Health Council of the Netherlands

Guideline for the identification and protection of high-risk groups

Gezondheidsraad
Health Council of the Netherlands

To
the Minister of Health, Welfare and Sport
the State Secretary of Infrastructure and the Environment

Subject : presentation of advisory report *Guideline for the identification and protection of high-risk groups*
Your reference : VGP/P&L 2581995
Our reference : I-696-05/HvD/pm/790-C
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Dear Minister and State Secretary,

I hereby submit the advisory report entitled *Guideline for the identification and protection of high-risk groups*. It was drawn up by a specially appointed expert committee, in response to a request for advice from both of your predecessors. During the preparation of this advisory report, the Standing Committee on Health and Environment was consulted, as were individual members of all of the Council's other standing committees.

Typically, the Council issues advisory reports on very specific issues, such as whether or not a given vaccination should be incorporated into the National Immunisation Programme, what constitutes an adequate intake of vitamins and minerals, or the concentration of certain medical interventions in a limited number of treatment centres. This advisory report involves a higher level of abstraction. It is one of a series of advisory reports on ways of dealing with health risks that the Council launched at the end of the twentieth century: *Not all risks are equal* (1995/06), *Risk is more than just a number (*1996/03) and *Prudent precaution* (2008/18).

The identification of high-risk groups and decision-making about policy-based dealings with such groups encompass all public-health-related policy domains. In their request for advice, your predecessors noted that such matters are dealt with separately in each individual policy domain, and that their goal was a more consistent approach spanning different policy dossiers. I fully endorse the importance of this approach, to avert the risk of arbitrary decision-making. Moreover, policy inevitably results in choices being made regarding high-risk groups. While this may not be explicitly stated, it is certainly implicit.

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In the interests of democratic control, I feel that choices need to be more explicit. This Guideline for the identification and protection of high-risk groups delivers the tools needed for dealing with high-risk groups consistently, systematically, and transparently in all policy domains. This involves an assessment framework for the systematic identification of high-risk groups and a decision framework to identify the various considerations affecting decisions on policy-based dealings with these identified high-risk groups.

I feel that the guideline's importance is not restricted to the policymakers and politicians who have to decide how to deal with high-risk groups. It is equally important for the numerous bodies who employ risk analyses in the field of health, in support of well-informed decision-making.

I recommend that the frameworks presented here be used in the development of new prevention policy, and when reviewing existing policy.

Yours sincerely,

(signed)
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President

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No. 2011/39E, The Hague, December 14, 2011

The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is “to advise the government and Parliament on the current level of knowledge with respect to public health issues and health (services) research...” (Section 22, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport, Infrastructure & the Environment, Social Affairs & Employment, Economic Affairs, Agriculture & Innovation, and Education, Culture & Science. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

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INAHTA

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Executive summary

Human diversity as a challenge

It is the government's constitutional responsibility to protect and promote public health. Instead of relying on the capacity of curative care alone, it is also active in the area of prevention. The government does everything in its power to provide protection for everyone. A complicating factor here is that people differ considerably in terms of their risk of disease and health impairment. How is the government to deal consistently with such variations in the population, across a range of policy issues? That is the subject of this advisory report. In this document, a Health Council committee formulates an assessment framework for the identification of high-risk groups, together with a decision framework to facilitate systematic decision-making on how such groups are to be dealt with in the context of policy. In this way, the Committee aims to bridge the gap between the domains of health protection, disease prevention and health promotion, while facilitating the exchange of knowledge, experiences and methods between disciplines.

High-risk groups

The Committee uses the term "high-risk group" to designate those groups within the population who are at increased risk of health impairment. In general terms, there are two approaches to what constitutes high-risk groups: those involving an

agent with properties that are hazardous to health, or those associated with a disease or disorder. Accordingly, a high-risk group can consist of:

- individuals with a particular trait that can adversely affect exposure to the agent, sensitivity to it, or both
- individuals with a particular trait that increases their risk of acquiring the disease or disorder in question.

"High-risk group" is a relative term. It refers to a subpopulation that is at greater risk of exposure to a given agent, or that is more susceptible to a given disease, than the rest of the population. In absolute terms, however, the risk involved may be quite small.

Inherent to the concept of "health risk" is the idea that there is a risk of exposure to "something" (an agent) that has the potential to harm health. Many factors can influence the risk of disease and health impairment:

- personal traits, including gender, age, genetic characteristics, and health status (i.e. fitness, pre-existing disease)
- lifestyle-related traits such as dietary pattern, exercise, and smoking;
- aspects of the physical and social environment, including environmental quality in residential areas and in workplaces, as well as food safety.

Assessment framework for identifying high-risk groups

The essence of the assessment framework outlined by the Committee in this advisory report consists of a systematic analysis of the impact (actual or potential) of personal, lifestyle, and environmental traits on the risk of health impairment or disease (see Figure A). This analysis is based on all of the available knowledge about an agent or disease (or both), depending on the approach selected. In this way, groups can be identified within the population at-risk whose increased risk results from one or more traits that adversely affect exposure, sensitivity, or both at the same time. In addition, a given disease may exhibit clear links to one or more traits, while nothing may be known about the underlying reasons for this. While this association might be based on causality, this is not necessarily the case.

The outlined approach is, in fact, a description of the common denominator of existing procedures used in many fields to assess the risk of disease or health impairment. However, this often involves a large degree of uncertainty, especially with regard to potential high-risk groups. Accordingly, going through the schedule is an iterative, dynamic process. It needs to be repeated whenever new information becomes available that might shed a different light on potential

high-risk groups. This involves a degree of interaction, as a growing understanding of high-risk groups for certain diseases or disorders can help to identify causes (agents) and mechanisms of action. Conversely, an understanding of causes can shed light on new high-risk groups.

Assessment frameworks are tools primarily intended for use by experts, as the identification of high-risk groups does require a degree of expertise. While these individuals could be trained scientists, this role could also fall to those who are experts by virtue of experience. They work closely with policy makers and, possibly, also with stakeholders. After all, the identification of high-risk groups always involves normative choices. For instance, this concerns the extent to which a given group's risk has to be increased before they can be designated as a high-risk group, the energy invested in identifying specific groups, and the degree of refinement of the analysis involved. The better an analysis reflects the information needs of policy makers and stakeholders, the more points of reference for policy it will ultimately provide.

Decision framework for decision-making with regard to high-risk groups

The analysis of possible courses of action is a necessary pre-requisite to decision-making on health issues. Accordingly, this is of particular importance when dealing with identified high-risk groups. A decision framework (see Figure B) illustrates the options available to decision makers. The first option is to deliberately make allowance for some or all identified high-risk groups through the implementation of generic measures that are geared to such groups, or to opt for individual, high-risk-group-specific policy interventions. Another option is to consciously take no account of some or all high-risk groups.

Before a choice can be made, the anticipated impacts of various courses of action on high-risk groups in particular, and on society as a whole, must be identified. This requires a range of analyses, in the areas of health, finance, economics, law, and ethics. The results of these analyses will involve a degree of uncertainty. Decision-making is not just about balancing costs and benefits. It also involves the allocation of responsibilities between government bodies, business and individuals, as well as an equitable distribution of advantages and drawbacks across population subgroups.

The Committee sees two general arguments for the protection of high-risk groups: 1. The protection of high-risk groups is sometimes the most efficient way of improving public health, 2. On occasion, justice dictates that special consider-

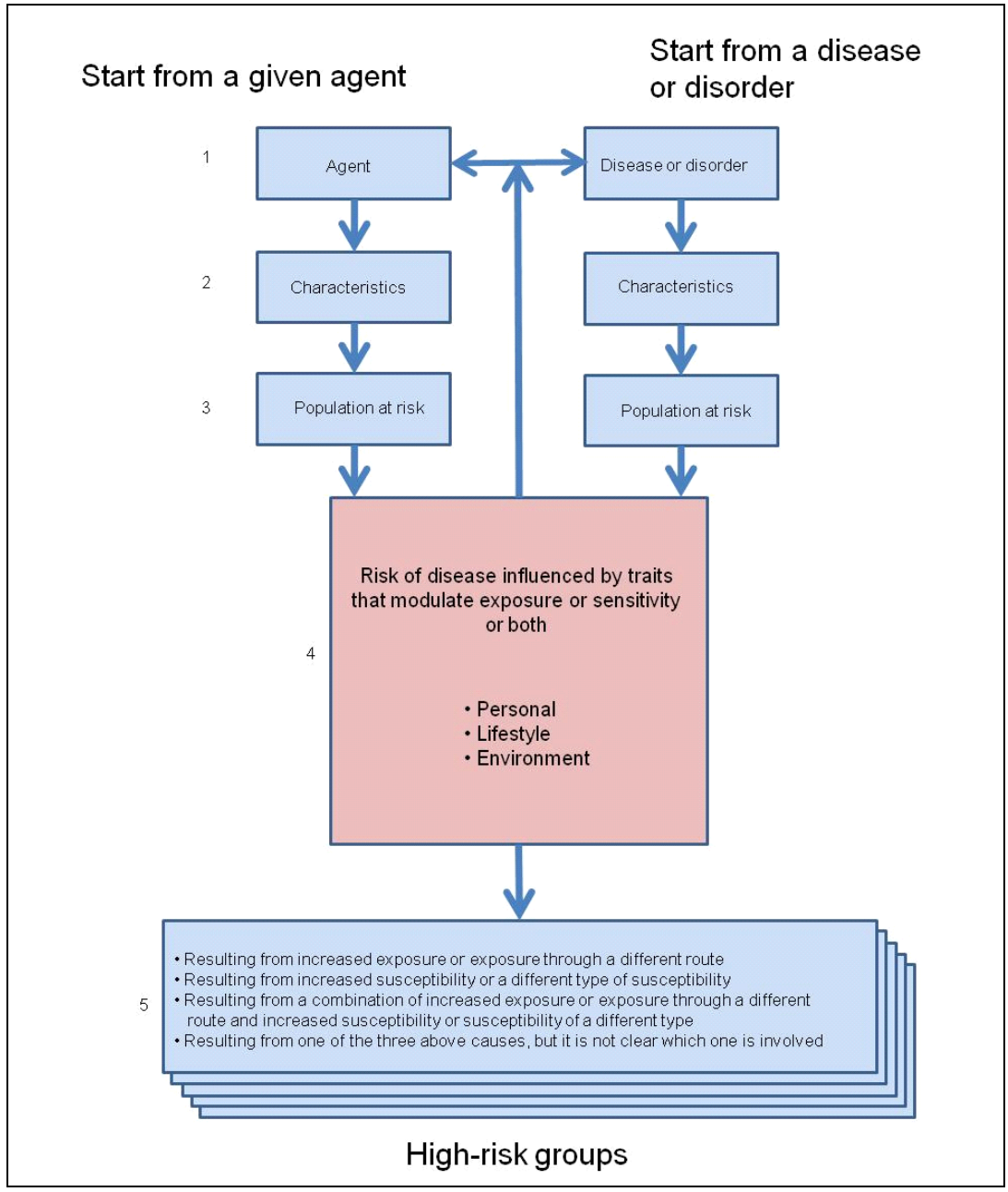

Figure A Assessment framework for identifying high-risk groups.

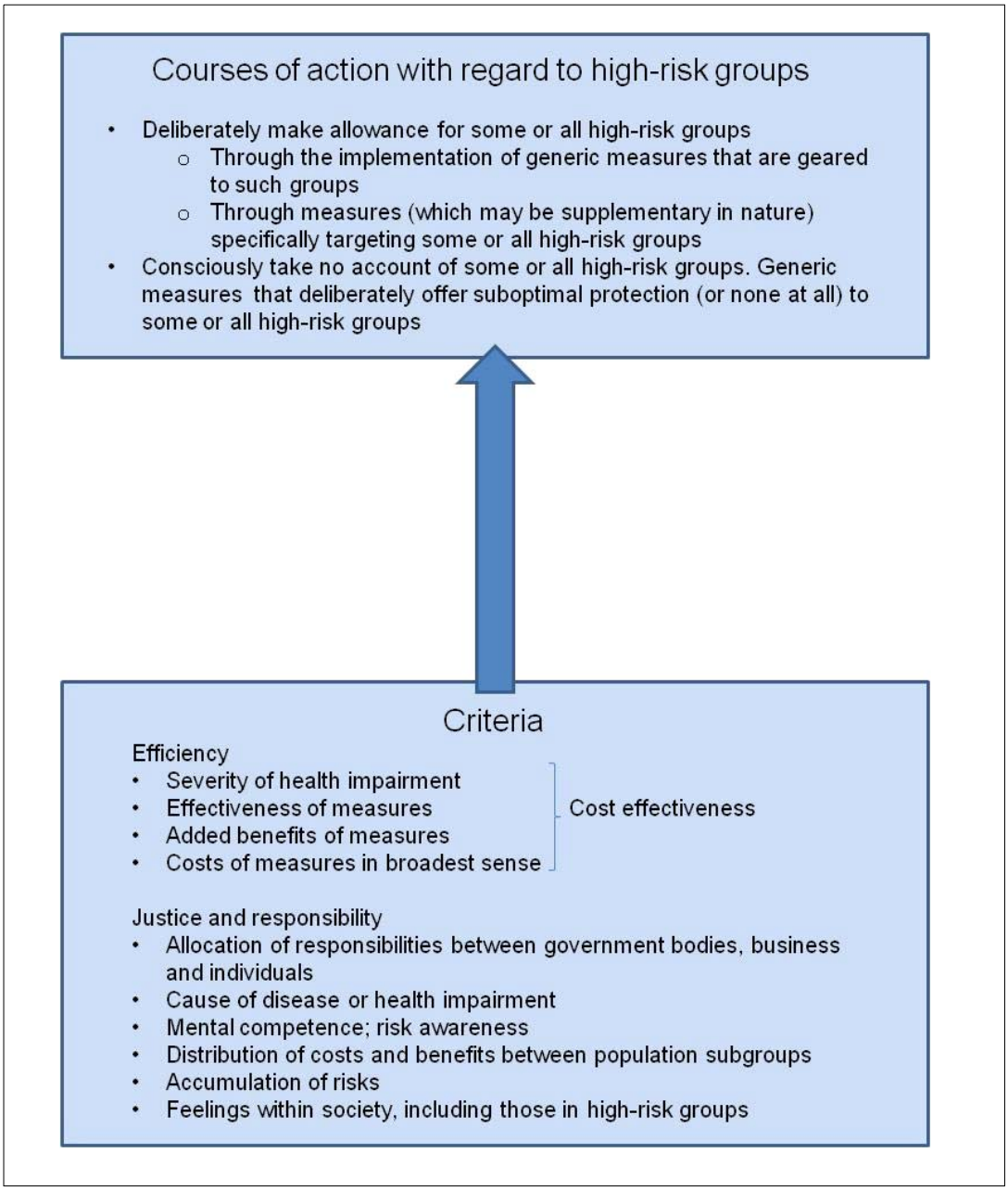

Figure B Decision framework for decision-making with regard to high-risk groups.

ation be given to reducing (unfair) socioeconomic health differences, for example, or to protecting people from risks caused by others. Assigning weighting factors to the various values at stake will ultimately enable policymakers to decide (either during– or following – consultations with stakeholders) which measure or combination of measures is preferable, and thus to determine the extent to which policy is geared to high-risk groups.

