendations made by the mid-term reviewer.

*This ability might be supported by the definition of predetermined breaking points already in the project plan, at which new decisions are made on the continuation of a project or some of its parts.*

Little attention was paid to interaction with or at least information of good other stakeholder groups, e.g. patient associations. In some projects, the benefits of research questions that meet well with the needs of the patients e.g. for the recruitment of participants in surveys was explicitly recognised, but in general little attempts were undertaken to actively involve patients and other stakeholders in the planning phase or at least disseminate results to the public or to specific target groups.

*Here a deficit has to be noted also with respect to the relevance of consumers on the political agenda that should be tackled in future project planning and dissemination.*

### 7.3.2 Selection of partners

The projects had an average number (median) of 7 partners. The size of the consortia was assessed controversially. Some argued that to have the choice among the best possible partners and to be able to compensate for eventual losses of partners it is better to start the initiation of a proposal with a relatively large group, maybe in the frame of a scientific meeting, and drop some partners if they don't fit well enough with the work programme. Despite the need to integrate complementary expertise, some redundancies were helpful to

cope with the loss of partners by taking over their tasks by another existing partner and to learn for one's own work from partners with similar tasks and expertise, e.g. by the exchange of scientific or lab personnel.

*Especially for public health and surveillance programmes, it was best to include as many partners as possible. On the other hand, a consortium should not be too large to assure efficient communication between the contractors.*

As compared to their respective number of contractors, the UK and the Netherlands had a relatively high number of coordinators, in the other Member States the relative numbers of contractors and coordinators were nearly equal.

There were relatively few partners and coordinators from the smaller Member States. The integration of the Accession Countries was attempted in many projects, partly supported by NAS extension grants, and especially for the public health projects this was seen as especially rewarding.

*From the perspective of the evaluation it cannot be determined if these still small numbers of partners from small Member States and Accession Countries are sufficient to meet the political aims.*

Among the non-EU countries, with the exception of Switzerland (50 participants), Norway (24 participants and 2 coordinators), Romania (7 participants), Iceland (6 participants), and Bulgaria (3 participants), the USA (9 participants), and Israel, which participated with 15 contractors and among them even four coordinators, third countries were not involved as partners in the KA2 projects to a large extent.

*This may mirror the political aim of funding in general researchers from the EU, but it should be considered to strengthen international collaboration. The model of collaboration with Switzerland, with Swiss partners normally contributing their own funding, could be extended to other non-EU partners if their specific expertise is helpful to strengthen the European research.*

For some of the poverty-related projects it was possible to collaborate with partners from the most affected countries and with WHO, which allowed the projects to act on the international stage and has clearly contributed to the recognition of EU-funded research in the world.

The selection of the best partners preceding the contract was very often not easy. The experiences show that this is a time-consuming but rewarding effort, because the success of the projects strongly depends on the selection of the partners. The selection should be based on

- the scientifically best partners,
- high motivation,
- very good collaboration, e.g. coming from earlier projects.

### 7.3.3 Industry involvement

An intrinsic goal of EU research funding is the collaboration of public research and industry. 45 of the 145 projects have at least one IND partner; in total 122 IND partners are involved. This is a share of around 9% of all 1370 participating institutions. 41 (33%) of the 122 IND partners are SMEs.

*With regard to the high priority that is given to the participation of industry and especially SMEs, the participation is not very high. This can be due to the strong administrative*

*requirements beginning with the writing of the research proposal which are especially difficult to manage by companies.*

While many researchers have a strong interest mainly on the scientific level, industry partners make researchers aware of the industry's needs.

*The direct inclusion of companies as partners who have an interest in marketing the project's products seems to be the best exploitation strategy. Besides sometimes difficult IPR issues in the contract and consortium agreement negotiations, the collaboration worked very well in those projects where IND partners were involved.*

In total, many drug and vaccine candidates have been developed which have a high potential for industrial exploitation. The division of labour between public research and companies seems to have worked well. For the exploitation, e.g. the common use of patented knowledge owned by different partners, interesting structures were developed: One consortium even established a foundation that would carry out the further clinical development.

However, the interface between EU-funded (normally preclinical) and industry-funded clinical development is difficult to manage, and the division of preclinical from clinical development was sometimes counterproductive.

