

**Research review**  
**Mathematical health modelling**  
**RIVM**

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Project number: 0656  
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# REPORT ON THE RESEARCH REVIEW IN MATHEMATICAL HEALTH MODELLING AT RIVM

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## **1. FOREWORD COMMITTEE CHAIR**

Review of research programmes by an independent committee can be extremely valuable. In the present review, the mathematical health modelling unit of RIVM provided an excellent detailed self-evaluation report as a starting point for the evaluation. Perceived strengths and weaknesses in this report could be confirmed, and other ones identified. Quite a few organisational and strategical problems had to be addressed by the committee.

It was helpful that all committee members had a strong and various background in the development and use of mathematical models in health care. Their joint experience has led to conclusions and recommendations which hopefully will lead to further strengthening of mathematical health modelling research at RIVM.

Dik Habbema  
Chair



## 2. THE REVIEW COMMITTEE AND THE PROCEDURES

### SCOPE OF THE REVIEW

The review committee in Mathematical Health Modelling (MHM) has been asked to perform an review of research of the virtual research unit in mathematical health modelling conducted by the RIVM. The term research unit refers to all RIVM employees who work in the area of the modelling of health and disease.

The review of this virtual research unit includes five research themes:

1. Population health and health care (PH);
2. Infectious diseases (ID);
- 3A. Infectious diseases, zoonotic transmission (IAFM);
- 3B. Food safety, microbiological contaminants (IAFM);
4. Food safety, chemical contaminants (FC)

The RIVM organisation consists of three domains, each containing staff with specific knowledge and expertise. Within these domains there is a wide diversity of knowledge and models. RIVM reorganised in 2013, which corresponds with the evaluation period 2013-2017. The three domains consist of twelve centres, six of which are involved in this research review.

In accordance with the Standard Evaluation Protocol 2015-2021 (SEP) for research reviews in the Netherlands, the committee's tasks were to assess the quality, the relevance to society and the viability of the scientific research at the research unit as well as the strategic targets and the extent to which the unit is equipped to achieve these targets. Furthermore, a qualitative review of the research integrity policy and a review on PhD training is executed. In addition, the MHM unit, in the self-assessment, asked the committee to address four questions, which will be dealt with throughout this report. The questions are:

- Are our models fit for purpose and are we addressing the right questions using modelling?
- Is the scientific and societal impact of our modelling work sufficient and ambitious enough?
- Is the modelling work embedded in an efficient and balanced way into the organisation of the RIVM?
- Which research fields need strengthening or more focus in the future? How do we involve society in our work?

### COMPOSITION OF THE COMMITTEE

The composition of the committee was as follows:

- Prof. Dik Habbema, chair, emeritus professor at Erasmus Medical Centre;
- Dr. Gary Barker, senior researcher at Quadram Institute Bioscience, Norwich (UK);
- Dr. Hubert Deluyker, scientific adviser at EFSA, Brussels (BE);
- Prof. Birgitte Freiesleben de Blasio, Norwegian Institute for Public Health and University of Oslo (NO);
- Prof. Martin O'Flaherty, professor at the University of Liverpool;
- Dr. Peter White, researcher at CIDSC and Imperial College London (UK);

The Curricula vitae of the committee members are included in Appendix 2.

The committee was supported by dr. M.J.V. Van Bogaert, who acted as secretary on behalf of QANU.

## INDEPENDENCE

All members of the committee signed a statement of independence to safeguard that they would assess the quality of Mathematical Health Modelling at RIVM in an unbiased and independent way. Any existing personal or professional relationships between committee members and the research unit(s) under review were reported and discussed in the first committee meeting. The committee concluded that there were no unacceptable relations or dependencies and that there was no specific risk in terms of bias or undue influence.

## DATA PROVIDED TO THE COMMITTEE

The committee has received the self-evaluation report of the unit under review, including all the information required by the SEP.

The committee also received the following documents:

- the Terms of Reference;
- the SEP 2015-2021;
- lists with an overview of publications;
- stakeholder assessment;
- assessment by department heads.

## PROCEDURES FOLLOWED BY THE COMMITTEE

The committee proceeded according to SEP. Prior to the first committee meeting, committee members independently prepared the site visit based on a preliminary assessment of the research unit under review based on the written information that was provided. The final review is based not only on the documentation provided by the research unit, but also includes the information gathered during the interviews with management and representatives of the research unit(s). The interviews took place on 19-21 April 2017 (see the schedule in Appendix 3) in Bilthoven.

Preceding the interviews, the committee was briefed by QANU about research reviews according to SEP. Also, the committee discussed the preliminary assessments and decided upon a number of comments and questions. The committee also agreed upon procedural matters and aspects of the review. After the interviews the committee discussed its findings and comments in order to allow the chair to present the preliminary findings and to provide the secretary with argumentation to draft a first version of the review report.

The draft report by committee and secretary was presented to the research unit concerned for factual corrections and comments. In close consultation with chair and other committee members, the comments were reviewed to draft the final report. The final report was presented to the Board of the university and to the management of the research unit.

The committee used the criteria and categories of the Standard Evaluation Protocol 2015-2021 (SEP). For more information see Appendix 1.

### **3. RESEARCH REVIEW MATHEMATICAL HEALTH MODELLING**

#### **3.1. MATHEMATICAL HEALTH MODELLING (VIRTUAL UNIT)**

##### **Introduction**

The research unit in Mathematical Health Modelling (MHM) at RIVM as reviewed by the committee is a virtual unit. The research in MHM is scattered in smaller and larger groups throughout six of twelve RIVM centres. The committee has decided to review the virtual unit with respect to its general findings regarding MHM at RIVM. In addition, all four research themes that are identified with respect to this review are assessed in a qualitative way, since these research themes are the actual groups within the RIVM centres that work on similar topics in MHM. The report is set up in a similar way; first a review of the virtual unit (findings, conclusions) and subsequently a review of each of the four research themes. A final chapter is dedicated to the formulation of recommendations by the committee. The committee would like to emphasize that all recommendations are directed to further improvement of the current situation, but without explicitly telling RIVM what it should do.