This decision-making process, too, is dynamic in nature. One reason for this is that new knowledge can cast fresh light on high-risk groups. Another is that, in a dynamic society, normative views about the balancing of costs and benefits, the distribution of advantages and drawbacks across population subgroups, and the allocation of responsibilities to government bodies, businesses and individuals are all subject to change.

Benefits of a systematic approach

To show how the assessment framework and the decision framework work in practice, the Committee has applied them to some public health and consumer protection issues. The Committee gives four examples: Q fever, diabetes, cervical cancer, and bisphenol A. These examples are offered purely for the purpose of illustration. They are not intended as critical analyses. The examples are given in Chapter 6.

The frameworks presented here provide a structured approach to the identification of high-risk groups and to decision-making on how to deal with such groups. The assessment framework triggers a systematic check of personal, lifestyle, and environmental traits that, separately or in combination, can affect the level of risk in terms of health impairment or disease. This reduces the likelihood of any relevant factors being overlooked, thereby facilitating a better and more refined characterisation of high-risk groups. One added advantage of this systematic approach is that it helps to uncover gaps in our knowledge, which in turn can influence the course of future research. The decision framework highlights the available courses of action with regard to high-risk groups, and helps those involved to make clear-cut choices with regard to a given approach.

Both frameworks provide a generic approach that is applicable to all prevention-related areas of policy. The Committee has broadly reviewed the extent to which allowance is made for high-risk groups in a number of policy areas (environmental policy, working conditions policy, consumer policy, and health policy). It found an occasional lack of clarity concerning the extent to which decision-making is geared to certain high-risk groups, and about whether decisions represent deliberate choices. Usually, consideration is indeed given to

the obvious high-risk groups. This often involves gender-related and age-related differences in risk. Only occasionally does decision-making appear to take account of other personal factors such as genetic background, physical condition, lifestyle, and environmental factors. The Committee notes that, at present, choices about whether or not to make allowance for high-risk groups are often implicit in nature. It recommends that the frameworks presented here be used, to make the choices in question more explicit. In addition, it recommends that those working in different disciplines put their heads together to see what they can learn from one another about how to deal with high-risk groups.

More specifically, the Committee notes that:

- A few years ago, the National Institute of Public Health and the Environment (RIVM) drew up the Framework for Decision making in the field of Environment and Health (FDE&H) to facilitate decision-making in the area of environmental policy. The only question about high-risk groups contained in this document does not provide a good enough guarantee that the profile of high-risk groups will be raised sufficiently for the purposes of decision-making. The Committee advocates that questions about high-risk groups be much more closely intertwined with the other questions in the FDE&H. This can be achieved by incorporating the assessment framework and the decision framework described in this advisory report into the FDE&H. In Annex C, the Committee shows how this could be achieved.
- Under the terms of REACH (legislation regulating the authorisation of chemicals within the EU), requirements concerning the scope of the toxicological studies to be carried out depend on the production or import volumes in question. This criterion involves the implicit choice not to take possible high-risk groups into account when production and import volumes are low. The Committee recommends that this choice be made more explicit.
- Infectious disease policy has traditionally placed great emphasis on high-risk groups, based on old age and pre-existing diseases. By contrast, the policy on exposure to harmful substances in the workplace, is traditionally geared to healthy young and middle aged workers. According to the Committee, this may need to be adjusted, now that everyone (including those with chronic disorders) is increasingly expected to continue working for longer, and in keeping with their ability.
- The same focus is seen in the authorisation policy for plant protection products, where residue levels in food are geared to the resilience of healthy individuals. The question is what this means for individuals with severe metabolic diseases, for example, or liver or kidney disorders.

These two frameworks, presented by the Committee, can assist in gathering and organising any available information and in clarifying the pros and cons that have to be weighed. The issue of how to properly weigh up the factors involved remains as thorny as ever. The Committee feels that the most appropriate approach would involve a process of governance, in which the government reaches a decision either during – or following – consultations with stakeholders. How exactly this should be organised is beyond the scope of this advisory report.

Chapter 1

Introduction

1.1 Government and public health

People see good health as a major asset. It contributes to people's well-being and enhances opportunities for personal development. Health is also a prerequisite for the effective operation of our society as a whole, and for maintaining our level of prosperity. It is the government's responsibility to protect and promote public health. That responsibility is legally enshrined in Article 22 of the Constitution. To this end, the government does not rely on the capacity of curative care alone. It also takes action to prevent as much avoidable health impairment as possible. It believes that everyone needs to get involved. To this end, it has drawn up a broad vision of health and prevention, which will provide reference points for the management of this process.[1] Once every four years, it will establish priorities for prevention policy.[2,3]

The vision of prevention defines prevention as the entire range of measures, both inside and outside the health service, aimed at safeguarding health by preventing illness and health problems.[1] In other words, the aim of prevention is to remove or reduce risks, in this case health risks. Prevention can take many forms. A classification system based on the nature of the measures to be taken, distinguishes between health protection, disease prevention and health promotion.[4] This type of classification system is used in a frequently presented model (Figure 1), which shows how an individual's health status is the sum total of many different, interacting factors. The factors in question are determinants of

health (physical and social environment, lifestyle, personal traits), health policy (prevention and care), and external developments (in areas such as demographics, economics, and technology).[5]

Health protection focuses on reducing exposure to health-threatening environmental factors through legislation, enforcement, or actual intervention in the environment concerned. This may include food and product safety, safe working conditions and a safe environment. Other aspects include measures in the areas of road safety and flood protection, as well as building codes.

Disease prevention includes measures for the prevention or early detection of certain diseases (or of an hereditary predisposition to such diseases). Some examples of these measures are the National Immunisation Programme, influenza vaccination, and the National Screening Programme. This includes the early detection of breast and cervical cancer by screening, and of metabolic disorders and cystic fibrosis by means of the Guthrie test (heel prick).

Finally, health promotion is aimed at fostering a healthy lifestyle. This could, for example, include public information campaigns and training courses aimed at influencing social norms and the behaviour of individuals. For instance, there are the BOB campaigns against drinking and driving, and courses to help people stop smoking. It also involves creating healthy living environments that encourage people to take more exercise.[7]

The distinctions between these different forms of prevention are far from sharp. They partly reflect traditions that have evolved over time.

The government places the responsibility for good health largely on individuals themselves.[1-3] This is especially true where their lifestyle and behaviour are concerned. In this context, the government feels that its involvement should mainly be confined to a supporting role. However, disease prevention and health protection are quite a different matter. Given the sheer scale and complexity involved, plus the allocation of responsibilities, there is generally little scope for effective action at the individual level. Any such measures must be taken collectively. Accordingly, they are the responsibility of government bodies, either at local, provincial, or national level. In many cases this may even require international cooperation, as with outbreaks of major infectious diseases, or where food safety issues are involved. The national government is increasingly tied to European or global agreements and laws and regulations.

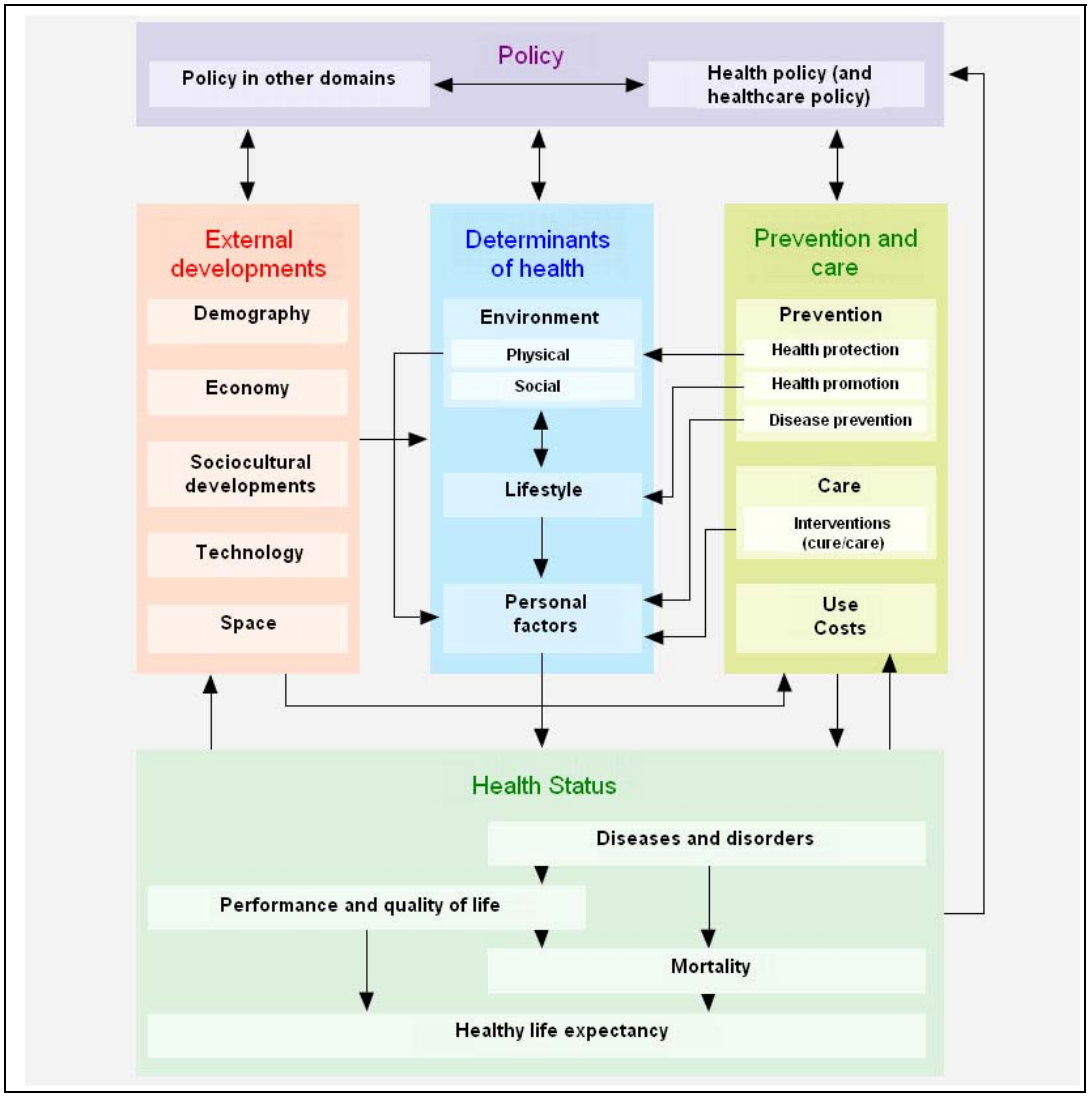

Figure 1 Conceptual model of health from the 2006 Public Health Status and Forecasts[5], derived from an earlier model by Lalonde.[6] The model primarily concerns the health status of individuals. However, aggregation of the data produces a description of public health and its determining factors.

By their very nature, preventive measures taken by the government to protect health and prevent disease can never be tailored to individuals. Whenever the government takes action, it always does so at a given collective level. In this way,

the government does everything in its power to provide protection for everyone. However, the enormous range of human diversity is a major complicating factor in this endeavour. Indeed, people differ substantially in terms of their risk of health impairment. For example, persistent hot weather in the summer or *Salmonella* infections have a much greater impact on very elderly people than on those who are young and in good health. In addition, chemical substances can have a very different effect in children than they do in adults. The risk of illness or health impairment is further exacerbated if adverse environmental factors combine or if they are associated with an unhealthy lifestyle or the lack of an effective health service. Accordingly, in a range of different domains, the government does not focus its prevention policy purely on 'Mr Average'. To some extent, it does attempt to take account of human diversity, using generic measures where possible, and additional measures for specific population subgroups where necessary.

1.2 The request for advice

Government policy is aimed at cutting health risks, or at least to reducing them to a given level. In this endeavour, the government is targeting a specific level of safety or protection.[8] This might mean that specific groups need extra protection, as they may be at greater risk due to increased susceptibility or to unusual dietary habits or lifestyles. At present, different policy domains each deal with such issues in their own way. Starting with the fields of environmental and consumer policy, the government aims to deal more consistently with such variations in the population across a range of policy dossiers. To this end, the Minister of Health, Welfare and Sport, also on behalf of the State Secretary for the Environment, has requested the Health Council's advice in this matter.

The Minister and the State Secretary have asked the Council to draw up an "assessment framework" which will provide a uniform basis for identifying population subgroups that are at increased risk. They have also urged the Council to design a "decision framework", as a way of determining whether given high-risk groups need to be taken into account when formulating policies or implementing measures. They have requested details illustrating the implications of both frameworks for policy across a range of areas. The Minister and the State Secretary have asked that the answers to their questions should incorporate the results set out in the National Institute of Public Health and the Environment (RIVM) publication *Assessment Framework for Health and Environment* (AFH&E)[9], the policy document *Coping rationally with risks*[8], the previous Health Council advisory report *Pesticides in food: assessing the risk to*

children[10] and the RIVM report on national and international developments in chemical risk assessment focussing on the risks to children[11]. The full text of the request for advice is set out in Annex A.

1.3 Committee, scope and procedure

The “High-risk groups” Committee was appointed and tasked with answering the questions posed by the Minister and the State Secretary. Details of the make-up of the Committee are given in Annex B.