*As many drug and vaccine candidates fail in the clinical phase, the possibility should exist to come back to EU-funded preclinical development with improved knowledge from clinical studies. This iterative process with smooth transitions from preclinical to clinical development and back to the preclinical phase seems not to be foreseen in the EU-funded projects.*

### 7.3.4 Implementation phase

Many factors are associated with the successful carrying-out of a project, although its contribution was not always inducible for each factor. Of overwhelming importance in the view of the researchers and mid-term reviewers is the communication between the participants and a strong coordination. Nearly all projects stated the need for at least 2 meetings of the whole group or of a steering committee per year and of additional personal meetings of subgroups, e.g. a special clinical trials committee. To assure the quality and standardisation of methods, the exchange of lab personnel was practised, although not always funded by the Commission contribution.

As mentioned above, technical problems emerged in a number of projects with the construction of databases, a problem which can be overcome if sufficient resources are dedicated to this task and if IT specialists are included in the consortia e.g. as subcontractors.

*Even with the best planning, some difficulties are not totally avoidable. In the development of drugs or vaccines, it is normal that most candidates have to be dropped during preclinical or clinical development. Projects need enough leeway to overcome this and redirect their ongoing work, sometimes to start again at the beginning with other promising candidates, although in advance, the necessary resources to do this can only be planned to a certain extent.*

The researchers felt overcharged by administrative tasks to meet with requests by the Commission that were sometimes perceived as unnecessarily rigid. This applies to the project contracts and contract amendments, e.g. with regard to changes in the partners, or inflexible cost categories which made it difficult to shift parts of the budget from one to the other purpose.

*The future will show if the "new approach" to project administration in the 6th framework programme makes these things easier, as it was hoped by some of the participants. As can be seen by today, a considerable amount of administrative work and responsibility has been shifted in FP6 from the Commission to the project coordinators, which rose concerns that a lot of administrative work has to be done by the scientific personnel.*

Another problem that sometimes even lead to delays in the start of projects or parts thereof were late payments by the Commission.

*The reasons for late payments cannot be assessed by the evaluation, but all possible measures should be taken not to slow down the projects for unnecessary administrative reasons.*

In many cases, the feedback and control by the Commission was appreciated by the projects. A good contact to the scientific officer and careful watching and keeping pressure by Commission were seen as helpful for the success of the projects. If this was not experienced, e.g. because there were no reactions by the Commission on the submitted reports or the representative of the Commission could not attend the mid-term review meeting, this was noted as hindering factor.

### 7.3.5 Exploitation and dissemination

Despite efforts of the pharmaceutical industry to bring their research scientists into closer contact with their colleagues from the universities, the two parties or "cultures" are still "worlds apart" (The communication barrier: Drug discovery's final frontier? (Editorial) 2004, p. 191). One approach to encourage cross-fertilisation between disciplines and research environments for the benefit of drug discovery is seen in the improvement of real and more open discussions on conferences (The communication barrier: Drug discovery's final frontier? (Editorial) 2004).

From the publication lists in the reports it can be seen that many contributions to scientific conferences were made by the KA2 projects. Dissemination to the scientific community was also ascertained by the generally large numbers of publications. However, there are only few reports on conferences that were organised by the projects themselves directed to their specific target groups including policy-making.

*More emphasis should be given to inform the public and the political level on the practical consequences of a project, e.g. in final workshops including policy makers, lay people and the press.*

*Although many industry partners were attached to the projects which can directly continue to develop products on the basis of the results of a project, more could be done to exploit the results with the industry, e.g. in the form of information events by projects in which no IND partners are available.*

Other examples in KA2 projects are publications not only in scientific but also in business journals, press releases and even a TV broadcasting.

## 7.4 Impacts

### 7.4.1 'Thematic' goals

The impacts with respect to the 'thematic' goals of the KA2 are clear and in general fulfil the expectations. In general, the projects attain or surmount their objectives, make significant contributions to science and end up with products of (mostly) high practical relevance, e.g. identified new therapeutic targets, patents on promising drug or vaccine candidates, enhanced diagnostic tools and standardised surveillance methods.