##### **The strategy and targets of mathematical health modelling**

The organisational structure at RIVM was reorganised in 2013 into three domains and twelve centres. As mentioned previously the activities in MHM at RIVM are presently conducted in six of twelve centres, and the total is in fact a virtual modelling unit.

There are four modelling research themes, all cherishing their independency and position within their own centre. There is little collaboration, hardly any coherence on mathematical health modelling and limited exchange of information and knowledge. This was most strongly evidenced in the interview with junior staff, who mentioned not knowing that other research themes in modelling existed at RIVM, or what they were working on. As mathematical models become increasingly sophisticated it will be necessary to become more systematic in the approach to model development, testing, and maintenance. This requires the sharing of good practice across the research themes in modelling at RIVM, and a systematic planning to increase inter-operability of models and algorithms where this is beneficial.

The committee recognises that modelling is an activity that requires not only the ability to write software code but also an in-depth knowledge of the diseases being modelled and this takes years to acquire – which means that modellers cannot be moved around from one area of activity to another on timescales of months. In this regard, modelling is very different from the more traditional statistics, in which it is possible for individuals to move rapidly amongst disparate disease areas. It is desirable for modellers to have close working relationships with other scientists working on the particular disease that they are modelling, and therefore it is desirable that modelling groups are embedded within RIVM, as at present, rather than being merged into centralised modelling unit. However, it is also desirable that modellers are able to work together and share expertise in areas of common technical interest, such as use of particular software platforms, use of fitting or optimisation techniques, individual-based modelling, etc. Different modellers will have different interests and needs, depending upon the particular requirements of their projects, and upon their previous experience and expertise.

Although the committee considers that more coherence and collaboration between the different centres and groups on MHM is necessary, the solution does not lie in setting up one centre on mathematical health modelling. This is not desired by any of the modellers, nor by the committee members since it will not benefit the quality of the research. Setting up a RIVM wide modelling

community requires an incentive for the modellers as well as a strategy and leadership. The diffuseness of activities does not allow increase of coherence to happen overnight and cannot be forced top-down, but should be facilitated by the central level. In its recommendations, the committee provides a number of suggestions to develop a modelling community.

In addition to the three domains and twelve centres, there is a team of six Chief Science Officers (CSO) who work across all centres and whose task it is to give strategic advice in their research fields and to connect research in different centres and fields. One of the CSOs covers the field of MHM and was appointed to strengthen the modelling aspects of research at RIVM. The positions of CSO create a matrix in which the CSOs run through the domains with their topic, but are not responsible for products or staff. The CSO supervises, stimulates and coordinates research ideas and plans. The CSOs have an overall budget which can be spent on innovative research proposals without strict rules. During the site visit the committee has extensively discussed the role and position of the CSO. According to the committee the role of the CSO in coordinating and helping modelling activities is a prudent advisory one, and not well defined. Whether this is the case only for the CSO in modelling, or also for the other CSOs is unclear to the committee.

As a result of the clearly fragmented modelling work at RIVM and considerable difference in size of the modelling groups, some research themes seem to be lacking critical mass. While the infectious disease modelling theme has critical mass, the smaller research themes do not, specifically the size of the PH research theme is below critical mass. The small sizes of the research themes make them vulnerable and – as will be described in more detail in the qualitative review of the research themes – there is the risk that the research output therefore has less impact than it could have.

### **Coding and version control**

Common coding often is not a usual practice between modelling research groups in the same institute, this also applies to MHM at RIVM. Nevertheless, exploration of the use of common coding standards where appropriate could be useful. In the short term, writing code with the intention that it should be generally applicable rather than specific to the immediate need, requires additional effort and it may not always be possible if time is limited. However, in the medium and long term it will increase efficiency and increase quality since having code that is used by multiple individuals leads to increased testing. The committee recognises that different models can require different approaches, and often legacy code has to be used and rewriting it may not be worth the effort. Therefore, it might be better to adopt an approach of applying a set of general principles rather than a set of rigid rules. Furthermore, the committee recognized limited use of version control. Good version control systems such as Git are available and would be of surplus value.

### **Research quality**

The quality of the research of MHM across the four research themes is of high international standards, and sometimes even world leading. This high quality is reflected in the scientific output and impact analysis of the output with the exception of the PH research theme. A number of reasons could be the cause this, this will be more extensively discussed in the qualitative review of the PH research theme.

Academic peers collaborating with MHM have also indicated to value the scientific quality as very high. Other stakeholders might not have clear understanding of the scientific quality of the modelling work, but overall stated to have trust in the models.

A major positive of modelling at RIVM is the fact that the modellers in the research themes are excellently close to data, data generation and experts for model building and validation.

Throughout the interviews it became clear that the modellers at RIVM are aware of the increasing importance of bioinformatics, or 'big data' for informing modelling. At present in RIVM the bioinformatics function is distributed amongst the laboratories and there is no centralised function, which limits the capacity for methodological development. According to the committee, it is outside the competence of MHM, let alone at the level of the research themes, to build all expertise required for dealing with big data. More worrying seems the fact that the ICT infrastructure at RIVM does not seem to perform at the level that is required to support high quality modelling. In several interviews the ICT infrastructure was reported to be inadequate. Specifically the fact that the latest versions of software required for modelling are typically not available. The ICT function is not sufficiently responsive in performing installations when required. Staff reported having to resort to running analyses on personal laptops, on which they were able to install the software that they require.

### **Relevance to society**

In addition to an informative stakeholder analysis that was provided to the committee prior to the site visit, the committee had conference calls with two stakeholders of MHM. Despite the fact that minor points of critique were given both in the analysis and in the conference calls, the committee concluded that stakeholders are overall pleased with the quality of the MHM work at RIVM and in general considered communication between RIVM and stakeholders to be good.

An area of potential improvement that is relevant to all MHM activity, brought up by the modellers themselves, concerns the development of scenarios to inform planning by policy-makers. This includes behavioural science work to understand public responses to interventions (e.g. uptake of vaccination or screening), applying methods of elicitation of expert opinion on future scenarios for the foresight group (e.g. societal change, technological development affecting screening, diagnosis, treatment), and public involvement in science and policy-making.