1.3.1 Scope and mission statement

The request for advice was prompted by requirements inherent to environmental and consumer policy. Accordingly, the Committee’s initial focus was along the lines of health protection. That approach primarily involves controlling exposure to potentially harmful agents via food, consumer products, the environment, or the workplace. Standard setting and product authorisation (registration) are important policy tools in this respect. Much of this is regulated by European legislation. However, the results of this advisory report are also relevant for other lines of prevention, specifically health promotion and disease prevention. Generic measures, such as standard setting and authorisation, are not necessarily always the most appropriate interventions for the protection of specific population subgroups. In some cases, especially in the area of health promotion, this could involve targeted information about healthy behaviour, for example. The identification of high-risk groups can also be useful in the prevention of specific diseases through vaccination or screening. The Committee also plans to address these types of prevention policy in its advisory report.

In considering the matter of health risks, the Committee has adopted a twin-track approach. The first line of enquiry involves a focus on specific diseases or disorders, such as diabetes and breast cancer. The second addresses health impairment associated with exposure to harmful agents. These might be chemical substances (either natural or artificial), physical agents (such as noise and radiation), or biological agents (such as viruses, bacteria and fungi). This will usually involve over-exposure to potentially harmful agents, although in other cases it might be a question of excessively low exposures to beneficial agents. For instance, deficits of important micronutrients like iodine, folic acid, and vitamin D can also lead to health impairment. Here too, the risk of “deficiency diseases” can vary from one individual to another. Given the

constraints of this advisory report, the Committee has focussed on risks associated with over-exposure.

Risk assessment has long been used in each of the policy domains mentioned. Two aspects of this are the identification of high-risk groups and decision-making with regard to such groups. Each of these domains differs greatly in terms of the approach used, nevertheless, the Committee suspects that they are all based on a similar system. The Committee plans to outline this, in the interests of consistency in policy. In this way, it also aims to bridge the gap between health protection on the one hand and disease prevention and health promotion on the other, while facilitating the exchange of knowledge, experiences and methods between different disciplines.

1.3.2 Pivotal questions

Guided by this definition of the scope of its remit, the Committee has decided to address the following questions in its advisory report:

Causes of differences in health risks

1 What factors determine the risk of health impairment or disease, and account for differences in risk between one individual and another?

Assessment framework for identifying high-risk groups

2 Is there a systematic approach that could be used to identify those subgroups within the population that are at increased risk of health impairment?

Decision framework for deciding about protection

3 What criteria can the government use to decide which high-risk groups should be taken into account when implementing protective measures?

Added value for various policy domains

4 How do different policy domains currently tackle the issues of identification and decision-making with regard to high-risk groups? Against this

background, what is the added value of the assessment framework and decision framework that have been presented?

1.3.3 Procedure

The Committee has based its advisory report on the international scientific literature and on reports issued by authoritative national and international bodies and organisations. The latter include previous advisory reports and background studies issued by the Health Council of the Netherlands (e.g.[12]) and the reports referred to by the Minister and the State Secretary in the request for advice.

1.4 Structure of this advisory report

In Chapter 2, the Committee first explores the nature of risks in general and health risks in particular. It then briefly covers developments in recent years, in terms of dealing with risks.

Each of the subsequent chapters is devoted to answering one of the pivotal questions. In Chapter 3, the Committee defines some key concepts associated with high-risk groups. It then explores at greater depth the question of why some individuals are at higher risk of health impairment than others.

In Chapter 4, the Committee then applies this knowledge to create an assessment framework for the identification of high-risk groups.

Chapter 5 examines the range of criteria that policymakers can apply when attempting to resolve the question of who should be protected, against what, to what extent, and at what price. Together, these constitute the required decision framework.

In Chapter 6, the Committee illustrates the use of the assessment framework and the decision framework by means of various case studies.

What are the advantages of the assessment framework and decision framework presented here? How do they supplement the identification and decision-making procedures currently used for high-risk groups across a range of policy domains associated with prevention? These issues are addressed in the final Chapter.

Chapter 2

Health risks and prevention

In this Chapter, the Committee briefly explores the nature of health risks, how they arise, and how they have shifted over time. It also presents a brief outline of developments in government policy, in terms of dealing with these risks.

2.1 Health risks

While “risk” mainly came into vogue in the twentieth century, the concept itself is much older. The term is used in various senses, among which there is considerable overlap, both in everyday life and in scientific disciplines such as epidemiology, psychology, environmental sciences and economics.[13] Almost all definitions of the concept make reference to “potential” and to “negative consequence” or “harm”. Rosa proposed the following very general definition of risk[14], which covers the spectrum of perspectives:

> A situation or event where something of human value (including humans themselves) has been put at stake and where the outcome is uncertain.

The uncertainty may include both the nature of the outcome and the probability that it will occur. Rosa’s definition stresses that risk exists only if something of value is at stake. If the valued item at stake is human health, then health risks are involved. It is risks of this kind that are addressed in this advisory report.

In a previous advisory report[15], the Health Council defined the term “risk” as:

> The possibility, with a certain degree of probability, of damage to health, environment and goods, in combination with the nature and magnitude of the damage.

For the sake of consistency, the Committee has adhered to this definition in its advisory report.

The literature sometimes distinguishes between the concepts of “risk” (in the strict sense: known consequences with known probabilities), “uncertainty” (known consequences with unknown probabilities) and “ignorance” (unknown consequences with unknown probabilities).[16] In its broadest sense, the term “risk”, as used by the Committee, combines these three concepts.

Risk arises when there is exposure to a hazard, or the possibility of such exposure. A hazard is “something” that has the potential to harm. That potential is based on an inherently threatening characteristic that, under certain circumstances, may give rise to damage. That “something” could be anything – animals, plants, bacteria, viruses, volcanoes, geological faults, weather, devices, products, working methods, or procedures. It might also be social circumstances, such as pressure of work, loneliness, or the threat of war. In other words, risk may derive from natural processes, human activities or combinations of both. The mechanism of harm may involve an accident or an undesirable (and often initially unsuspected) side-effect of a process that operates according to plan. One example of the latter is the eutrophication of surface waters by fertiliser use in agriculture, another is the development of antibiotic resistance.

Throughout much of history, the risks to which people were exposed were predominantly of natural origin. Infectious diseases, in particular, were a major threat. Over the centuries, however, and especially in the modern era, mankind has gradually gained the upper hand. By contrast, human action itself has become an increasingly important factor in the emergence of risks. Scientific and technological developments, population growth and social globalisation are gradually changing the nature of the risks to which people are exposed. Many “new” risks are not confined to particular places or times.[17,18] When damage occurs, it often does so on a global scale, as in the case of climate change, the “hole” in the ozone layer, urban air pollution, endocrine disruption, and BSE.

The wide range of technological developments has also had an impact on people’s individual lifestyles, of course. The increased prosperity of Western society, together with our heightened technical capabilities in areas such as information, communication, and transport, has affected many aspects of daily life. These include dietary patterns, physical activity, use of stimulants and

medications, travel behaviour, pursuit of hobbies, and sexuality. These lifestyle changes also involve new risks, not least for health. In past times, hunger was a serious health threat in our part of the world. These days, the same is increasingly true of excessive consumption. Not too long ago, medicinal products were a scarce commodity. Today, adverse interactions between concomitant medications are an increasing problem, especially in the elderly.

2.2 Dealing with health risks

As the products of science and technology entered general use at an ever increasing rate and on an ever increasing scale, it quickly became important to consider the associated risks. Accordingly, "risk thinking" is now an integral part of many policy domains that are directly or indirectly significant in terms of public health (see Figure 2).

Figure 2 "Risk thinking" is part of many policy sectors that are significant in terms of public health.[8]

Those in the area of health protection felt perhaps the greatest need for risk assessment. They needed to assess not only the nature and extent of potential damage, but also the likelihood that this would actually occur. Quantitative risk

analysis was developed in the 1980s, for the domains of the environment and public safety. It makes use of cause-effect chains to describe, in scientific terms, how material and energy can be released, and how they might harm human health and that of the environment. This approach was adopted in the policy document *Coping with risks*, which the Dutch government published in the late 1980s as an annex to its *National Environmental Policy Plan*.[19] In this way, the government endeavoured to provide everyone with at least a minimum level of protection, and to deal with risks from various hazardous agents in a more uniform way[20]. Another of its goals was to provide the business community with a degree of legal certainty. This approach did indeed appear to provide scientifically-based certainty. Furthermore, the results of the analyses appeared to provide a basis for the comparison of risks of various kinds, which made it easier to set priorities when tackling them. Quantitative risk analysis also facilitated rational decision-making about the acceptability of apparently hazardous activities, and about the nature and extent of the action needed to keep risks within acceptable bounds. Quantitative risk analysis became established not only in the environmental policy domain, but also in the field of occupational health and safety and the field of food safety.

For various reasons, however, this approach ran into a number of practical problems. Given its perspective, quantitative risk analysis is restricted to data that scientists consider to be sufficiently robust and that is, to some extent, quantifiable. Psychological research has also shown that, in addition to rational aspects such as the likelihood and the degree and extent of any damage, more affective aspects are also important to the social perception of risks.[21] These include people's awareness of the risk in question, and their assumptions concerning the degree of control involved. Moreover, no assessment of the risks can be divorced from an evaluation of the benefits delivered by the risk-generating activity in question. Decision-making usually requires difficult trade-offs of disparate costs and benefits. Very often, these also involve uncertainties, and they are almost always unevenly distributed across subgroups within the population. In addition to their scientific aspects, risk issues always have a socio-economic dimension. In addition to the bare facts, value judgments (partly motivated by interests) inevitably play an important part in decision-making. For this reason, government bodies are increasingly seeking to arrive at policy decisions in consultation with stakeholders. The term "governance" is now commonly used to describe this approach.[22] It must take the form of a multi-stage assessment and decision-making process, centred on clear communication between all stakeholders (Figure 3).

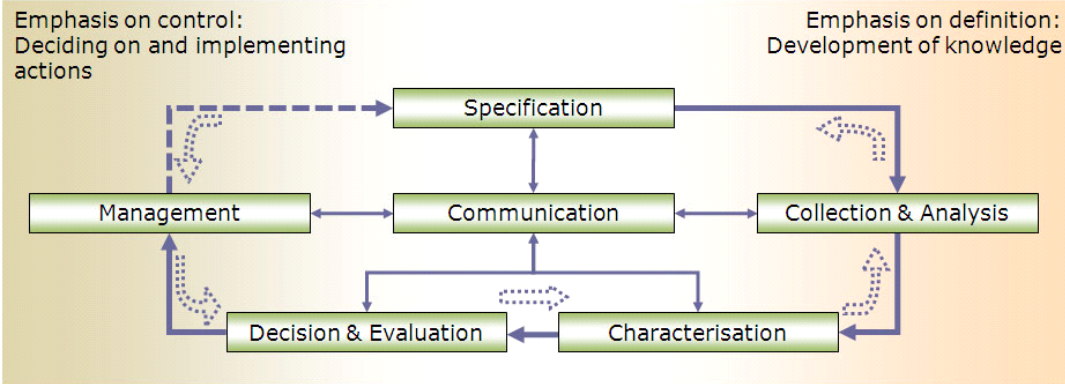

Figure 3 Flowchart showing how to deal with risk issues.[17]

In the Netherlands, this governance approach was reflected in the 2003 report by the Environmental Assessment Agency (MNP) and RIVM, entitled *Coping rationally with risks*[23]. This was followed in 2004 by a policy document from the Ministry of Housing, Spatial Planning and the Environment (VROM)[8], and in 2006 by a Government Vision Document bearing the same title[24]. The latter states that, based on the principles of good governance (e.g. legal equality and legal certainty) generic policy is considered desirable. At the same time, however, effectiveness (and cost effectiveness) is an important consideration in policymaking. There is a social need for specific agreements in certain situations, in other words for customisation. This could mean that the general principles are no longer universally applicable, and that – in practice – varying levels of safety will have to be accepted.[24]

Drawing on *Coping rationally with risks*, the Health Council recently noted that, with regard to many contemporary risk issues (e.g. the risks of nano-technology), decision-making is hampered by a lack of scientific knowledge.[17] It believes that uncertainty about risks does not constitute a reason for inaction. Quite the opposite, in fact. The Council calls for a careful approach to the uncertainties involved. It advises policymakers and politicians to assess the various courses of action (each of which has beneficial, adverse, certain, and uncertain repercussions) on their merits, and to weigh them against one another in a careful and transparent manner. It urges those involved not to lose sight of distributional issues, such as the distribution of risks and benefits among different population subgroups, or between current and future generation. It takes the view that the choice of the best risk control option should not be based purely

on the likelihood of each of those effects, which people attempt to derive from the – often limited – available evidence. Account should also be taken of the importance assigned in advance to the adverse effects of cautious and less cautious courses of action. Policies that are pursued to mitigate potential risks in situations involving uncertainty are usually referred to as precaution. Where sufficient knowledge is available to underpin policy choices, this is described as prevention. There is not a sharp distinction, however. In synchronicity with the Health Council, the Scientific Council for Government Policy advocated a more alert and careful approach when dealing with uncertainties.[25] The government recently endorsed most of the recommendations put forward by both advisory councils on this issue.[26]

Human diversity is a recurring challenge to those charged with developing policy for dealing with risks. Risks (just like benefits) resulting from human activities or natural processes tend to be unevenly distributed across the population. Simply put, some individuals are more at risk than others. This means that policymakers must make choices. To what extent should prevention be geared to those who are at greater risk, what price are we as a society willing to pay, and how do we deal with people's willingness to put themselves at risk? Before such choices can be made, it is important both to identify subgroups within the population who are at increased risk and to better understand the nature and extent of that risk. Chapter 4 explains how this can be addressed in a systematic manner. However, the Committee will first provide a more detailed explanation for the variation in risk from one individual to another.

Chapter 3

High-risk groups - reasons for differences in risk

In this Chapter, the Committee defines several terms associated with high-risk groups. It goes on to demonstrate how people's personal, lifestyle, and environmental traits determine their level of risk, in terms of health impairment or disease.

3.1 Definitions

Before outlining a systematic approach to the identification of high-risk groups, the Committee defines some commonly used terms.

Population at risk

Various definitions can be used, depending on the context. In disease prevention, which is generally aimed at preventing a specific disease or condition, the following definition is commonly used:

That section of the population at risk of suffering the disease or condition in question (compare[27])

The population at risk will therefore vary, according to the disorder or disease in question. For instance, the population at risk of prostate cancer consists of all adult men, for neural tube defects it is confined to unborn children, and for flu it corresponds to the entire population.