The longer-term specific impacts of the projects are not easy to assess because no follow-up data are available on the use of the results by the different target groups, and for many projects even no final report could be analysed.

*Based on strong dissemination activities directed to the scientific community, it can be assumed that the results of the projects will be useful for further research. Where hospitals and laboratories were included in the development of diagnostic methods or data collection standards, the reports give hints that the participating institutions will in general use the enhanced methods also in their day-to-day work.*

### 7.4.2 'Non-thematic' goals

With respect to the 'non-thematic' goals of KA2 and the FP5 QoL research programme (see chapter 3.2), the impact assessment results in a more diverse picture. Especially the public health projects with their emphasis on harmonisation of research and laboratory methods as well as treatment standards, but also the other projects with participants from smaller or larger numbers of Member States had an impact on the policy goal of European integration. EU and national research was partially combined, including additional funding from national grants.

*The transnational character of the projects and the fact that in most cases the EU was the only possible source of funding for this kind of projects, the collaboration of experts from the Member States, and the standardisation of methods and communication of results across borders show a clear EU added value.*

The integration of industry partners as another explicit goal has worked very well in such projects where a market for the products of a project is in sight. However, the number of industry partners was still low.

*The actual usefulness of the results for policy-making is not easy to determine. From the weak dissemination activities in this direction it can be concluded that there are opportunities for improvement. Probably the Commission should insist more on the projects meeting thematic and non-thematic policy goals.*

This is most relevant for public health projects, but even research that is totally basic in character and far away from practical application can make a contribution to the non-thematic goals.

### 7.4.3 EU as research area

The projects have generated new networks of institutions which will potentially or certainly continue to work together in similar activities. Although much depends on a sometimes

changing funding policy which can also impair functioning collaborations in fields which are no longer on the political agenda, these emerging networks are a contribution to the European research area.

*To make best use of the new, tried and tested relationships and maximise their utility to strengthen the European research, steps should be taken to keep track of the well-functioning networks and use and possibly extend their competencies.*

The European Commission wants to play a central role in the system of international cooperation on infectious diseases proposed by the WHO (IP/03/1282; European Commission 2003a). This stronger role could be supported by the suggested European Centre for Disease Prevention and Control (ECDC). Especially in the light of the enlargement by countries with a higher burden of infectious diseases and less developed health infrastructure, a central institution would be welcomed (A European CDC 2003).

The plans of the European Commission to launch a European Centre for Disease Prevention and Control are assessed differently by scientists in the literature. The Commission's plans are for a small centre which mainly oversees the existing network for the Epidemiological Surveillance and Control of Communicable Diseases using training programmes, expert groups and international collaboration, to prevent duplication of national activities. Some scientists, however, argue in favour of a larger central organisation closer to the model of the US Centers for Disease Control and Prevention (Europe trims plans for infectious disease agency 2003).

*With its task to look after the existing scientific networks, the central institution would have the chance to draw on results and working groups of KA2 projects.*

# Annexes

Annex 1: Literature

Annex 2: Documentation sheet for telephone interviews

Annex 3: List of projects for closer evaluation and interview partners

Annex 4: Infectious Agents and respective Diseases

# Annex 1: Literature

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# Annex 2: Documentation sheet for telephone interviews

**Project ImpactInfect**

Stand 16.10.2003 /BUE

| | |
|---|---|
| ID-Nr. Project | |
| Acronym | |
| Interviewee | |
| Institution | |
| Interviewee's Role | |
| Date | |
| Interviewer | |

## Documentation sheet for telephone interviews with project co-ordinators

## 1 General information on the project

## 2 Project implementation

### 2.1 Would the project have received funding from other sources if there was no funding by the Commission?

❑ **Yes** ❑ **No** ❑ **Don't know**

## 2.2 Employment: How many persons are employed in the project (scientists, doctoral students, technicians…).

| | already existing | newly employed for project | total |
|---|---|---|---|
| scientists | | | |
| doctoral students | | | |
| technicians | | | |
| | | | |
| | | | |

### 2.2.1 How important is the money for personnel compared to other costs in the project, e.g. travel expenses, instruments or materials?

## 2.3 What can you tell me about the qualification of scientific staff during the project, e.g. number of PhDs acquired

How many persons received or will certainly receive a scientific degree based on the work in the project?