A topic of discussion between committee and the stakeholders was the desire to improve modellers' understanding of the roles and needs of policy-makers and improving policy-makers' understanding of modelling. As an example of this need, the chronic disease model (CDM) is currently underused, which appears to be due to a lack of questions being asked by policy-makers which might be due to a lack of awareness of what questions the model can be used to answer. Considering the importance of chronic disease this represents a missed opportunity for beneficial societal impact.

### **Viability**

All research themes, except for Infectious disease, face budget challenges for the near future. The Public health and health care (PH) research theme is clearly underfunded, while there is barely sufficient funding for Infectious diseases, zoonotic transmission and Food safety, microbiological contaminants (IAFM) and Food safety, chemical contaminants (FC). Thus far MHM has not succeeded in a stable expansion of the budget by acquiring national and international research grants. Only FC has many international links for funding but IAFM has an established link with EFSA. For the successful continuation of the high quality research, more funding is crucial. The committee considers that required maintenance of the important and high quality models, which is time-consuming and expensive, should be part of the basic funding.

In addition to budget challenges most research themes face continuity problems with regard to personnel. Filling vacancies of new scientists is difficult, particular at senior level. This is particularly an issue for the smaller modelling groups, which do not have the high profile of the larger infectious disease modelling group. By joining forces in the MHM 'virtual unit' the respective themes could have a higher profile than any of the individual modelling groups and this could assist with recruitment. Specifically the smaller modelling groups are critically dependent on a single senior scientist for some or all of the activities, and some of these critical individuals' are

approaching the end of their careers. Scientific institutes often recruit from MSc and PhD students. There is a considerable number of them in the ID research theme, but not in the other themes. In addition to difficulties recruiting senior staff, the scarcity of students limits the recruitment options of the junior staff.

The Infectious diseases (ID) research theme is large and has a high profile, which means that it is able to more easily recruit students and staff more competitively. It has staff at various levels of seniority, which is an advantage for succession planning which is not apparent in the other themes. However, it was commented that staff are ambitious and there is not necessarily a career structure that enables them to progress as scientists rather than having to become managers. Retention of experienced staff through enabling career progression is a critical component of succession planning, enabling individuals to 'step up' when a senior modeller leaves.

The smaller modelling groups in particular find it difficult to balance meeting the requirements for answering questions in the short term with developing methodology to meet future needs. Greater collaboration between the modelling groups could ameliorate this issue to some extent because it is likely that at present there is some duplication of effort, with one group developing code to solve a problem that has already been solved by another group.

## 3.2. RESEARCH THEME POPULATION HEALTH AND HEALTH CARE

The review of this research theme was complicated by the fact that no distinct organisational unit exists within the area of population health and health care modelling, but exists rather as three organisational units that each employ mathematical modellers working on chronic disease modelling part-time. Furthermore, with a total of 2.8 research fte in 2017 and one PhD student, the research theme critical mass is very small.

### **Research quality**

The research theme Population Health and health care (PH) is involved in state of the art modelling activities, with consistent high methodological quality, recognized nationally and internationally. Examples of well-known models are the chronic disease model (CDM) and Dynamo HIA, with proven ability to answer a wide range of policy questions relevant to population health.

The staff members within this research theme are internationally recognized as leaders in modelling methodology, with active national and international collaborations and participation on advisory groups. There is evidence of strong work on aspects of modelling methodology that are increasingly attracting the attention of stakeholders and the academic community (e.g. model cross validation). Also the links to universities seem strong and the quality of the work is highly valued by peers.

The research theme kept its momentum in MHM methodological innovation by developing a comprehensive microsimulation model of chronic disease (CDM), building on their work on Dynamo HIA. This approach could ensure continued methodological innovation and will prove essential to engage on emerging policy debates around noncommunicable disease prevention, thus becoming an important strategic activity for the group.

From the CWTS analysis that was provided to the committee during the site visit, it became clear that the research theme has relative lower bibliometric performance compared to the field with an average productivity compared to the other modelling research themes at RIVM. The committee did not identify a clear academic publication strategy to be in place, which may be linked to a lack of available resources and the under-utilizing of PhD's. If scientific impact is considered to be important by RIVM, a publication strategy should be designed and implemented. This subsequently requires a change of culture within the research group and focus more on publications on diseases and policy issues rather than on models. From the interview during the site visit, the committee observed a sharp vision on the future of chronic disease modelling, but specific development plans to implement this vision are not evident.

Concluding, the scientific quality is high, but this is not reflected in academic publication metrics. The group has kept the ability to innovate and the research theme has considerable modelling expertise and an internationally high valued track record. However, there is a need to develop a plan in order to ensure the continuing development of a world class modelling resource. PH can aspire to be a global leader in chronic disease modelling.

### **Relevance to society**

The current Foresight activities in PH ensure a continued need for expertise in modelling chronic diseases at RIVM. The need for this activity is clear and recognized internally as well as externally, and is likely to continue.

The group has a substantial track record on transparency and documentation of their modelling activities, and expressed aspirations to maintain this distinctive approach to disseminate their modelling work. This is consistent with emerging trends in the field calling for increased openness, validity and transparency. It appears that the Dynamo HIA model is used more than the academic outputs record suggests. However, it is not clear to what extent this activity is managed and resourced by RIVM. Given the maturity and quality of Dynamo HIA, managing and resourcing this use might help in enhancing the global reach and funding stream of the research theme.

Recent developments of the main model, which has now been implemented as a microsimulation model, mean that it is capable of much more sophisticated analysis than was previously possible. Microsimulation allows consideration of individual-level variation, multiple interacting risk factors, and of the life-course history of individuals. Combining improved modelling methods with improved data means that modelling can be much more useful for informing policy-making than previously.

The level of academic, policy and public engagement is adequate, but could be improved. This said, it is clear that the group work is highly dependent on external actors to identify problems to tackle. The ongoing methodological developments could support a responsive and flexible approach to policy questions in the mid to short term, and enable the theme to originate policy analysis under their own initiative.

The research theme is providing relevant policy analyses using appropriate modelling methods. Also, PH is currently enhancing its ability to engage in emerging policy debates using innovative modelling approaches. However, a more direct and proactive engagement with internal and external stakeholders to develop a shared work plan can further enhance the quality and societal relevance of the modelling solutions that are provided.