For a more agent-oriented approach (which is commonly used in health protection) the following definition would be more appropriate:

> The section of the population that is potentially exposed to the agent in question and that is therefore at risk of health impairment (compare[28])

In one sense, this latter definition refers to a more restricted group, as the population at risk is confined to those who have a realistic risk of exposure to the agent in question. Accordingly, individuals who have no contact whatsoever with that agent do not feature among the population at risk. As a result, the population at risk varies from one agent to another.

Risk group/High-risk group

Dutch scientific literature and policy documents use two different terms – "*risicogroep*" (risk group) and "*hoogrisicogroep*" (high-risk group) – in this context. The Committee takes the view that these terms are usually synonymous. They both have drawbacks. The Committee feels that "risk group" is not sufficiently distinct from the term "population at risk". This is because every individual in the population at risk is, by definition, at risk. The precise meaning here is that a section of the population is at increased risk. This is better expressed by the term "high-risk group". However, the latter term gives the impression that the "high risk" involved is high in the absolute sense, and that is not necessarily the case at all. The term is primarily a relative concept, one that conveys no indication of the absolute level of risk involved. A tenfold or even a hundredfold increase in risk may still involve a very low level of risk, in the absolute sense. With this in mind, it might be better to use a term such as "elevated risk group". However, this is not used in the literature. Given its commitment to the use of conventional terminology, and as there are more profound objections to "risk group" than to the term "high-risk group", the Committee has opted to use the latter term in the remainder of this advisory report.

Here too, the disease-oriented approach uses a slightly different definition than the agent-oriented approach. The former uses the following definition:

> A subgroup within the population at risk that is at increased risk of suffering the disease or condition in question. This consists of individuals with a particular trait that is associated with an increased risk of acquiring the disease or disorder in question.

The existence of this association has been established by scientific research. While this can be causal in nature, this does not necessarily have to be the case. The former designates the trait as a “risk factor” while the latter uses “risk indicator” or “risk marker”, but the terms are often used interchangeably (see[29]).

The agent-oriented approach generally uses the following definition:

> A subgroup within the population at risk that is at increased risk of health impairment. This consists of individuals with a particular trait that can adversely affect either exposure or susceptibility (or both) to the agent in question.

The trait could adversely affect exposure in a number of ways. For instance, it could result in increased exposure, alternatively it could mean that exposure takes place via another route (e.g. by inhalation rather than orally). An adverse effect of the trait on susceptibility could be quantitative in nature, i.e. it might involve increased susceptibility. This might mean that a given health effect would occur at a lower level of exposure, that it would progress more rapidly, have a more serious course, or persist for longer. However, the influence of the trait could also be qualitative. In such cases, the health effects involved differ in nature from those in other subgroups.

The comparison (elevated relative to what?) always involves individuals with variations of the same trait[30]. For instance, men versus women, individuals with a given genetic disorder versus those without that disorder, or smokers compared to non-smokers. The extent to which a level of risk has to increase before a group can be described as “high risk” is seldom, if ever, defined. This is, to some extent, a normative choice. Clearly, however, it makes more sense to designate high-risk groups within the population at risk if large increases in risk and/or large groups are involved. Of course, there is often considerable variation within any given high-risk group. Individuals in high-risk groups may have other traits that further increase their risk of a given disease or of health impairment in general. The practical benefit of dividing high-risk groups into ever smaller subgroups of increasing risk (an approach known as risk stratification) is something that has to be determined on a case by case basis. Various factors can serve as useful guidelines in this regard, including the size of the subgroup and the severity of the risk involved.

In the literature, there are frequent references to the terms “susceptible group” or “sensitive group”).[12,31] The Committee sees this as a high-risk group whose increased level of risk is due to an increased susceptibility to the agent in question. Frequent use is also made of the term “vulnerable group”.[31,32] This term has varying shades of meaning. It is sometimes used to denote susceptible

groups, sometimes high-risk groups, and sometimes population subgroups with an accumulated risk. Given this lack of clarity, the Committee prefers not to make use of this term.

3.2 Traits responsible for increased risk

The above description of a high-risk group shows that two factors are usually involved in the onset of illness. The first of these is exposure to a pathogenic agent, and the second is the individual's susceptibility to that agent. Infectious diseases, for example, involve exposure to a pathogenic microorganism in combination with little or no immunity. In reality, this almost always features a range of exposure and/or susceptibility-enhancing traits, which (either individually or in combination) must be sufficiently extreme to result in a given disease (cf. [12,33,34]). Individuals who combine more of these traits are at greater risk of developing the disease in question. In the following sections, the Committee explores these traits in greater detail.

3.2.1 Traits that can affect exposure

Table 1 contains a list of traits that affect human exposure to harmful agents. The list is not exhaustive. These traits can be personal, lifestyle-related, or environmental in nature. While the traits can indeed be classified separately in this way, the fact remains that they strongly influence each other. In reality, any given situation usually involves a complex interplay of these factors.

Table 1 Traits that can affect exposure to various agents.

Personal	Lifestyle	Environmental
Gender	Dietary pattern	Living environment
Genetic profile	Smoking	Indoor environment
Age	Alcohol use	Working environment
Pregnancy	Use of medication	Food safety
Health status/disease	Hygiene	Drinking water quality
Character	Physical activity	Quality of products
Educational background	Use of consumer products	
Family background	Hobbies	

Personal traits

Personal traits can be genetic, acquired, or a combination of both. They have a huge influence on people's exposure to a range of different agents. This is largely

because they help determine people’s lifestyle choices and surroundings. For example, on average, women tend to use different types (and greater quantities) of cosmetic products than men. Accordingly, their exposure to the substances present in such products is also higher than average. Children’s food preferences differ from those of adults. For instance, they eat more apples and drink more lemonade than adults, but consume negligible amounts of alcoholic beverages. Young children also put their hands into their mouths more often than adults, and spend more time crawling around on the ground.[10] Older people spend more time indoors than younger people, which increases their exposure to agents typically found in indoor environments such as radon, endotoxins, and dust mite allergens. Conversely, this behaviour decreases elderly people’s exposure to sunlight, for example.[35] In addition, this group uses a relatively large number of medicinal products. In some cases, a cognitive decline in old age can make it difficult for people to recognise hazards. As in the case of children, this can exacerbate exposure. An individual’s educational level can also be a factor here. Finally, a person’s character can also play a part. For instance, those who are habitually casual when handling chemicals (either at work or at home) will suffer greater exposure than those who are more prudent in this regard.

In addition, personal traits can sometimes directly determine the amount of exposure involved. Children have relatively high energy requirements, compared to adults. Accordingly, they ingest more food and water, and breathe more air, per kilogram of body weight per day than adults. They also have more body surface area per unit of weight than adults, which has the same effect in terms of dermal exposures.

Lifestyle traits

An individual's lifestyle has a major influence on the nature and extent of exposures to harmful agents. People’s lifestyles are determined by a range of personal and sociocultural factors. There are a number of significant differences between individuals or groups. These include the use of stimulants (tobacco products and alcoholic drinks), dietary patterns, leisure-time activities, and sexual behaviour. Those who frequently visit discos are exposed to loud music. Unprotected sex increases the risk of venereal diseases. These differences are partly related to differences in socioeconomic status, such as smoking habits.[36] To some extent, they are ethnically determined. Individuals of Surinamese or Chinese origin, for example, have very different dietary patterns from those of native Dutch people. They also differ in terms of their manner of dress. People who like to sunbathe for hours while scantily clad, or who make regular use of

sun beds, have increased exposure to UV radiation. Those who always wear concealing clothing, on the other hand, will suffer less exposure. This relates not only to the level of exposure, but also to its distribution over time (peak exposures). Frequent, long-distance travellers are at greater risk of acquiring tropical diseases.

Environmental traits

Levels of exposure are also determined by the quality of the physical environments in which we live. This includes our living environment, our indoor environment, and our working environment. It also relates to the quality of the products that people use or consume.

Increased exposures can be linked to specific localities. For instance, this might involve the emission of harmful substances into the air by traffic, industry, or agriculture in the immediate area. Alternatively, it might be related to the presence of radio transmission towers. The type of building materials used, or inadequate ventilation, can also produce elevated exposure in indoor environments. Other forms of exposure might involve contaminants in locally grown vegetables or in local sources of drinking water. Here, too, differences in exposure are, to some extent, related to socioeconomic factors.[39]

Increased exposure in the workplace often results from the specific tasks carried out by certain workers. One notorious example is exposure to asbestos. The route of exposure is of particular importance. For instance, work-related exposure to alcohol, via the skin or the respiratory system, cannot be directly compared to exposure through the consumption of alcoholic beverages. Again, differences between individuals are partly related to socioeconomic factors, in the sense that the lower socioeconomic classes are more often exposed to unhealthy working conditions.[37] However, there are exceptions. Animal husbandry professionals are at increased risk of zoonoses. For instance, veterinarians and poultry farmers are at increased risk of avian influenza.

Aside from the physical environment, the social environment is also important with regard to exposure. This affects exposure to noise or pathogens, for example. For instance, families with children of school-going age are at greater risk of infection with the influenza virus.[38] Exposure to factors which we less readily associate with the word “agent”, such as aggression or loneliness, is also determined by the social environment.

3.2.2 *Traits that can affect susceptibility*

Table 2 contains a summary of traits that can affect an individual's susceptibility. To some extent, these are the same traits that can affect exposure. This list, too, is not exhaustive.

Table 2 Traits that can affect an individual's susceptibility to various agents or diseases.

Personal	Lifestyle	Environmental
Gender	Dietary pattern	Physical agents
Age	Smoking	Chemical agents
Pregnancy	Alcohol use	Biological agents
Health status/disease	Use of medication	Social agents
Adaptation	Hygiene	
Genetic profile	Physical activity	
Epigenetic profile	Use of consumer products	

These traits may influence people's susceptibility to agents via a range of different routes, by affecting:

- Kinetics (how the body affects the agents)
- Dynamics (how the agents affect the body)
- Reserve capacity.

Certain changes in kinetics, dynamics, or reserve capacity can make people less susceptible or more resistant to the agent in question. Immunity to a pathogen, whether this is acquired naturally or by means of vaccination, is one example. Another is the induction of detoxifying enzymes that accelerate the breakdown of toxic substances. Other changes, however, can actually increase susceptibility. Some examples are the increased absorption of a harmful agent from the environment or from food, reduced inactivation by binding proteins in the blood, reduced detoxification, enhanced bioactivation by liver enzymes, or reduced excretion by the kidneys. All these changes boost the concentration of the agent in organs and tissues.

Reductions in reserve capacity also make individuals more susceptible to disease and increase their risk of health impairment. For instance, elderly individuals can be affected by osteoporosis, a condition in which bones gradually lose minerals and structure. This causes their bones to become brittle, thereby increasing the risk that a fall will result in a broken hip or wrist, for example.[40]

A given trait may operate via several of these mechanisms to affect people's susceptibility to specific agents. Further details are given in the brief summary below.

Personal traits

Gender influences the effects of agents in a variety of ways. However, given the limitations of our current level of knowledge, it is not always possible to predict the exact mechanism involved. In addition, this influence is often age dependent. It is reasonable to expect that the greatest differences in susceptibility would occur in relation to agents that directly affect the genitals or the endocrine system. Women, for example, are very much more susceptible to breast cancer than men. The susceptibility of other organs and tissues can also be gender dependent. Sex hormones often play a prominent part in this regard.[42] The most important factors appear to be differences in dynamics. While there is a wide range of differences in terms of kinetics, these generally appear to be less significant.[43,44]

Genetic factors can significantly affect an individual's susceptibility to various harmful agents or diseases. Some well known examples of the genetic factors in question are polymorphisms in the genes coding for enzymes involved in the conversion and excretion of chemical substances. Differences in the enzymes involved in the breakdown of alcohol mean that Asians generally do not tolerate alcohol as well as Westerners.[45] Individuals with an abnormal form of factor V (factor V Leiden) are at increased risk of thrombosis.[46] The vast majority of disorders, including diabetes, cancer, and cardiovascular diseases, involve a much more complex relationship between genetics and susceptibility. They result from interactions between many different genes and environmental factors.[47] By regulating the activity of specific genes, epigenetic factors (which can be inherited) can affect an individual's susceptibility to certain diseases.[47]

Another characteristic that can determine susceptibility is age. Children exhibit different kinetics (e.g. reduced metabolic enzyme activity) especially in the first few months of life. That can work both ways, either increasing or decreasing susceptibility to harmful substances. There are also significant differences in dynamics. This is particularly true during the genesis of organs in the embryonic phase, as well as during their subsequent maturation when organ development is particularly susceptible to disruption by a variety of agents (e.g. substances, radiation, viruses, and bacteria). The Health Council will explore the effect of prenatal exposure to chemical agents in greater detail in an advisory report that is scheduled for publication at a later date.

The ageing process is much less rigidly defined than child development. To a great extent, it depends on what the individual in question has experienced during their lifetime. Accordingly, there is considerable inter-individual variation. Ageing seems to impair the ability to convert and excrete substances.[48,49] This will often lead to increased susceptibility. However, it can occasionally result in reduced susceptibility, for instance in cases where a metabolite is more toxic than the parent compound (bioactivation). For obvious reasons, more elderly people generally have little to fear from the long-term effects of exposure. As people age, their immune systems also become less effective, which results in increased susceptibility to infectious diseases. Another significant factor is that reserve capacity and resiliency generally decline with age, so minor disruptions can have major consequences.[48,50]

Numerous physiological changes take place in the body of the expectant mother. These are designed to optimise the supply of nutrients to the foetus, and the removal of waste products. Such changes can affect the absorption, distribution, conversion, and excretion of substances. For this reason, women may require different doses of medicinal products during pregnancy than at other times.[51,52] The immune system also undergoes a number of changes.[53] As a result, pregnant women are more prone to (or more severely affected by) certain infectious diseases, including malaria, measles, and food borne infections such as Listeria.[54,55]

Finally, susceptibility can also be affected by pre-existing diseases. For instance, kidney and liver disorders can increase an individual's susceptibility to toxic substances or medicinal products[56,57], calcium or iron deficiency can increase susceptibility to heavy metal poisoning[58,59], and an atopic constitution can increase the risk of sensitisation to chemical substances.[60] Individuals with impaired immune systems (e.g. due to AIDS or the use of certain medicinal products) are more susceptible to infectious diseases and carcinogens.[61]

Lifestyle traits and environmental traits

The impact of lifestyle factors and environmental factors on the body can produce acquired personal traits that increase the individual's susceptibility to a second, external factor. A birth weight that is either too high or too low (resulting from maternal influences), for example, can increase an individual's susceptibility to developing obesity in later life.[62-64] This may result from epigenetic changes induced in the prenatal phase. It should be noted that this involves an obligatory sequence of events. Firstly, an exogenous factor must induce an endogenous change, which in turn will determine the individual's

susceptibility to a second exogenous influence. That initial exogenous factor might have been exposure, in the distant past, that caused permanent endogenous changes. This is more or less the case in the obesity example cited above. However, exposure to both exogenous factors could also take place virtually simultaneously, as in the case of exposure to combinations of toxic substances. If one chemical interferes with the body's detoxification mechanisms, this will immediately boost the individual's susceptibility to the second substance.