## 2.4 How do you assess the methodological quality of the study and validity of the results

new methodological approaches,

shortcomings (e.g. because of lack of funding) ?

## 2.5 Interlinking of the project activities with other national or Community activities and projects

How do you collaborate with other national of EU initiatives (research, industry, administration...)

### 2.6 Which measures are taken or planned to promote the use of the results?

Technology implementation plan? Patenting? Publication?

## 3 General outcomes

### 3.1 Project outcomes relative to its objectives

How would you assess the results of the project compared to its aims?

### 3.2 Which specific in-sights into the research field did you achieve, what is the contribution to actual research questions in the field?

### 3.3 Possible effects on employment based on the products/technologies developed in the project?

Are there results of the project that will open new opportunities for employment?

❑ **Yes** ❑ **No** ❑ **Don't know**

### 3.4 What activities will persist after the funding has finished?

### 3.5 Will there be proposals for further projects?

❑ **Yes** ❑ **No** ❑ **Don't know**

# 4 Technology transfer/ Practice impact

4.1 Which impact of the results do you expect on national and Community practice?

4.2 Are the developed methods used or expected to be useful in day-to-day life, e.g. in laboratories or health care?

❑ Yes ❑ No ❑ Don't know

4.3 Money for IPR issues has been available but rarely asked for. Did the projects apply for this?

**❑ Yes ❑ No ❑ Don't know**

4.3.1 If not: Why?

# 5 Policy impact

5.1 Transfer into policy making: What measures are planned to disseminate the results to the respective authorities?

5.2 How will the results serve as input for policy making?

### 5.3 What is the impact of the results on national and Community policy making

### 5.4 EU added value: What are the specific results from the fact that the project received funding from the EU? What is the contribution of the project to the EU as a whole?

## 6 Science impact

### 6.1 Transfer into science: What measures are planned to disseminate the results into the scientific community?

## 7 Additional information

### 7.1 Which factors influence the attainment of the project goals and the utilisation of the results in a positive or negative way

#### 7.1.1 Positive

#### 7.1.2 negative

# Annex 3: List of projects for closer evaluation and interview partners[10]

| ID-Nr. | Acronym | Title | CO first name | CO last name | Organisation | Reason for selection | Date of interview |
|---|---|---|---|---|---|---|---|
| PROJ_38 | MUCADJ | Dr. | Audino | Podda | Chiron Vaccines Clinical Research/Chiron SPA | DM | 24.11.2003 |
| PROJ_205 | SalVac | Prof. Dr. | Michael | Hensel | Universität Erlangen-Nürnberg | Salmonella | 24.10.2003 |
| PROJ_49 | HCVACC | Prof. Dr. | Willy | Spaan | Leiden University Medical Center | largest of HCV projects | 29.10.2003 |
| PROJ_50 | MenB vaccine | Dr. | Nicholas | Lecrenier | GlaxoSmithKline Biologicals | completed | 30.10.2003 |
| QLK2-1999-00429 | NEOVAC-EC | Prof. | Paul-Henri | Lambert | University of Geneva | Children | 16.10.2003 |
| PROJ_57 | PEPSAC-MIMIC | Dr. | Marco Rinaldo | Oggioni | Università degli Studi di Siena | basic research | 30.10.2003 |
| PROJ_60 | TB VACCINE CLUSTER | Prof. | Brigitte | Gicquel | Institut Pasteur | TB, large, 49 partners | 04.11.2003 |
| PROJ_45 | EUROVAC | Prof. Dr. | Peter | Liljeström | Karolinska Institute | HIV, overall most expensive project | 11.11.2003 |
| PROJ_176 | Reo ID | Dr. | Peter Paul Clement | Mertens | Institute for Animal Health, Pirbright Laboratory | no 1st report, reoviridae, expensive | 20.10.2003 |
| QLK2-2000-00542 | ESEN 2 | Dr. | Elizabeth | Miller | Health Protection Agency - Communicable Disease Surveillance Centre | Public Health | 23.10.2003 |
| QLK2-2000-01166 | Novel antimalarials | Dr. | Henri | Vial | UMR CNRS 5539, Université Montpellier II | Malaria, innovative approach | 29.10.2003 |
| PROJ_113 | EBP | Dr. | Giulio | Ratti | Chiron Vaccines | TN | 04.11.2003 |
| PROJ_119 | ARPAC | Dr. | Fiona | MacKenzie | University of Aberdeen | Antibiotic resistance, nosocomial infections | 20.10.2003 |
| PROJ_123 | PSEUDOMONAS VIRULENCE | Prof. Dr. | Arnaud | Ducruix | IFR 71 des Sciences du Médicament | Nosocomial infections | 29.10.2003 |
| PROJ_148 | ECHINORISK | Prof. Dr. | Peter | Kern | Universität Ulm, Medizinische Fakultät | Zoonosis | 05.11.2003 |