### **Viability**

Compared to the other research themes in this review, the small size of the group as well as low direct and external funding seems to be a significant limiting factor to the performance. Whereas funding has increased, this was mainly related to contract research and from the RIVM strategic programme, while direct funding and research grants decreased. The absence of critical mass and low resource level, combined with leadership issues at various organisational levels over the past years, might compromise the ability of maximizing impact of academic and societal outputs and of increasing the acquisition of external funding. The underutilization of PhD students to run projects in order to enhance academic output (both in quality and quantity) adds to this.

The low level of basic funding creates potential issues on retention and recruiting of new staff to maintain skill sets, particularly since modellers and ICT staff are shared with other themes. The organizational embedding of the research theme has been challenging over the period of review. For example, it was decided that the Statistics, informatics and Modelling group (SIM) would be coordinating the research theme, but it is not coordinating the incoming work. Modellers are part of different RIVM centres under responsibility of different centre heads, which is likely a factor in reducing the group's ability to produce high impact research.

The committee identifies a number of barriers and enablers on expansion of the portfolio of activity. First is the relationship with the Ministry which currently limits the options for development, for example in developing revenue streams with industry or pharma. Whereas, the group is not entirely "academically independent" from the ministry, it certainly can influence the research and policy agenda from their valuable expertise and experience. A more proactive approach could thus be used to maintain and increase a stream of relevant and doable policy questions to answer. The fact that there are no restrictions in publication or academic products is a substantial advantage that can and should be further exploited. Second, to impact the ability

to proactively develop methodology and pursue strategic research questions, time should be provided to the research theme. It did not become clear to the committee how activities are currently being coordinated or managed. Furthermore, external collaboration is possible, but might require more resource investment in the increasingly competitive environment. Finally, there is potential to influence data collection and process through internal links at RIVM with data holders and producers.

In conclusion, the present funding level and lack of an explicit plan to implement the vision and strategically prioritize service and research tasks appears to be key limiting factors for the research themes performance.

### 3.3. RESEARCH THEME INFECTIOUS DISEASES

The committee encountered a very strong research theme in infectious disease (ID) modelling at RIVM. ID is a solid and substantive group, with its own gravity and vibrancy, working with good processes and team management and a clear scientific vision for the future. The committee observed some good practices in this group that could be of use to the smaller modelling research themes at RIVM.

#### **Research quality**

The research theme ID is conducting research at a very high level with a clear international scientific impact. The modelling activities cover a large breath of topics and approaches with methodology of high quality. Examples of recent activities include the Burden of disease model allowing for consistent comparison of the population-level impact of infections, the Phylbreak model implementing sequence data for source attribution in outbreaks and the HPV model used to inform policy-makers on recommendations of vaccination.

The publication output from the group is significant in size and volume and the research is often published in high impact journals; many of the papers are highly cited including seminal papers on age-specific social mixing as drivers of transmission. At national as well as international level, the research theme ID has strong links with universities through collaborations and visiting professors, documenting the international recognition and leading position of the group.

With 19 staff members and 6 PhD students the size of the ID research theme is large compared to the other research themes in mathematical health modelling at RIVM. The staff group consists of several senior researchers with individual and complementary competences that allows for collaboration internally and strengthen the group. Some senior staff members are affiliated to universities and maintain links with teaching at the graduate level, which according to the director, is important for recruitment of PhD students and post-doctoral staff.

Most of the models in the ID research theme are tailor-made for a single purpose, while some are made for the long-run work, e.g. the burden of disease model. During the site visit the head of the department - in which the majority of the research theme is embedded - expressed that the embedding of the modelling group is crucial because it facilitates direct contact between the modellers and the epidemiologists/surveillance and outbreak specialists. This interaction stimulates the quality of the research and exchange of ideas. The access to large amounts of in-house data is clearly important for the success of the research theme, clearly arguing in favour of embedding the modelling research themes within different centres.

The management of the research theme shows signs of good leadership, and was rated excellent by the head of the centre in the self-evaluation report. The research theme develops 5-yearly research strategies to prioritize on areas for research that ensures a continuous evolution of the research while building on the strength and competences within the group. The group is well balanced in terms of mixing junior and senior staff and this is part of a deliberate strategy to ensure the continued development of the group. The research theme is proactive and innovative in identifying new areas for research, e.g. by the study of individual incentives for vaccination and use of novel data types.

Concluding, the committee has met an internationally leading modelling group that is clearly capable of producing innovative methodological research of high quality, with good leadership and ambitious plans for the future.

## **Relevance to society**

From the documentation and the interviews during the site visit it became clear that the modelling work in the research theme ID is critically important for advising policy makers on infectious control measures. The modelling work in the department is used extensively to support and inform policy decision-making. For example, in contributing knowledge base for the introduction of the HPV vaccination.

The advice towards the ministry is often communicated in reports to the Ministry of Health, Welfare and Sport. This interaction is rather indirect, while direct and frequent contact with people from the ministry is scarcer. According to one stakeholder from the Ministry of Health, Welfare and Sport, the overall cooperation with RIVM is good. Minor concerns regarding communication are mainly directed at the balance in communication of the complete and scientific results on the one hand and the information provided in a press release on the other hand. Although this is an issue that should be dealt with, this should be done by the RIVM since the issue is not exclusively related to the research theme ID.

During the interview with the research theme staff, the wish to improve the scenario-based approach to modelling was clearly expressed as well as the wish to make use of behavioural data in models. Also, the intensification of stakeholder engagement in the modelling process was discussed with the staff to ensure the relevance and use of the models. The committee concurs that building better alternative scenario's for policy advice is an ambition to pursue. By introducing more behavioural sciences into the modelling work and scenario-based forecasting, expert opinions can inform modelling scenarios. Involvement of stakeholders in the early stages of modelling projects will allow

Overall, the modelling work of this research theme has strong societal impact and is critical to informing policy makers on infection control measures.

## **Viability**

Overall, the research theme seems well equipped to maintain and develop the strong research profile in the years to come. In particular, the group has critical mass and a good mixture of senior and junior staff. The budget and funding prospects are good and the size of the group allows for flexibility in terms of innovation and maintenance of models.