Smoking increases an individual's susceptibility to numerous harmful agents. In cases of asbestos exposure, for example, smokers tend to develop lung cancer more often than non-smokers.[65] They are also more susceptible to noise-induced hearing loss[66-70] and to respiratory tract infections.[41]

The elderly are the largest consumers of medicinal products.[71] They often use several medicinal products at the same time (polypharmacy). That gives rise to a risk of interactions. One medicinal product can either stimulate or inhibit the enzymatic conversion of the other. This can lead to a reduced therapeutic effect, or to harmful adverse effects.[50,72,73] In the same way, the use of medicinal products alters an individual's susceptibility to contaminants in the environment or in their food. Conversely, contaminants can also undermine the efficacy of medicinal products.[50]

Exposure from the environment can also change an individual's susceptibility. For example, exposure to asbestos increases smokers' susceptibility to lung cancer.[65] Those who have had an infectious disease develop a specific immunological memory that reduces their susceptibility to re-infection by the same organism or other, closely related, pathogens. For example, milkmaids who had previously been in contact with cowpox were not susceptible to smallpox.[74] The development of modern-day vaccinations against infectious diseases was prompted by these findings.

Chapter 4

Systematic identification of high-risk groups

Here the Committee presents a system for identifying high-risk groups, which is based on information from the previous Chapter. This constitutes the requested "assessment framework for the identification of high-risk groups".

4.1 A general system for identifying high-risk groups

The previous Chapter presented details of the traits that can affect an individual's exposure to harmful agents or their susceptibility to health impairment and disease. This information forms the basis of a system for identifying high-risk groups. The Committee illustrates this in graphical form, in Figure 4. This amounts to a systematic description of the common denominator of the procedures currently being used in many domains to assess the risk of disease or health impairment. It symbolises an iterative, dynamic process. The schedule needs to be repeated whenever new information becomes available that might shed a different light on high-risk groups for a given disease or for health impairment resulting from a given agent. The schedule has been applied to numerous diseases and agents in recent years. As a result, the associated high-risk groups are slowly but surely becoming more clearly defined. The schedule is primarily intended for use by experts, as the identification of high-risk groups is mainly a task for those with expertise in such matters. While these individuals could be trained scientists, this role could also fall to those who are experts by virtue of experience. Their input is absolutely essential. When dealing with risk

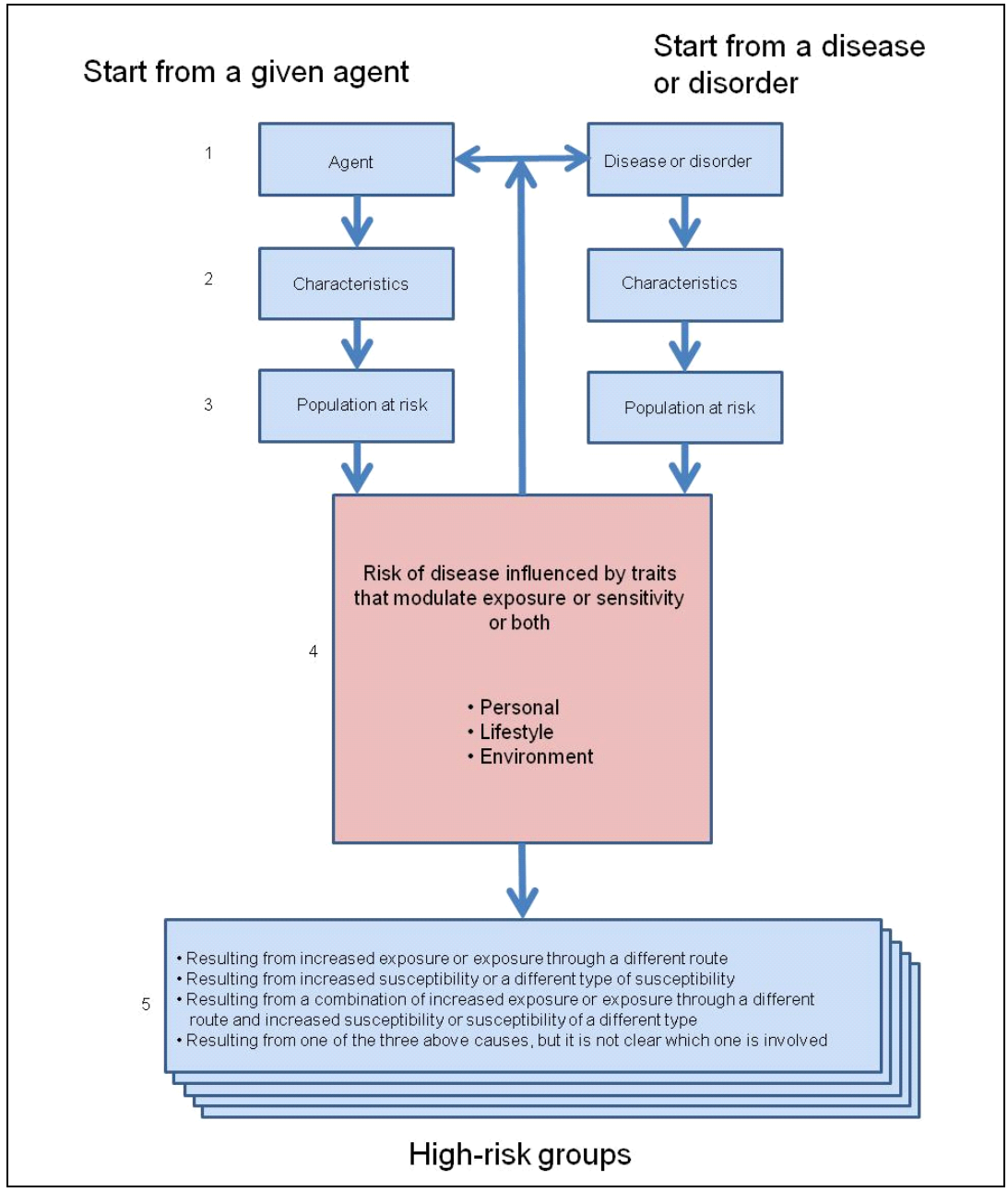

Figure 4 The systematic identification high-risk groups.

issues and health problems, the instrument must be used in the "Collection and Analysis" stage (see Figure 3 on page 31), in which experts take the lead. They work closely with policymakers and, where appropriate, with stakeholders. After all, the identification of high-risk groups always involves normative choices. For instance, this concerns the extent to which a given group's risk has to increase before they can be designated as a high-risk group, the energy invested in identifying specific groups, and the degree of sophistication of the analysis involved. The better an analysis reflects the information requirements of policymakers and stakeholders, the more points of reference for policy it will ultimately provide.

The identification of high-risk groups involves the following stages:
1 Starting with a given agent or disease
2 Characterisation of the agent or disease
3 Identifying the population at risk
4 Identification of traits that might influence the risk of disease by modifying exposure or susceptibility
5 Demarcation of high-risk groups.

The Committee discusses each of these stages individually below.

1 Starting with a given agent or disease

Either cause or effect can serve as the starting point when assessing the risk of disease or health impairment. By extension, this also applies to the identification of high-risk groups. The choice depends on the purpose or, in this case, the policy domain being served by the assessment in question. In the case of policy domains in the field of health protection (which generally focus on the regulation of potentially harmful agents), the agent in question is usually the starting point. With regard to domains that deal with disease prevention or health promotion, then the starting point is usually a given disease. Simultaneous departures from both starting points are also possible. For instance, in the domain of infectious diseases such as influenza, the processes for assessing the agent and the disease usually go hand in hand. Wherever possible, such a twin-track approach is to be preferred (compare with[75]).

2 Characterisation of the agent or disease

If an agent is to serve as the starting point for the assessment then the first thing to do is to find out everything about it. Is it chemical, physical or biological in nature? What other characteristics does it possess that could, in any way, affect people's exposure and any resultant health impairment ? It is important not to be too quick to conclude that the way in which the agent is used precludes any risk of human exposure, after all, improper use and accidents can never be ruled out entirely.

If a given disorder or disease is to serve as the starting point for the assessment, then its characteristics must first be identified. What is the nature of the disease or disorder in question? What are the symptoms? Which organs or organ systems are affected? What is known about the possible causes and course of the disease?

An agent's characteristics, such as a substance's chemical structural formula or toxicity data, or a parasite's life cycle, can provide information about the nature of potential health problems. That may indicate that there is also a need to gather information about the disease itself. Conversely, the very nature of a particular disease can point to the involvement of a specific agent, which can then provide an additional avenue for information gathering. This is represented by the arrow linking the blocks labelled "agent" and "disease".

3 Identifying the population at risk

The information gathered can be used to identify individuals among the general public who are at risk, i.e. the members of the population at risk. If an agent is to serve as the starting point for the assessment then the risk of being exposed to that particular agent, in combination with the risk of suffering health impairment as a result of that exposure, determines which individuals or groups belong to the population at risk. Because the nature of the adverse health effect itself is not the main issue here, the risk of exposure will generally be the determining factor. This population at risk should be defined as clearly as possible. Searching for possible trends over time is also a worthwhile exercise. Can the number of exposed individuals be expected to increase in the future? This gives an indication of the possible health interest involved. If the prevention of a disease or condition is to serve as the starting point for the assessment, then the population at risk is limited to those who are susceptible to that specific disease.

4 Traits that might influence the risk of disease by modifying exposure or susceptibility

This is the central stage of the identification process. Here, the variability of the population at risk has to be translated into the variation in risk. If a given agent is to serve as the starting point for the assessment, then the question is whether there are individuals with given health problems that they, or suitably qualified experts, believe are related to exposure to the agent in question. Of course, this is subject to the agent in question being on the market, or present in the environment. If such a group of people does indeed exist then it is important to characterise this sub-population as clearly as possible, using their personal, lifestyle, and environmental traits. It is also worth finding out whether such associations are based on factors influencing exposure to the agent in question, susceptibility to that agent, or both. In the first and last cases, individuals with health problems (especially those with severe health problems) will have a higher average exposure to the agent than those with milder symptoms (or none at all). Alternatively, their exposure may proceed via a different route. Neither of these considerations apply to the second case. Data from epidemiological studies can be supplemented with information from studies in experimental animals, *in vitro* studies, and mechanistic studies. When combined with information on geographical distribution and trends over time, this data provides evidence of a possible causal relationship. In fact, here too, there is a switch from an agent-oriented to a disease-oriented process. This is indicated by the vertical arrow pointing upwards.

If, from the outset, the approach taken involved a given disease or disorder, then a patient population will usually be involved. In these cases, the approach may be largely the same as that described above. It involves a search for associations between patients' personal, lifestyle, or environmental traits and their risk of developing the disease (or the severity of that disease). Some of the requisite data is often recorded in centralised registration systems. The investigation is restricted to those traits that, on the basis of current knowledge, can reasonably be expected to be associated with the disease in question. In general, these might be traits that affect an individual's exposure to a causative agent, those that influence an individual's susceptibility to such an agent, or both. However, the cause of any given disease is often poorly understood. Frequently, there is also a lack of clarity concerning the interpretation of any associations derived from epidemiological research. Nevertheless, the characterisation procedure occasionally delivers evidence for the involvement of a specific agent. Also, studies in experimental animals, *in vitro* studies, and research into

mechanisms of action can sometimes reveal a previously unsuspected link between the disease in question and an agent that is on the market, or present in the environment. From that point on, both the disease-oriented approach and the agent-oriented approach can be taken into consideration. Here too, this is indicated by the arrow pointing upwards.

It also shows that there is a substantial interaction between identifying high-risk groups and tracking down the causes of disease. The high-risk groups that have been identified in connection with a given disorder can provide clues about its cause. Conversely, any new causes that are discovered can help to shed light on new and existing high-risk groups.

In many cases, the risks associated with a given agent need to be assessed in advance, i.e. before the agent comes onto the market, or enters the environment. For instance, this might be a novel chemical substance that a manufacturer wants to market, or a new device that emits electromagnetic radiation. Alternatively, it could be a harmful microorganism or parasite whose expanding range is ultimately expected to incorporate the Netherlands. In such cases, there are no exposure measurements or figures on diseases or health problems on which to base an assessment, although data of this kind may be available in other countries. This situation should be resolved by data from other sources, such as calculations based on exposure models, experimental animal studies, and *in vitro* studies, as well as analogies with related agents. This, in turn, will make it possible to evaluate the influence of the personal, lifestyle, and environmental traits of those within the population at risk in terms of the extent and route of exposure to the agent in question, the degree of susceptibility involved, and the nature of possible health effects. Once again, this analysis is restricted to those traits that, on the basis of current knowledge, are considered to be relevant.

5 Demarcation of high-risk groups

This exercise identifies high-risk groups for a given agent or disease, within the population at risk. That can be just one group, or several. In Figure 4, this is represented by a number of blocks positioned one in front of the other. It is theoretically possible that there might be no high-risk group at all. However, the Committee finds it difficult to conceive of a harmful agent or disease that poses exactly the same risk to everyone, regardless of their personal, lifestyle, or environmental traits. A given subpopulation within the population at risk could be considered a high-risk group if its traits result in:

- Increased exposure to a harmful agent, or in exposure via a different, more harmful route;

- Increased susceptibility to a harmful agent, or in health effects of a different nature;
- A combination of increased exposure to a harmful agent (or exposure to such an agent via a different route), and increased susceptibility (or some other type of susceptibility).

This is illustrated graphically in Figure 5.