[10] The selection of the projects for closer evaluation was agreed upon with the Commission at the interim meeting in Brussels, Sep. 4, 2003

| ID-Nr. | Acronym | Title | CO first name | CO last name | Organisation | Reason for selection | Date of interview |
|---|---|---|---|---|---|---|---|
| PROJ_150 | HIV PR Inhibitors | Prof. Dr. | Hans-Georg | Kraeusslich | Universitatsklinikum Heidelberg | No 1st report; early start date, NAS extension | 04.11.2003 |
| PROJ_36 | RASTUD | Dr. | Peter | Brown | Cell Analysis Ltd. | CRAFT | 10.11.2003 |

# Annex 4: Infectious Agents and respective Diseases

red: infectious agent covered by at least one KA2 project
blue: infectious agent or diesease on the DG SANCO list of infectious diseases for special surveillance[11]
green: infectious agent from "bug list" covered by KA2 project

| Infectious Agent | Disease | Comment | KA2 project | SANCO bug list |
|---|---|---|---|---|
| **Viruses** | | | | |
| ADV (Adenovirus) | Respiratory disease | | X | |
| CMV (Cytomegalovirus) | Normally without symptoms, fever, pneumonia etc. in immune-depressed persons | | X | |
| Enterovirus | e.g. Hepatitis A | | X | |
| Hantavirus | Hantavirus Pulmonary Syndrome HPS, hemorrhagic fever with renal syndrome HFRS (in part zoonosis) | e.g. Hantaan-Virus | X | X |
| Hepatitis-Virus | Hepatitis | | X | |
| – HAV (Hepatitis A virus) | Hepatitis A | | | X |
| – HBV (Hepatitis B virus) | Hepatitis B | | X | X |
| – HCV (Hepatitis C virus) | Hepatitis C | | X | X |
| HIV | AIDS | | X | X |
| HPV (human papilloma virus) | Papilloma (benign tumor as a wart) | | X | |
| HSV-1 (herpes simplex virus) | Herpes simplex | | X | |
| Influenza-Virus | Influenza | | X | X |
| MPV (Metapneumovirus) | Respiratory disease | | X | |

[11] Annex I of Commission Decision 2000/96/EC, cf. European Commission 2000

| Infectious Agent | Disease | Comment | KA2 project | SANCO bug list |
|---|---|---|---|---|
| Paramyxovirus | Measles, mumps, respiratory disease, atypical Pneumonia in children, bovine disease... | e.g. RSV, partially zoonoses | X | |
| – RSV (Respiratory syncytical virus) | Respiratory disease | | X | |
| – Measles-Virus | Measles | agent = Briarcus morbillorum, type of Paramyxovirus | X | X |
| – Mumps-Virus | Parotitis epidemica (=Mumps) | agent = Rabula inflans, type of Paramyxovirus | | X |
| Poliomyelitis-Virus | Poliomyelitis | | | X |
| Rubella-Virus | Rubella | | | X |
| Reoviridae | Diarrhea, vomiting, pharyngitis, rhinitis | Family of RNA-Viruses, e.g. Rotavirus | X | |
| – Rotavirus | Gastroenteritis in children | | X | |
| Variola-Virus | Variola = Smallpox | agent = Borreliota variolae | | X |
| Viral zoonoses | e.g. rabies, toxoplasmosis | zoonoses | X | |
| – Rabies-Virus | Rabies | zoonosis | | X |
| – e.g. Dengue-Virus, Hantaan-Virus | Viral haemorrhagic fevers | e.g. Dengue-fever, Tula-fever | | X |
| **Bacteria** | | | | |
| Bacteria, gram-positive | | | X | |
| Bacteria and fungi | | | X | |
| Bacillus anthracis | Anthrax | partially zoonosis | | X |
| Bordetella pertussis | Pertussis (=whooping cough) | agent = Haemophilus pertussis | X | X |
| Brucella | Brucellosis | zoonosis | | X |
| Campylobacteria | e.g. sepsis, meningitis, gastritis | | | X |
| Chlamydia | Chlamydia infections | | | X |
| Clostridium botulinum | food-borne intoxication, botulism | | | X |
| Clostridium tetani | Tetanus | | | X |