Entering the world of big data, successful continuation of this research theme is dependent on the availability of new and high-quality data. This applies in particular to genetic data, and the strengthening and build-up of competence in bio-informatics is critical, but also to other types of big data derived from social media etc. From the interviews it became apparent that although data accessibility in general is easy, there may be considerable delay in the time before modellers get access to data due to protective behaviour among the researcher who collect data. A potential threat to a good viability is the IT-infrastructure that is currently lacking. It is important, not only for this research theme, to provide better access to software and programming facilities.

There are clear opportunities for greater international policy impact for the research theme, a strategy in this area should be developed. One suggestion by the committee is to make better use of developed models, e.g. by doing work for foreign governments connected to advising on vaccines. There is a strategy and operational plan for the content direction of the research theme, but not yet a clear strategy on how to accomplish a number of ambitions.

In conclusion, the group in this research theme seems well equipped to maintain and develop the strong research profile in the years to come due to a successful recruitment policy and well balanced mixture of senior and junior researchers, the large size of the group and the overall positive financial situation.

### 3.4. RESEARCH THEME INFECTIOUS DISEASES, ZONOTIC TRANSMISSION AND FOOD SAFETY, MICROBIOLOGICAL CONTAMINANTS (IAFM)

The research theme Mathematical modelling in relation to zoonotic disease and microbial food safety (IAFM) has a complex organizational structure. In fact, there seem to be two research themes, reflected by two separate SWOT analyses and by two separate quantitative self-assessments. Modelling in relation to zoonotic diseases and microbial food safety is distributed across three research departments (Non alimentary, Food, Environment) within the centre of Zoonosis and Environmental Microbiology. Currently there are approximately 10 staff members identified with mathematical modelling in relation to zoonotic disease and microbial food safety

#### **Research quality**

With respect to mathematical modelling of IAFM, RIVM has a strong reputation for high quality research and several current and past staff members are identified as international experts. The research theme has contributed to several internationally recognised efforts (e.g. a European effort to model Salmonella in Pigs) and to significant national programmes (e.g. estimating the burden of disease in the Netherlands). The CWTS analysis that was provided to the committee during the site visit indicates a performance that is consistent or superior to other modelling efforts at RIVM and which is internationally competitive.

The scores by heads of centres in the self-evaluation report on the modelling of the research theme indicate good or very good performance, but also indicate some concern regarding the functioning of the work programme and about accuracy of outcomes and calculations.

Although the research theme includes a very large number of related subject areas, it is not clear how modelling effort is coordinated within the centre and integrated across research topics. Elements of mathematical modelling in the research theme, e.g. burden of disease, are primed for collaboration across RIVM health modelling activities, but mechanisms for integration are unclear.

The research theme provides a good environment for PhD student training, but the throughput is relatively small compared to some other groups.

The committee concludes that the research theme is an essential component of Health Modelling at RIVM and fits clearly within the core activity of the organization. It has established an international reputation for high quality science and has embraced the emergence of challenging new information sources and technologies and it will be essential to develop strong commonalities with other RIVM health modelling groups particularly in relation to shared resources (e.g. data management and bioinformatics). Finally, there are some opportunities to initiate a much stronger integration of modelling within this research theme with health modelling in other themes at RIVM

#### **Societal impact**

Reported outputs from this research theme IAFM are dominantly single domain (and often single user) and so it is difficult for the committee to assess their impact. Attempts to communicate complex microbiological risk modelling information to non-expert stakeholder groups (e.g. a rapid risk assessment tool) have not always been successful.

In the self-evaluation report the centre heads generally indicated a good performance, but identify communication as a particular weakness. From the stakeholder assessment similar concerns were expressed.

The mathematical modelling of zoonotic disease and microbial food safety at RIVM do not deliver direct products for, or indicate recognition by, societal groups even though it is a clear food safety modelling covers several prominent societal issues.

In conclusion, modelling within the research theme IAFM currently seems to underachieve with respect to its societal impact and, currently, stakeholder involvement does not seem to be a major priority.

### **Viability**

The senior scientists within the research theme have identified important developments, and significant emerging methodological issues, within their areas and this provides a clear reasoning for the maintenance and strengthening of their efforts. The integration of mathematical modelling within other science is a particular strength of the centre for Zoonosis and Environmental Microbiology.

There is a significant mismatch between the number of active modellers in the research theme and the range and depth of topics that are being considered so that capacity issues are a constant challenge.

Modelling activity, and particularly leadership, in the research theme has been strongly affected by the loss of some significant senior researchers and the identification and recruitment of suitable replacements has been problematic.

Leadership and planning activities that can support progression of the research theme are unclear and possibly not fully defined (the centre head, chief scientific officer, senior science advisor and the department heads are all potentially involved in leadership).

The committee concludes that recent changes, including the loss of important senior members of staff and the rapid emergence of several technological issues such as the impact of WGS, have made the organization and development of a viable modelling activity in food safety risk assessment very challenging. There is some uncertainty concerning the organization and leadership of health modelling in the research theme that is detrimental to overall performance and sustainability.

### 3.5. RESEARCH THEME FOOD SAFETY, CHEMICAL CONTAMINANTS (FC)

#### **Research quality**

The total number of publications is rather small, which is obvious when considering the size of the research theme. The results of the citation scoring of the published papers, however, show that the scientific quality is widely recognized at an international level. This recognition is also demonstrated through the involvement in various externally-funded international research projects.

A key strength of the approach taken by this research theme, lies in the fact that the group has developed a complementary set of modelling tools that covers the full cascade of chemical risk assessment. This has put the RIVM in a rather unique position of strength in this area.

The committee concludes that the activity in this research theme has clearly gained an international reputation among peers and stakeholders. All in all, the research theme is very productive with the limited resources available. It serves as a model of what a 21st century EU Reference Lab for software models would look like. However, the maintenance of this international leadership is currently uncertain. This is because of a workload that may grow both for maintenance and keeping up with evolving needs. In addition, the transfer of knowledge to a new generation of scientists seems to be lacking at the moment.

#### **Relevance to society**

Through the models that have been developed the group is strategically very well positioned in its area of expertise. By constantly reaching out to potential users the group has made sure its work is highly relevant, i.e. the models are used both at national, European and international level. In this the research theme has set a very good example for others to potentially consider.