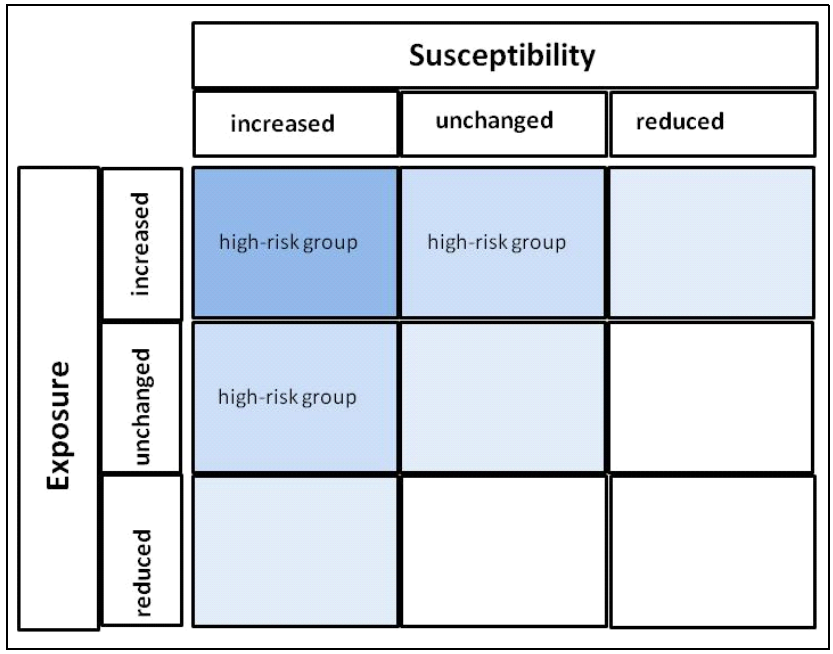

Figure 5 Distinguishing between high-risk groups on the basis of the influence of personal, lifestyle, and environmental traits on their susceptibility and exposure.

Epidemiological studies sometimes indicate that a given subpopulation is at increased risk of a disease or condition, while it is – as yet – unclear which of the above three reasons is involved. For this reason, the Committee has identified a fourth scenario:

- The exact reason is unclear, but it is known to be one of the three listed above.

This is often the case. The lack of clarity is a direct result of numerous, highly convoluted personal, lifestyle, and environmental traits, many of which influence

both exposure and susceptibility, as the Committee demonstrated in the previous Chapter.

Sometimes, subpopulations within the population at risk combine exposure-boosting traits with traits that decrease their susceptibility (resistance-promoting traits). The opposite can also be true. Subpopulations with susceptibility-enhancing traits can also possess exposure-reducing traits. Accordingly, when all this is taken into account, such groups do not need to be designated as high-risk groups. Thus, if traits have opposing effects, they can partially or completely nullify each other's influence on the risk in question. Conversely, several traits can each contribute to a larger effect. This accumulation of adverse factors can leads to an extra high risk. The ultimate risk depends on the net cumulative effect of the entire range of traits. This opens the door to risk stratification. Here, high-risk groups that are demarcated by a given trait can be further divided into smaller subgroups using a second, third, or fourth trait that increases the risk still further. These subgroups are then characterised using a given set of traits: the risk profile.

When identifying high-risk groups, the key question is always: which of the many possible personal, lifestyle, or environmental traits exhibited by individuals or groups within the population at risk are capable of modifying the risk of a particular disease (or health effects generated by an agent)? Any such traits need to be included in the risk assessment procedure. The less that is known about the disease or agent in question, the more difficult it is to answer this question. With many diseases, our knowledge of their exact aetiology is relatively limited. This hampers attempts to identify high-risk groups. The potential health risks of many commercially available products have to be assessed before marketing, based on widely varying amounts of data concerning the nature and application of such products. As a result, this often makes the identification of high-risk groups more difficult and less reliable. In all cases, the identification of high-risk groups remains a matter for the experts. Given all the uncertainties involved, it is vital that they consult the schedule presented here whenever new information becomes available that might be relevant to the exposure and/or susceptibility of subpopulations within the general population. In this way, the detection of high-risk groups becomes an iterative, dynamic process.

A better understanding of the cause of a given increased risk offers the prospect of identifying clues for possible policy measures. These might involve health protection, health promotion, or disease prevention. Even without such an understanding, or in the absence of details underpinning an association between particular personal, lifestyle-based or environmental traits, effective preventive

measures are still possible, making the identification of high-risk groups worthwhile. In the next Chapter, the Committee examines this issue in greater detail.

Chapter 5

Reaching decisions on high-risk groups

In terms of protecting public health, it seems self-evident that the government should focus on high-risk groups as a matter of priority. Nevertheless, it is important to clarify the normative foundation on which such policies are based. This can then serve as a guideline for subsequent choices, such as at what point do we consider an increased risk a problem that needs to be addressed? Which individuals would require extra protection, against what, how, to what extent, and at what price? After a brief explanation of the general principles, the Committee lists the courses of action that the government can theoretically use when dealing with high-risk groups. It also puts forward various criteria that could help the government to make choices. Together, options and selection criteria make up the required decision framework.

5.1 General principles

When dealing with risk and health issues, the government must decide whether and, if so, to what extent they should fine-tune preventive measures to high-risk groups that have been identified. Various general principles can underpin this decision-making process. The protection of public health (and, by extension, the welfare of individuals) and a fair distribution of health are two reasons *why* the government is focusing on high-risk groups as a matter of priority. It is the government's constitutional responsibility to protect and promote public health. To this end, it aims to achieve quality, efficiency, and accessibility at the system

level. A high-risk group approach may, in some cases, be the most *effective way* to exercise that responsibility (e.g. in the case of some vaccination programmes). One way to assure accessibility is to guide high-risk groups through the preparatory phases of the intervention in question, and to provide them with clear and objective information. In addition, policies aimed at high-risk groups can be justified from the standpoint of *fairness*. It could, for example, reduce unfair socioeconomic health inequalities,[76] or protect people against risks caused by others.

On the other hand, respect for the autonomy of private citizens imposes limits on government measures to protect public health. The recognition of that autonomy means that, to a large extent, people are free to live their own lives, and are considered to be capable of doing so. The other side of the coin, however, is that the risks they take are primarily their own responsibility and not that of the government. While health protection measures are often mandatory in nature (e.g. wearing seatbelts), health promotion measures enable individuals to live healthily but do not enforce compliance. This involves the principle of informed choice. A recognition of autonomy also implies protection of privacy.

With regard to health policy, another "restrictive" consideration is that measures to promote public health should not themselves affect peoples' health or welfare.

In theory, these considerations apply across the board, in all areas of prevention, i.e. health protection, disease protection, and health promotion. However, putting them into practice is not always a simple matter. Conflicts between the underlying principles can give rise to dilemmas. Such cases call for clear assessment and decision-making. In this connection it is important to identify the underlying cause of this conflict and to indicate which principle, in the situation at hand, will ultimately be the deciding factor.

5.2 Deliberations and decision-making in connection with high-risk groups

The main question is whether and, if so, to what extent, policies on a given risk issue or health issue should be geared to the high-risk groups that have been identified. This might involve measures in the fields of health protection, health promotion, disease prevention, either individually or in combination. In theory, the following courses of action are available to the government:

- Deliberately make allowance for some or all high-risk groups:
  - Through the implementation of generic measures that are geared to such groups;

    - Through measures (which may be supplementary in nature) specifically targeting some or all high-risk groups.
- Consciously take no account of some or all high-risk groups; generic measures that deliberately offer suboptimal protection (or none at all) to some or all high-risk groups.

If the government decides to take account of high-risk groups, then it basically has two options: a high-risk group approach and a population approach. The British physician-epidemiologist Geoffrey Rose has compared these two options.[77] The high-risk group approach is a more clinically oriented approach focusing on those individuals who are most at risk. The aim is to help such individuals reduce their high level of exposure (or high degree of susceptibility) to a given pathogen. The population approach, on the other hand, focuses on public health and assumes that a change in the general population* ultimately prevents a greater amount of disease burden than an approach based solely on the high-risk groups. Elevated plasma cholesterol levels can cause coronary artery disease. According to Rose, the population's average cholesterol level is a reasonably good predictor of the proportion of people with elevated levels. The greatest burden of disease results from the mass of people with mildly elevated cholesterol levels and the associated slightly increased relative risk, rather than from those few individuals with highly elevated cholesterol levels and a significantly increased relative risk. In much the same vein, based on the close correlation between the number of problem drinkers in a given country and average national alcohol consumption, he suggests that a reduction in that average value (e.g. through price controls) would probably automatically result in fewer problem drinkers. The strengths and weaknesses of the high-risk group approach and the population approach (as generally described by Rose) are summarised in Table 3. The Committee points out that the value of the strengths and weaknesses of both approaches can only be assessed in the context of a specific health issue or risk issue.

* This could be limited to the whole population at risk, or it could encompass the entire population (i.e. including those who are at no risk whatsoever).

Table 3 The strengths and weaknesses of various prevention strategies, according to Rose.[29,77]

High-risk group approach
Strengths
• Intervention can be customised • No impact on those who are not at increased risk • Compatible with the ethical and cultural values, organisation and economics of the existing system • Selectivity makes it more likely that resources will be used in a cost-effective way
Weaknesses
• The medicalisation of prevention • Success can be both palliative and temporary in nature • This may be of only minor benefit to general disease-control efforts within the population • In behavioural or cultural terms, the intervention may be largely inadequate or unsustainable • It is difficult to predict which individuals will benefit from the intervention
Population approach
Strengths
• Is a more radical approach, the social and political approach tackles the problem at its roots • In cultural terms, it may be more appropriate and sustainable to pursue general changes in behavioural standards and social values than to try to change behaviour at the level of the individual, which – in essence – is socially determined
Weaknesses
• Of only limited benefit to each individual participant • Requires major changes in economic and social performance • Less advantageous timing of costs and benefits (costs further outpace benefits)

The following criteria (which are classified into the categories of efficiency and fairness) can be used to determine the most appropriate choice in any given situation:

Efficiency

1 How does health impairment in the high-risk group relate to the rest of the population at risk?

In this connection, the following matters must be considered:

- The nature of the health effect, disorder, or disease in question
- The reversibility of the health effect, disorder, or disease in question
- The extent to which the health effect, disorder, or disease in question responds to treatment
- The size of the high-risk group in question

- The risk (or additional risk) of developing the health effect, disorder, or disease in question
- The contribution to the sum total of similar disease burdens in the high-risk group

2 Are any effective measures available? In other words, measures capable of delivering a substantial reduction in health impairment in the high-risk group in question.

In this connection, the following matters must be considered:
- The theoretical efficacy of possible measures
- The efficacy of possible measures in practice, concerning issues such as the identifiability and accessibility of those in high-risk groups.

3 Do these measures have any additional benefits?

This could involve:
- Health benefits for those who are not in any high-risk groups
- Ecological benefits
- Economic benefits
- Confidence in the safety of products.

4 In the broadest sense, do the benefits of the measures in question justify the cost involved?

These costs include:
- Adverse side effects on health, or on any other interests of the high-risk group in question
- Adverse side effects on health, or on any other interests of those who are not in any high-risk groups
- The financial costs of the measures
- Possible drawbacks associated with individual identification
- Potential restriction of people's autonomy and an invasion of their privacy

Justice and responsibility

5 Do the health inequalities between the high-risk group and the rest of the population at risk involve any unfairness? Who is responsible for the risk (or increased risk)?

Points to be considered:

- Allocation of responsibility to government, business, and private citizens
- The cause of the increased risk (natural, voluntary, other individuals)
- Mental competence; risk awareness
- Distribution of risks and benefits among different population subgroups
- Accumulation of risks
- Feelings in society, including those in high-risk groups.

Together, the courses of action and criteria mentioned at the start of this section constitute the decision framework requested by the Minister and the State Secretary (see Figure 6). Here, the Committee has included brief explanations of the various criteria involved (see below).

5.2.1 *Substantial health impairment*

There are two aspects to health impairment, how it affects individuals and its impact on the population as a whole. At the level of the individual, severe health impairment involves death, serious complications, or debilitating residual symptoms. Children may be far more severely affected than adults by exposure to harmful agents. Anything that disrupts the development of the unborn child or of young children can cause irreversible and untreatable health impairment. Other important factors are whether or not a disease is life-threatening, and the impact of any treatment.

At population level, it is the number of new cases of the disease each year (the incidence) that is of significance. Another question concerns the extent to which the burden of disease is concentrated in high-risk groups. Two aspects are crucial in this regard. Firstly, this is dependent on the size of the high-risk groups in question. This can either be small (e.g. a small group with a genetic disorder, or a profession practised by relatively small numbers of people) or very large (e.g. unlike men, women are a high-risk group for breast cancer). Two other large groups are children and the elderly; everyone was a child once, and everyone hopes to live to a ripe old age. Secondly there is the important consideration of how much more risk high-risk groups run compared to the rest of the population, and how much more severely they are affected in terms of health effects or disease course. Consideration also has to be given to the contribution of a given causative factor in a particular burden of disease suffered by a high-risk group.