| Infectious Agent | Disease | Comment | KA2 project | SANCO bug list |
|---|---|---|---|---|
| Corynebacterium diphtheriae | Diphtheria | | | X |
| Coxiella burnetii | Q-fever | zoonosis | | X |
| E.coli (Escherichia coli) | extraintestinal infections of humans and animals | | X | |
| – Enterohaemorrhagic E. coli | Infection with Enterohaemorrhagic E. coli | | | X |
| Francisella tularensis | Tularaemia | zoonosis | | X |
| Gonococcus | Gonococcal infections (e.g. gonorrhoea) | agent = Neisseria gonorrhoiae | | X |
| Haemophilus influenza group B | Bacterial influenza | | | X |
| Leptospira | Leptospirosis | zoonosis | | X |
| Listeria monocytogenes | Listeriosis | | | X |
| Meningococcal disease | | | | X |
| – Meningococcus B | Meningitis | | X | |
| Mycobacteria | | e.g. leprosis, TB | X | |
| – M. tuberculosis | Tuberculosis (TB) | | X | X |
| – M. paratuberculosis | Paratuberculosis | | X | |
| Legionella pneumophila | Legionellosis | | | X |
| Pneumococcus | Pneumococcal infections | | | X |
| Pseudomonas aeruginosa | Sepsis | | X | |
| Salmonella | Salmonellosis | partially zoonosis | X | X |
| Shigella | Shigellosis | bacterial infection affecting the intestinal tract | X | X |
| Staphylococcus | | e.g. meningitis, abscesses, wound infections | X | |
| Streptococcus | | e.g. respiratory infection, scarlet fever, rheumatic fever | X | |
| Treponema pallidum | Syphilis | | | X |
| Vibrio cholerae | Cholera | | | X |
| Yersinia | Yersinosis | e.g. Plague | X | X |
| – Yersinia pestis | Plague | | | X |

| Infectious Agent | Disease | Comment | KA2 project | SANCO bug list |
|---|---|---|---|---|
| **Miscellaneous** | | | | |
| (Alveolar) Echinococcus | Echinococcosis | tapeworm infection, zoonosis | X | X |
| Cryptosporidium | Cryptosporidiosis | | | X |
| Fungi | | mycoses | X | |
| Giardia lamblia | Giardiasis | =type of protozoa, e.g. diarrhoea | | X |
| Leishmania | Leishmaniasis (chronic inflammation, ulcera) | vector: sand fly | X | |
| Mosquito-borne diseases | | | X | |
| – Plasmodium (falciparum or malariae or ovale or vivax) | Malaria | | X | X |
| (Pneumonia) | Pneumonia or other lung infections | | X | |
| Pneumocystis carinii | PCP esp. related to HIV-infection | | X | |
| Tick-borne diseases | | e.g. FSME, borreliosis | X | |
| Toxoplasma gondii | Toxoplasmosis | =type of protozoa, zoonosis | | X |
| Transmissible spongiform encephalopathies, variant CJD | | all projects excluded from evaluation | (X) | X |
| Trichinella spiralis | Trichinosis | zoonosis | | X |
| Yeast | | | X | |
| Zoonoses | Zoonoses | examples from "bug list" e.g. Anthrax, Leptospirosis, Salmo-nellosis, Yersiniosis | X | (X) |
| Nosocomial infections | | special health issue on "bug list" | X | X |
| Antimicrobial resistance | | special health issue on "bug list" | X | X |