One consideration that is and will remain important for public bodies is the transparency of the models including how the underlying calculations are carried out. This illustrates the need for transparency in coding through adherence to accepted coding standards. A strength of RIVM is its independent position and ability to be transparent, this should be cherished.

#### **Viability**

By growing its leadership in particular models and by seeking national and international collaborations, the research theme is currently very well positioned at an international level.

The challenge is now how to maintain this wide suite of packages such that it remains relevant in the future, considering the available resources. This also raises the question as to whether all available packages are equally strategically important. Importance will - in part - be determined by the uniqueness of each of the models. For example does the PBPK modelling represent a core strength or are there other non-RIVM packages available that could be integrated?

To remain relevant the models will need to undergo new developments to maintain and improve. In particular at least one of the tools will be affected by the clear and continued move to non-animal based testing in toxicology. The research theme seems to be well aware of this. Much of the research this model is involved in, is conducted outside the RIVM. Therefore, collaboration with Centres deeply involved in the development and validation of these models is needed. This has been recognized and is in fact already beginning to be implemented through EU 2020 projects.

The group is not particularly well resourced and there are quite a few Single Point of Knowledge cases. Furthermore, it is mainly composed of very experienced staff which may leave in short time span and in a not too distant future. Thus, the research theme faces the need to transfer knowledge to a new generation of modellers as retirements are likely to take place in the upcoming period.

The research theme does already reach out to other research themes in RIVM for support in new areas e.g. web-based applications. This does not, however, address the need for succession planning of core competencies. While successful in attracting research grants the group appears to experience difficulties in attracting PhD students. To ensure continuity it may be necessary for the RIVM in general, and for this research theme in particular, to be (even) more pro-active to attract potential new staff by offering e.g. training opportunities to Master level students.

The hiring practices of modellers seem to be carried out by each Centre and research theme separately rather than be shared. This further handicaps a small group such as the research theme FC. Also, induction training of staff seems to be variable between research themes or non-existent. The setting-up and the costs of induction training of new staff could be shared among the different modelling research themes as a smaller unit - such as this one - can hardly afford to set up such an activity on its own.

There probably is also efficiency to be gained from systematically logging and providing access to models across modelling units. This seems to be done on *ad hoc* basis at the moment rather than being part of a structured and coordinated approach. In addition the group is fairly dependent on grants. Funding for model maintenance may be very difficult to obtain via this route. Hence baseline funding through national and/or European customers is essential.

### 3.6. PHD PROGRAMME

Although all research themes host a number of PhD students, the RIVM is not officially employing all of these PhD students. Each PhD student is also connected to a Dutch university and part of a graduate school at that university. In practice, however, many PhD students consider the RIVM as their working place and have very little contact with the university. Therefore the committee has discussed a number of topics with PhD students regarding their supervision, training and progress.

As is also mentioned in the review of the research themes, the number of PhD students strongly differs between the four research themes. This difference was also reflected in the selection of PhD students the committee talked to, with a majority of PhD students from the research theme ID. This might have had an effect on the topics discussed and the feedback provided by the PhD students.

Overall the PhD students are very satisfied by the supervision they receive by daily supervisors and promotors. Being part of a graduate school at different universities result in different possibilities and funding for courses as well as attending seminars and (inter)national conferences. All PhD students the committee talked to were happy with the possibilities. There were three topics that were more extensively discussed.

One point of discussion is the connection between PhD students from different research themes as well as between PhD students and staff from other research themes. As mentioned earlier in the report, this issue is not limited to PhD students. Although there is a RIVM wide PhD network, this has a low visibility and is not focussed on modelling. The committee considers that, in line with creating a modelling community at the RIVM, consideration should be given to creating a modelling PhD community. This will help PhD students find peers who work in different research themes, but on similar topics and can stimulate training for modellers. Suggestions by the PhD students were creating a website, buddy system and create cohorts with other PhD students who started at the RIVM around the same time and giving them a joint introduction.

The second topic was raised by some PhD student, but was not a shared experience by all. It relates to the checking of code/syntax by supervisors or other experienced researchers. PhD students are trained in coding techniques, but many do not have a background in computer science and have not been taught how to structure their code to maximise reliability. When the modelling becomes more complex, a small coding error that is not detected early in the process, might lead to loss of work. PhD students understand that checking all code is not realistic considering resources. For more information, also see chapter 3.7. Research integrity policy.

Finally, there were complaints regarding the ICT services at the RIVM. This is also not restricted to an issue at PhD student level and should be dealt with. For more information, see page 9.

### 3.7. RESEARCH INTEGRITY POLICY

In the teleconference with stakeholders it became clear that they are overall pleased with the integrity of RIVM work and according to the committee there are no problems that should be highlighted. However, as models become more sophisticated, there is simultaneously an increased risk of errors occurring and an increased difficulty in identifying errors. A systematic approach to software coding and testing is part of the solution. Regarding this, the quality assurance processes could be strengthened, taking into consideration that this needs to cover not only the software code but also the interpretation of data, representation of natural history, etc.

## OVERVIEW OF QUANTITATIVE ASSESSMENT

Research quality: 1-2 (very good to excellent)

Relevance to society: 2 (very good)

Viability: 3 (good)

## 4. RECOMMENDATIONS

### THE MATHEMATICAL HEALTH MODELLING “VIRTUAL UNIT”

1. In view of the increasing strategic importance of the mathematical health unit (MHM) for RIVM, and the high quality of modelling research, the future of MHM should be actively safeguarded at RIVM level as well as at the level of the centres.