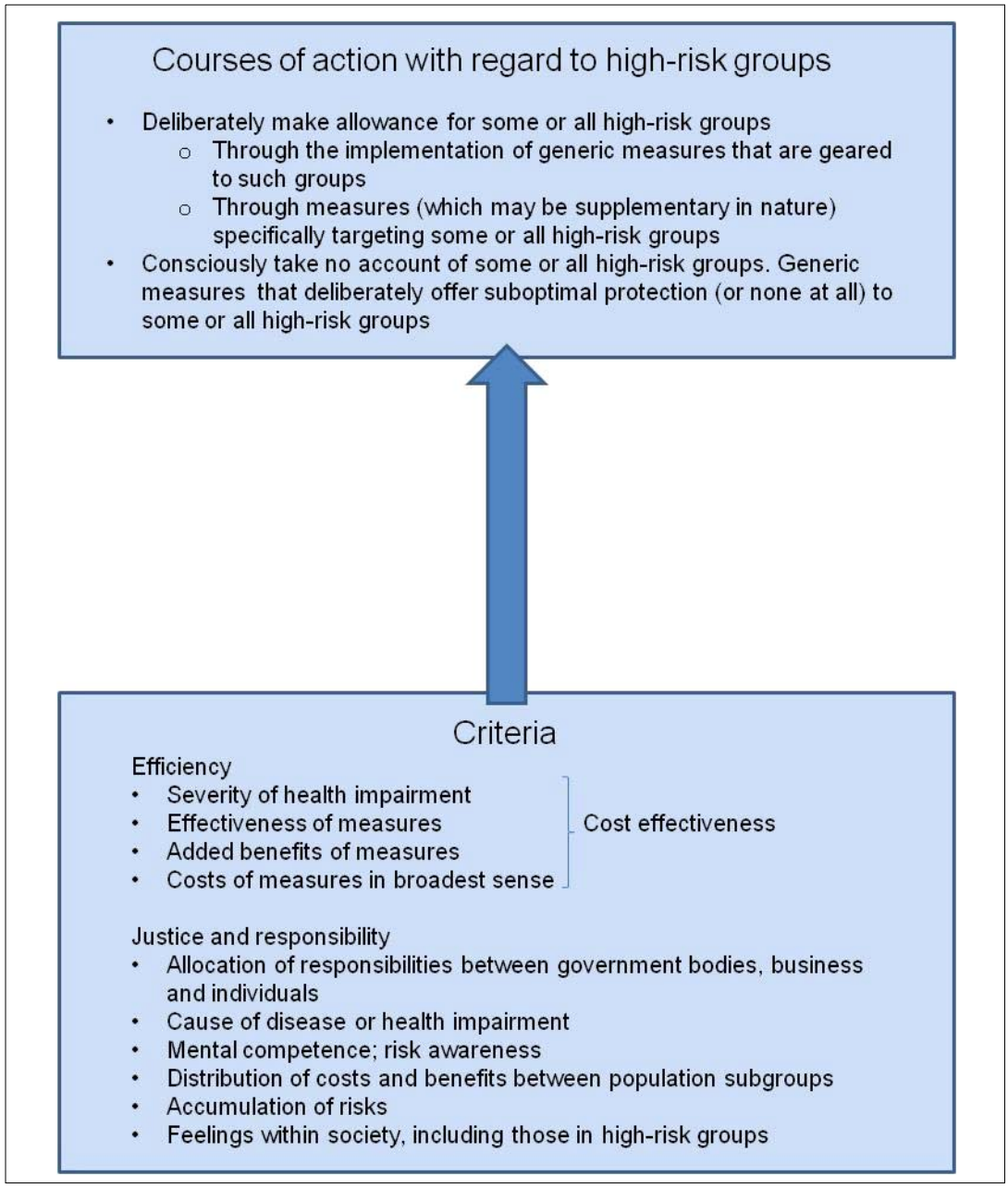

Figure 6 Decision framework for decision-making with regard to high-risk groups.

5.2.2 *Effective measures*

The first condition to be satisfied by a suitable measure is that it must be effective, i.e. it must reduce the risk involved. Ideally, people want to know in advance how effective a given measure will be in practice, but it is often the case that this cannot be determined until afterwards, and even then not with any degree of certainty. Another factor here is the degree of confidence concerning the cause of certain diseases or health problems.

In theory, measures can be taken either at source or at the stage when the recipient becomes involved. In the former case, these are always focused on limiting exposure. The latter case can involve both limiting exposure and reducing susceptibility. In theory, measures taken at source are to be preferred, subject to a review of what is both feasible and efficient. To protect high-risk groups, it is important to have a clear picture of the causative factors underlying their risk (or increased risk). Does this involve traits that increase exposure, traits that increase susceptibility, or both? It is sometimes impossible to reduce susceptibility (e.g. in the case of phenylketonuria, PKU), and measures to reduce exposure (labelling) are the only option. The reverse is also true (e.g. vaccination against influenza).

An important consideration here is whether the individuals in the high-risk group in question can be identified in practice. If that is indeed the case, then specific measures targeting the group in question could also be an option. The individuals belonging to certain high-risk groups can be easily identified. This is true of people of a certain age group, a particular gender, with a certain lifestyle or dietary pattern, or a given profession. For other groups that is seldom, if ever, the case. For instance, this generally applies to high-risk groups whose increased susceptibility is due to a genetic predisposition. In some cases, there is a detailed (or reasonably good) understanding of their prevalence within the population, but the identity of specific individuals with the disorder in question is not known. Screening is not always either possible or desirable.[78,79] The only feasible measures in such cases are those that are implemented at the level of the entire population.

5.2.3 *Additional benefits*

Measures taken in the interests of public health may simultaneously deliver benefits in another area. For instance, stricter exposure standards for a given harmful agent, geared to certain high-risk groups, can deliver additional

environmental benefits. Benefits can also surface in a different area altogether, such as increased consumer confidence in product safety, reduced workplace absenteeism, or preventing social disruption. Finally, society as a whole can gain by combating infectious diseases in specific groups, to ensure that these do not spread to the rest of the population.

5.2.4 *The costs involved, in the broadest sense*

One major issue concerns the amount of money that society is prepared to devote to health gains for the population as a whole, or for high-risk groups. This must, of course, be weighed against the costs of inaction. The potential health gains involved are usually expressed in terms of QALYs*.[80,81]This makes it possible to set limits to the cost per QALY, which in turn enables the advisability of a given measure to be assessed. In practice, vaccinations administered in the context of the National Immunisation Programme, for example, are subject to a limit of €20,000/QALY. This system can also be used to compare different measures and to set priorities. A cost-effectiveness analysis can be very useful way of weighing the relative merits of a high-risk group approach and population-oriented approach. One drawback, especially in relation to high-risk groups, is that some groups (such as the elderly and the chronically ill), by their very nature, involve fewer QALYs. A purely utilitarian approach, aimed at the greatest possible health gain (in QALYs) per euro spent, puts groups such as these at a disadvantage.[80] Choices like these involve the time-honoured trade-off between equity and efficiency.

Those wishing to be scrupulously fair in their dealings with some high-risk groups can opt for a more flexible interpretation of the cost-effectiveness criterion. If this approach is applied to high-risk groups of low socioeconomic status, for example, it can be of use to those endeavouring to reduce health inequalities between various groups in society.

On occasion, policy measures that specifically target high-risk groups will be more likely to meet a given cost-effectiveness criterion than interventions aimed at the general population. This is due to the potentially greater benefits involved when dealing with high-risk groups (see Table 3).

Aside from any positive effects (i.e. involving risk reductions), some measures can also pose new risks to health (e.g. adverse side effects of

* Quality Adjusted Life Year: a year of life, corrected by a factor of between 0 and 1 for the actual quality of life experienced during that year. In this system, 1 represents optimal quality and 0 minimum quality (= death).

vaccinations), give rise to discomfort or impact the interests of the high-risk group in other ways. If that is indeed the case, it is usually only advisable to proceed with the measure in question if the net balance of its effects is positive. That balance is more likely to be favourable for high-risk groups than for the entire population, given the greater potential benefits involved. This may be a further argument in favour of targeting policy interventions at certain high-risk groups, or restricting them to such groups entirely (see Table 3). If, however, generic measures are implemented, then the benefits for high-risk groups must outweigh the disadvantages for those who are at little or no risk at all. Financial considerations are not the only "costs" involved. Others include restrictions on freedom of choice, coercion, interference, or infringement of privacy. If two measures are equally cost-effective in terms of risk reduction, the preferred measure should be the one with the least impact on people's autonomy.

It should be pointed out that comparisons between measures need not necessarily be limited to those employed in a preventive setting. The cost benefit ratio can also shift towards the curative side, especially in the case of rare, difficult to detect, and eminently treatable health effects or diseases.

5.2.5 *Justice and responsibility*

Determining the acceptability of a given risk (or increased risk) is a complex matter that involves normative choices. The relevant factors here include the cause of the risk (or increased risk), the degree of conscious acceptance, and the extent to which the risk (or increased risk) in question is an integral part of an individual's identity or culture. Risks can be natural in origin, such as earthquakes or influenza pandemics. In cases such as these, the government is often expected to take preventive action. The government can also intervene in the case of risks resulting from the actions of others. On the basis of justice and, more particularly, the harm principle (prevention of harm to others), the government can require the causative party to curb the risks in question. However, where people voluntarily expose themselves to increased risk, through their own lifestyles and choices, obligations are rarely imposed. After all, members of the public also have a degree of individual responsibility with regard to risks. It is a well-known fact that members of the public more readily accept risks with which they are familiar and which they believe they can control.[82,83] This applies, for instance, to lifestyle-associated risks, such as smoking and alcohol use, or to the pursuit of risky hobbies such as mountaineering, boxing, or motorcycling. That easier acceptance stems from the fact that, for many members of the public, health is not the only value of importance in their lives.

Each individual makes their own compromises in terms of these values. This balance is not based purely on rational arguments, as affective aspects are also involved.[21]

It is worth noting that individuals are always exposed to a variety of factors, both social and otherwise, that tend to promote unhealthy behaviour. The social and physical environment in which people are raised and lead their lives, as well as the addictive nature of some stimulants, have a major impact on people's behaviour. This does not mean that, as a result, people are unable to control their own behaviour, or that they bear no responsibility for their actions. However, it is equally inappropriate to take the view that people are entirely responsible for their own behaviour (be it healthy or unhealthy), while taking no account whatsoever of social factors. The judgment about the extent to which people are responsible for the consequences of their own behaviour is a complex ethical issue. However, the government has every reason to induce members of the public to adopt healthy behaviour. One approach is to provide incentives that nevertheless offer them sufficient scope to make alternative choices.[84]

In addition, there is the issue of partial or complete mental incompetence, which applies to groups such as children and people with intellectual disabilities. When it comes to defending their interests (including their health), such groups are largely or completely dependent on others. In this respect, they are especially vulnerable. That might be an argument for offering them extra protection.

The members of economically disadvantaged socioeconomic groups often have to deal with an accumulation of various risks and social constraints. Moreover, there is no easy way out of this situation. The associated health inequalities may be regarded as unfair. The acceptability of certain socioeconomic inequalities has been addressed by various politico-philosophical theories, each of which has produced a different answer.[85] This is pre-eminently a matter of normative choice.

The causes of disease or health impairment are often unclear. Some people may ascribe their health problems to exposure to a specific environmental factor, possibly in combination with a particular type or degree of susceptibility. In the absence of scientific evidence to confirm the existence of a causal link (in some cases, despite extensive research), those involved will continue to hold differing views regarding the extent to which existing symptoms result from the effects of the physical environment, or from psychological factors. In this situation, the question of what measures (if any) are appropriate remains unanswered. Furthermore, if they are required, who is to be responsible for their implementation?

5.3 Knowledge and value judgments

Both knowledge and value judgments have a major influence on decisions about how to deal with high-risk groups. The task of identifying, as far as possible, the consequences of various courses of action with respect to high-risk groups falls mainly to scientists and experts. It goes without saying that this involves impacts on public health. However, it also addresses all of the other costs and benefits, and how these are distributed across population subgroups. One problem here is that, unlike details on "Mr and Mrs Average" (as Rose calls them), knowledge about "mavericks" and "outsiders" is often in particularly short supply.[77] All such information has to be grouped together at the "characterisation" stage of the assessment and decision-making process (see Figure 3 on page 31).

Value judgements are particularly important when deciding which of the outlined courses of action to implement. Many, if not all, of the criteria presented are inherently normative. What degree of health impairment or what burden of disease can appropriately be described as "substantial"? How far should causative parties go in taking steps to mitigate the risk suffered by high-risk groups? At what point can a given measure be deemed sufficiently effective? How can one weigh up the relative importance of dissimilar costs and benefits? What might be considered a fair distribution of costs and benefits? What can we reasonably ask of "Mr and Mrs Average", in order to protect high-risk groups? In terms of solidarity, Rose argues that "*it is the necessary price of being members of a society rather than solitary individuals*".[77] Which considerations and arguments should be assigned the greatest weight? Individuals and stakeholders may tend to disagree about the answers to all these questions. This is even more the case when there is uncertainty about the nature and extent (or exact cause) of possible health impairment. Accordingly, the question of how to deal with high-risk groups lends itself perfectly to the risk governance approach mentioned in Chapter 2. Here, during or after consultation with all of the stakeholders, policymakers and politicians decide which course of action is appropriate. This is the "evaluation and decision" stage (see Figure 3 on page 31). Views on this matter can change over time, giving rise to a dynamic decision-making process.

In the following Chapter, the Committee will illustrate the use of the assessment framework and the decision framework using various specific examples.

Chapter 6

How the assessment framework and decision framework are used

In this Chapter, the Committee illustrates the use of the assessment framework in identifying high-risk groups. It also shows how the decision framework is used to reach decisions about these groups. For these purposes it uses various examples from the policy domains of public health and consumer protection. The emphasis here is on the step-by-step use of the assessment framework in identifying high-risk groups. Using the decision framework, the Committee has put forward various arguments and questions of relevance to existing policy measures, and to those that have yet to be implemented. These are not presented in sequence, as the various deliberations are more likely to be made concurrently rather than sequentially. The Committee would like to emphasise that the descriptions presented here are not intended as critical analyses of the approach in question.

6.1 Q fever [86-88]

Characteristics

Q fever is an infectious disease caused by the bacterium *Coxiella burnetii*. It is a Gram-negative, obligate intracellular bacterium found in the phagosomes of monocytes and macrophages. Many species of wild animals, pets, and farm animals can act as a host. The same is true of humans. Spore-like stages in the bacterium's life cycle enable it to survive for long periods of time outside its host. Humans can become infected through contact with infected animals or animal

products. In the Netherlands, however, it appears that the inhalation of aerosols is by far the most important route of infection. Dairy sheep and goats are the main sources of new human infections. Infected pregnant sheep and goats are at increased risk of abortion. Both normal births and abortions release huge numbers of bacteria, which can spread far beyond the animal pens. In addition, contaminated blood products and human tissues are a possible source of human-to-human transmission.

In humans, the process of infection is symptom-free in up to 90% of cases. Those who do become ill can develop one of two different types of Q-fever: acute or chronic. The former gives rise to influenza-like symptoms, plus pneumonia and hepatitis in varying degrees of severity. This form is generally self-limiting. Yet, after one year, 40% of patients continue to experience health problems, especially prolonged bouts of fatigue. The much rarer chronic form (which involves 2% of all cases) mainly causes an inflammation of the heart valves and the lining of the heart (endocarditis). This is a serious condition which, if left untreated, can result in death. The chronic form can occur without being preceded by a diagnosed acute form.

There are indications in the scientific literature that Q fever during pregnancy can also lead to premature birth, abortion, and neonatal mortality in humans. This can even occur in infected pregnant women who show no signs of illness. However, data on this topic is very limited and potentially biased. Further research is currently in progress.