#### Organisation and operation of the virtual including its working methods

2. The exchange of information and collaboration between modellers and themes should be strengthened while keeping the independent position of research themes in the centres intact.
3. The committee suggests taking a “bottom-up” approach, in which individuals self-organise according to their needs, rather than a “top-down” approach. The committee suggests the following initiatives to foster a common MHM corporate culture:
  - Induction process; an introduction for new modellers at MHM should be developed (see also below). This should include meeting modellers from other themes face-to-face, being provided with an overview of MHM activities, and reviewing general modelling concepts and terminology.
  - Use of common software platforms where appropriate. Collaboration should be encouraged, both for modellers facing the same ad-hoc problems, and for modelling groups addressing similar methodological problems, like the burden of disease estimation.
  - Use of common coding standards where appropriate. It is recommended to adopt an approach of applying a set of general principles for coding rather than a set of rigid rules.
  - Development and implementation of an appropriate quality assurance process, including guidelines for model development and testing, and version control.
  -

#### Staffing

4. To secure appropriate staffing, long-term strategic thinking by the centre heads and senior modellers should be encouraged.
5. To retain experienced modellers, with their rare combination of breadth and depth of knowledge and skills, career progression paths should be introduced to create a long term perspective on their position and possibilities at RIVM.
6. The four research themes should develop a plan for attracting more MSc and PhD students, as a means for recruiting future staff members. It appears valuable to maintain links with teaching at the graduate level to attract PhD students and post-doctoral staff.

#### Internal support

7. The ICT services of a central bioinformatics unit should be strengthened. The MHM staff should conduct an analysis of the issues with respect to data handling capacity and other requirements that need to be addressed and collaborate with ICT staff to find solutions.

8. The rationale, role, responsibilities and embedding in the RIVM research organization of the chief science officer (CSO) should be evaluated.

### **Interaction with stakeholders**

9. The MHM as a virtual unit should examine ways to pursue opportunities for improvement in the areas with respect to relevance to society. With regard to public involvement, a lot of work has been done in the UK, particularly by the National Institute for Health Research (NIHR), which RIVM may wish to examine.
10. Specifically raising awareness among relevant stakeholders of the utility of modelling should be a priority. The MHM could consider involvement of stakeholders in user forum in larger modelling projects, running training workshops and sharing experience of senior modellers who have engaged with policy-makers.
11. MHM should more actively explore the use of their models for more policy issues than they are currently used for, especially in international collaborations. In this way MHM should try to acquire more national and international research grants.

## **POPULATION HEALTH AND HEALTH CARE RESEARCH**

A "Roadmap for chronic disease model development" should be developed, including the identification of possible modelling problems and a model innovation development plan, including stakeholder involvement in model development, scenario design and interpretation, to enhance societal impact.

The group should develop a strategy to enhance quantity and impact of publications, including more emphasis on applied policy analysis alongside methodological papers, and awareness of the trend in the field toward open data, open access and open source.

The group should consider developing plans to proactively implement existing models to other populations, through external funding internationally, particularly in Europe. In order to be able to recruit sufficient and well trained (junior) staff, the number of PhD and MSc students should increase, adopting best practices used elsewhere in RIVM.

## **INFECTIOUS DISEASES**

In agreement with observations by the group in this research theme, it should be explored how behavioural sciences can contribute in developing relevant scenarios will help stakeholders make policy decisions.

There are clear opportunities for greater international outreach and policy impact for the research theme. The group should develop a strategy in this area, for example to make better use of developed models at an international level.

Being the largest research theme in MHM at RIVM and being well organised, the infectious disease theme should take its responsibility and initiate and support activities that are suggested in the first recommendation of the virtual unit.

## INFECTIOUS DISEASE WITH ZOOONOTIC TRANSMISSION AND MICROBIAL FOOD SAFETY

The appointment and strong support for an appropriate leader of modelling within the research theme should be a priority.

Increased collaboration between the modelling with the research theme and with other RIVM health modelling themes is recommended.

An increased throughput for PhD students within the research theme is recommended

The development of interactions between the research theme and stakeholders, particularly societal groups, is considered to be important.

## FOOD SAFETY, CHEMICAL CONTAMINANTS

A strategic review is required as to which of the models are key to be both maintained, properly funded and further developed; thereby making them less dependent on *ad hoc* funding.

For these key models, consideration may be given to their potential uses of them in other areas. In particular the use of the MCRA may be much wider than the current focus on chemical residues in food. For example in the areas of nutrition and medicines.

There is a need to ensure that key modelling competences are transferred to a new generation of staff and this in a not too distant future.

## APPENDICES



## APPENDIX 1: EXPLANATION OF THE SEP CRITERIA AND CATEGORIES

There are three criteria that have to be assessed.

### A. Research quality:

- Level of excellence in the international field;
- Quality and Scientific relevance of research;
- Contribution to body of scientific knowledge;
- Academic reputation;
- Scale of the unit's research results (scientific publications, instruments and infrastructure developed and other contributions).

### B. Relevance to society:

- quality, scale and relevance of contributions targeting specific economic, social or cultural target groups;
- advisory reports for policy;
- contributions to public debates.

### C. Viability:

- the strategy that the research unit intends to pursue in the years ahead and the extent to which it is capable of meeting its targets in research and society during this period;
- the governance and leadership skills of the research unit's management.

Category	Meaning	Research quality	Relevance to society	Viability
1	World leading/excellent	The unit has been shown to be one of the most influential research groups in the world in its particular field.	The unit makes an outstanding contribution to society	The unit is excellently equipped for the future
2	Very good	The unit conducts very good, internationally recognised research	The unit makes a very good contribution to society	The unit is very well equipped for the future
3	Good	The unit conducts good research	The unit makes a good contribution to society	The unit makes responsible strategic decisions and is therefore well equipped for the future
4	Unsatisfactory	The unit does not achieve satisfactory results in its field	The unit does not make a satisfactory contribution to society	The unit is not adequately equipped for the future



## APPENDIX 2: CURRICULA VITAE OF THE COMMITTEE MEMBERS

**Dr. G. (Gary) Barker** was trained as a theoretical physicist and has worked at the Institute of Food Research / Quadram Institute since 1984. His research has centred on the application of theoretical and computational techniques in Food Materials science and Food Safety science. Current research interests include the integration of molecular data and systems biology models into risk assessments, integration of user centric information sources into risk communications and a stronger appreciation of global food chains with respect to food safety and food security. Barker is a STEM ambassador and has been member of the UK Advisory Committee on Microbiological Safety of Foods since 2012.

**Professor B. (Birgitte) Freiesleben de Blasio** is Head of the Department of Infectious Disease Epidemiology and Modelling at the Norwegian Institute of Public Health and has a position as Professor II at the Department of Biostatistics, University of Oslo. She holds a PhD degree in theoretical physics from the Niels Bohr Institute at Copenhagen University. Her main research interests include mathematical models that predict the effectiveness of interventions against transmissible diseases to assist policy decision-making, models for disease burden estimation and forecasting, and network methodology for improved understanding of the spread of infections in populations. She is board member of the research-based innovation centre BIG-INSIGHT in Oslo, dedicated to the development of statistical methodology for personalized health using big data

**Professor em. JDF (Dik) Habbema (chair)** studied mathematics at Eindhoven University of Technology and received his PhD at Leiden University. He was professor of medical decision sciences at the Department of Public Health of the Erasmus MC Rotterdam. He was coordinator of the decision sciences research programme, which has evaluation of early detection of disease, (tropical) infectious disease control, health impact of interventions, model building and validation, prediction and evaluation, optimizing the choice of interventions, and cost-effectiveness analysis as important activities. He has (co-) authored several hundreds of scientific publications in these fields. Habbema served on many advisory boards, among others for the Health Council of the Netherlands, the Netherlands Committee for Medical Research, and the World Health Organization.

**Dr. H. (Hubert) Deluyker** is EFSA's Scientific Adviser, providing the Executive Director with advice on issues related to EFSA's scientific activities and working in close cooperation with the Authority's scientific directors. He holds a PhD in Epidemiology. Before working for EFSA, Deluyker was a clinical research scientist in the field of animal health for Pfizer Belgium, where he led a range of multidisciplinary and multinational research and development projects. He was Associate Professor in Epidemiology between 1991 and 2000 at the School of Veterinary Medicine of the University of Ghent, Belgium and worked as District Veterinary Officer for the Belgian Ministry of Agriculture.

**Professor M. (Martin) O'Flaherty** is professor of Epidemiology at the Department of Public Health and Policy of the University of Liverpool. He was trained as a physician and developed an interest in Public Health and Epidemiology. His main research interests are in cardiovascular epidemiology and in using a modelling approach to inform the decision making process in healthcare. He is leading a number of projects on modelling Food policy and other preventative interventions to reduce the burden of non-communicable diseases, including cardiovascular disease, cancers and dementia.

**Dr. P. (Peter) White** is Head of the Modelling & Economics Unit in the Centre for Infectious Disease Surveillance & Control (CIDSC) at Public Health England and has a position in the MRC Centre for Outbreak Analysis & Modelling at Imperial College London. White is also Deputy Director of the new NIHR Health Protection Research Unit in Modelling Methodology at Imperial College London in partnership with Public Health England. White's research interests include health systems research, statistical analysis and mathematical modelling of the epidemiology of, and the effectiveness and cost-effectiveness of interventions against, sexually transmitted infections (including HIV), tuberculosis, and influenza. He is member of the steering group of the Infectious Disease Research Network, Fellow of the Winston Churchill Memorial Trust, and a NESTA Crucible awardee (2006). In addition to lecturing to under- and postgraduate students at Imperial, White gives MPhil lectures at Cambridge University.

## APPENDIX 3: PROGRAMME OF THE SITE VISIT

### Day 1: Wednesday 19 April 2017

Start	End	Activity
09.00	10.30	Deliberation on: <ul style="list-style-type: none"> <li>• Introduction</li> <li>• Assessment procedure</li> <li>• Terms of Reference / SEP</li> <li>• Writing of assessment report</li> </ul> Individual findings based on received documentation
10.30	11.00	<ul style="list-style-type: none"> <li>• Meeting with RIVM board (prof. Jaap van Dissel, Walter van Wijngaarden, Prof. Jantine Schuit)</li> </ul>
11.00	11.30	Walter van Wijngaarden, Jaap van Dissel, Els van Schie, Chief Scientific Officer Mirjam Krezschmar: Introduction CSO function at RIVM <ul style="list-style-type: none"> <li>• Introduction RIVM</li> <li>• Introduction task and responsibilities</li> <li>• Introduction liaison officers and their tasks in the audit</li> <li>• Introduction research unit and scope of the audit</li> </ul>
11.30	13.30	Interview of the committee with heads research unit, project leaders and CSO
13.30	15.00	Research theme 1: Public Health and Health Care Hendriek Boshuizen, Jantine Schuit, Jeljer Hoekstra, Astrid Kloosterman, Jaap van Delden, Henk Hilderink
15.00	15.15	Deliberation committee
15.15	16.45	Research theme 2: Infectious Diseases other than zoonotic transmission Jacco Wallinga Hans Bogaards, Marianne van der Sande, Don Klinkenberg, Scott McDonald
16.45	17.00	Deliberation committee
17.00	17.15	Teleconference stakeholder I (Ministry of Health, Welfare and Sport), policy advisor of the Department of Food, Health protection and Prevention
17.30	18.00	Deliberation committee

**Day 2: Thursday 20 April 2017**

Start	End	Activity
09.00	9.15	Teleconference stakeholder II (Health Council)
09.15	9.30	Teleconference LO's (J.P. Mackenbach) and Prof Van der Meer
09.30	10.00	Deliberation committee
10:00	11:30	Research theme 3: Food safety chemical contaminants Anton Rietveld, Jantine Schuit, Wout Slob, Jacob van Klaveren, Marco Zeilmaker
11:30	12:00	Deliberation committee
12.00	13.30	Interview and lunch with PhD-students Irene Man, Joram Hoogink, Loes Soetens, Maarten van Wijhe, Maarten Reitsema, Koen Fussenich
13:30	15:00	Research theme 4: Infectious diseases zoonotic transmission from animal population to a human population & Food safety microbiological contaminants Arno Swart, Arjen van de Giessen , Peter Teunis
15:00	15:30	Deliberation committee
15:30	16:30	Art walk around RIVM
16.30	17.00	Interview with heads of centres involved in the audit
17.00	18.00	Preparation final report by committee

**Day 3: Friday 21 April 2017**

Start	End	Activity
09.00	12.00	Deliberation committee
12.00	13.00	Lunch
13.00	14.00	Closing meeting (final conclusions and recommendations)
14.00	14.45	Final deliberation A committee – draft preliminary findings
14:45	15.15	<ul style="list-style-type: none"><li>• Presentation for employees and Liaison Officers</li><li>• Closing by chair</li></ul>