Up until 2006 Q fever was a rare disease, involving around twenty cases per annum. However, there was then a sharp rise to 168 cases in 2007, 1000 in 2008, and 2354 in 2009. It is not known what caused this sudden increase. It is unclear whether a new, more virulent bacterial strain has emerged. Over the past two years there has been a decline in the number of new cases, with 504 reports of acute Q fever in 2010, and just 37 in 2011 (up until mid-June).

Population at risk

Probably the entire population

Traits that might influence the risk of disease by modifying exposure or susceptibility

How environmental traits influence risk

This disease occurs mainly in intensive goat-farming regions in the provinces of Noord-Brabant and Limburg. Studies carried out in the area surrounding an infected farm showed that individuals living within a radius of 2 km are more than thirty times more likely to have Q fever than those living more than 5 km away. This is probably due to the fact that the population living in the immediate vicinity has a higher level of exposure to *Coxiella burnetii*.

Individuals who work with sheep and goats in the course of their professional activities also have increased exposure to the bacterium. These include dairy goat farmers and dairy sheep farmers, those members of their families who live on the farm, sheep shearers, agricultural contractors, and veterinarians. Serological testing in the Netherlands has shown that 80% of Dutch dairy goat farmers and veterinarians are currently (or have previously been) infected with the bacterium. Yet, to date, the burden of disease within this group has been very limited in its scope and severity.

How personal traits influence risk

Chronic Q fever occurs more frequently in individuals with underlying conditions, such as overt or hidden heart valve defects. They are at increased risk of complications, particularly endocarditis. In a retrospective study, French researchers estimated that approximately 40% of Q fever patients with heart-valve deficiencies go on to develop endocarditis. Since 2008, Q fever has been diagnosed in 10-20% of all endocarditis patients treated at the St. Radboud University Medical Centre in Nijmegen. Before that time there were virtually no such cases at all. In the provinces of Noord-Brabant and Gelderland, 50 to 75 patients with severe cardiovascular disorders are currently receiving long-term antibiotic treatment to counter the effects of chronic Q fever.

It has been suggested that chronic Q fever is more common in pregnant women, but the evidence is still inconclusive. Also at risk are those who, for medical reasons, have been given blood or other human tissues. If this donor material was infected, these patients' reduced immunity puts them at increased risk of developing the disease.

Despite their increased exposure, the number of cases among those working in the field of animal husbandry is comparable to that in the general population.

The reason for this is – as yet – unclear. One possible explanation is that the group may have built up immunity after years of contact with less virulent strains, and that this offers a degree of protection against any new, more virulent bacterial strains that arise. In that case, anyone planning a future in this area of animal husbandry, such as trainee veterinarians, may be at increased risk.

High-risk groups

Resulting from increased exposure or exposure through another route:
- Those living in the immediate vicinity of infected farms
- Fully qualified professionals and trainees who have not yet built up any immunity.

Resulting from increased susceptibility:
- Patients with cardiovascular disorders
- Pregnant women?

Resulting from a combination of both
- Recipients of contaminated blood and other human tissues

Policy measures

In 2010 and 2011, in accordance with the harm principle, the government enacted various measures to reduce the risks of Q fever. The first of these concerned measures taken at source.[89] For instance, dairy goat farmers, dairy sheep farmers, and veterinarians are now subject to a notification requirement with regard to suspected cases of Q fever in animals. Following the outbreaks, as a one-off measure, pregnant animals on infected farms were culled. Under certain circumstances there is a ban on breeding. Many sheep and goats undergo mandatory vaccination against the disease. Farmers who keep other types of goats and sheep voluntarily opt to have their animals vaccinated. At all farms with flocks of more than fifty animals, bulk tank milk samples are regularly tested for the presence of the bacterium.

In addition to these source-oriented measures, people can also be vaccinated against Q fever. Decisions about vaccination involve difficult considerations. For instance, to whom should the relatively unknown Australian vaccine be offered, and how do the complications of Q fever weigh up against the possible adverse effects of that vaccine? In 2010, the Health Council advised the Minister of Health against vaccinating the entire population against the disease, but

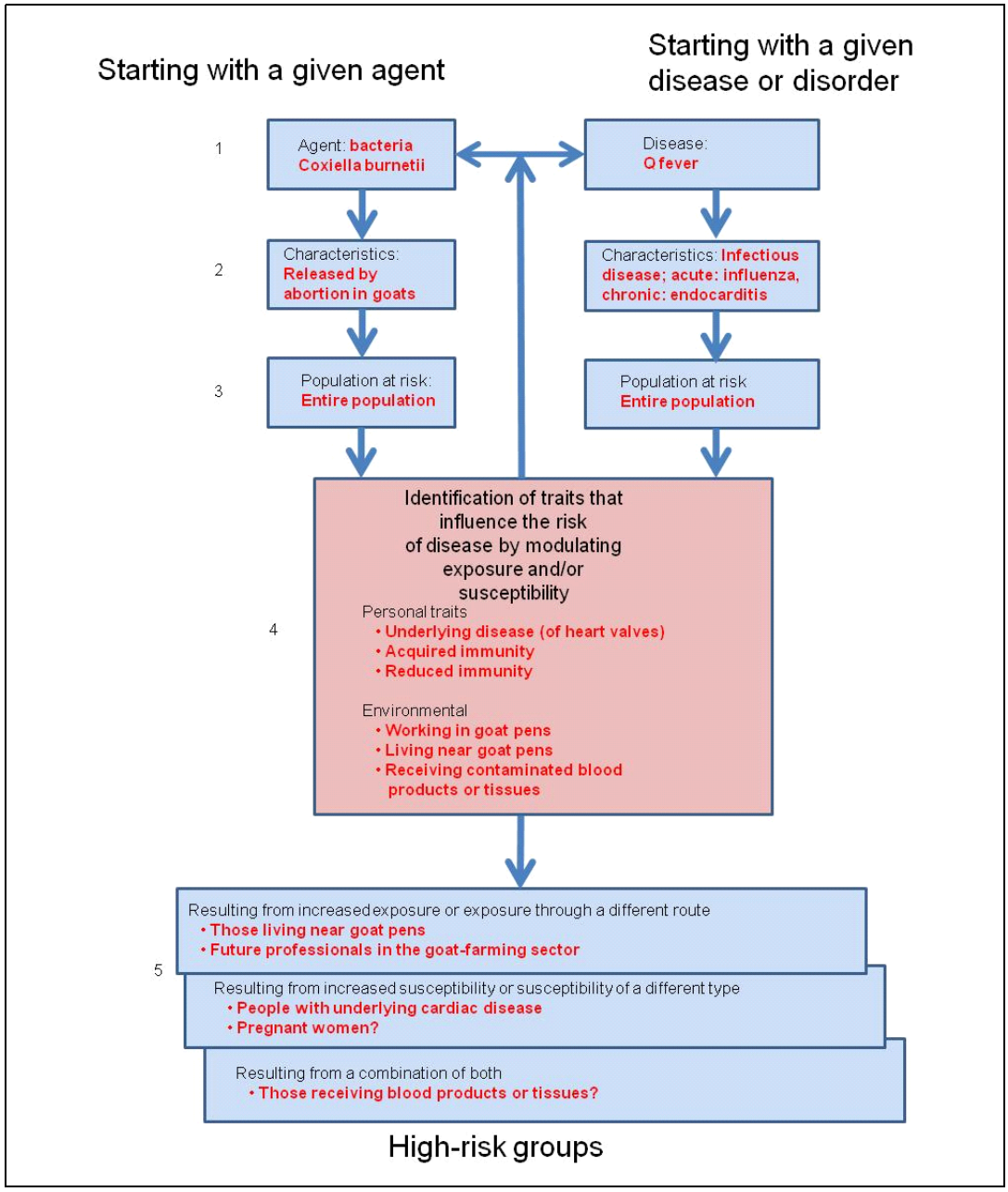

Figure 7 Use of the assessment framework to identify high-risk groups for Q fever.

recommended that vaccine be actively offered to individuals with cardiovascular diseases, in line with the individual care of patients.[86] The Council takes the view that, in these groups, the balance between the possible complications of Q fever and any adverse effects of the vaccine tips in favour of vaccination. The decision to vaccinate is the responsibility of the attending physician, in consultation with the patient. The Council recommends that a vaccination programme should be initiated in the high-risk areas in Noord-Brabant and Limburg. Beyond these areas, the Council feels that attending physicians have an important part to play in decisions on vaccination. Given the lack of familiarity with the vaccine, the Council advises against vaccinating pregnant women, young children and the local or regional population in Q-fever areas. From the perspective of a public vaccination programme, the Council feels that it would not be appropriate to vaccinate animal husbandry professionals, given the limited burden of disease involved. The Minister has recently adopted the Health Council's recommendations.

In a subsequent advisory report, the Council recommended that trainee animal husbandry professionals should also not be vaccinated, partly because the falling number of Q fever cases means that the expected burden of disease in this group is limited.[87] This recommendation was also prompted by public health considerations. According to the Council, an approach from the point of view of working conditions might well lead to different outcomes. Furthermore, the Council finds that more research is needed to assess the usefulness of testing blood donors for Q fever. It recommends that the costs and benefits of any such testing be identified before a decision is made. With regard to organ donation, however, measures are needed to prevent the transmission of Q fever, or to curtail its impact.[88]

6.2 Type 2 diabetes mellitus[90]

Characteristics

Diabetes mellitus is a chronic metabolic disorder associated with excessively elevated blood glucose levels. In diabetes mellitus, the body is unable to process glucose properly. This can be caused by deficient insulin production, and/or by the body becoming desensitised to this hormone. Insulin is necessary for the transport of glucose from the blood to the body tissues. In the absence of insulin, cells have difficulty in absorbing glucose, which causes blood glucose levels to increase. This gives rise to all manner of symptoms and complications.

There are two types of diabetes. In type 1, which mainly affects young people, insulin-producing cells in the pancreas are destroyed, possibly as a result of an infection. While this is the most common type of childhood diabetes, it is still quite rare. Type 2, which is also known as adult-onset diabetes, is the most common form of this disease. It occurs as a result of reduced insulin secretion coupled with reduced efficacy of the remaining insulin in tissues (insulin resistance). The disease has a very gradual progression. In the first phase (pre-diabetes), insulin resistance causes the pancreas to produce ever greater quantities of insulin. Blood glucose levels are normal, but insulin levels in the blood are elevated. The following phase involves an insulin-production deficiency, causing insulin levels to fall and glucose levels to rise.

The initial symptoms of type 2 are typically rather vague, involving excessive drinking, overeating, frequent urination, fatigue, and dizziness. It may be a long time before a diagnosis is made. Such patients have often had high blood-glucose levels for many years, without being aware of it. The high glucose levels, together with an abnormal profile of plasma lipids, damage blood vessels causing complications such as cardiovascular diseases (myocardial infarction, stroke, circulatory disorders of the legs). There is also damage to the retina, kidney disease, and numbness and/or pain in the limbs. The disease progresses through a number of stages: impaired glucose tolerance (pre-diabetes), type 2 without complications, and type 2 with complications.

On 1 January 2007, there were 670,000 diabetes patients in the Netherlands. In the course of that year, around 71,000 new patients were diagnosed. Approximately 90% of these had type 2 diabetes, the rest had type 1. In 2007, there were 10,811 deaths in which diabetes was cited as the primary or secondary cause of death. This figure is equivalent to 8.1% of the total number of deaths in 2007. Many deaths result from the complications of diabetes. In the past, this meant that diabetes was not always recorded as the cause of death. Between 1990 and 2007 there was a sharp rise in the prevalence and incidence of diabetes. This is primarily due to a rapidly ageing population, more active detection, greater public awareness due to information campaigns, and an increase in the number of individuals with risk-enhancing traits.

Population at risk

Probably the entire population

Traits that might influence the risk of disease by modifying exposure or susceptibility

How personal traits influence risk

Diabetes in children is almost exclusively type 1 (98%), but recent years have seen a rise in the number of children and adolescents with type 2. In the 40 to 70 age group, diabetes is more common in men than in women. The opposite is true of the group aged 75 and above. In 2007, the average age of all patients (with either type of diabetes) was 64 for men and 68 for women. About 30% of people over the age of 60 have pre-diabetes. It is estimated that at least one third of those with pre-diabetes go on to develop type 2 diabetes within a period of six years.

Interactions between risk factors are involved in the gradual development of insensitivity to insulin (insulin resistance) and the associated high blood-glucose levels. In adults, obesity is a major risk factor for the development of type 2 diabetes. The magnitude of this risk depends on the degree of obesity and on the distribution of body fat. Abdominal obesity (colloquially known as “belly fat”) is worse than fat on the hips.[91,92] The link between obesity and type 2 diabetes is partly attributed to substances released into the bloodstream via fatty tissue. Once people have developed pre-diabetes, they are at high risk of eventually developing the disease itself.

Genes that influence the onset of type 2 diabetes are often involved in the formation and functioning of the pancreas’s insulin-producing beta cells, as well as in “fasting” glucose levels and obesity. Estimates of the number of genes involved range from approximately eighteen to over fifty. Remarkably, only a fraction (about 4%) of the total risk for type 2 diabetes can be accounted for by the sum total of all known genetic variations.

Various Dutch studies have shown that the prevalence of diabetes mellitus in some ethnic groups is higher than in the general population. The highest prevalence is seen in those of Indian-Surinamese origin, especially in the older age group (37% in individuals over the age of 60). Prevalence among people of Turkish, Moroccan, and African-Surinamese origin is broadly similar, at around three to six times that of the native Dutch population. In these groups of immigrant origin, prevalence is higher among women than among men. The studies in question made no distinction between type 1 and type 2 diabetes.

There is no simple explanation for the increased prevalence of diabetes among these ethnic groups. A possible cause might be a genetic profile adapted to the sparse availability of food in the country of origin, coupled with a sudden transition to a Western country where large quantities of food are readily

available. In addition, young people in immigrant populations are more prone to obesity and severe obesity than those of the native Dutch population.

The main risk factors for type 2 diabetes in young people are severe obesity (45-90% of young people with type 2 diabetes are severely obese), genetic factors (ethnic origin and familial history of diabetes are risk factors), female gender (55-70% of young people with type 2 diabetes are girls), high birth weight (more than 4500 grams) or low birth weight (less than 2500 grams), and a mother who has had gestational diabetes.

How lifestyle traits influence risk

Regardless of body weight, physical inactivity and an unhealthy diet (too much saturated fat and too little dietary fibre) have been identified as significant risk factors for diabetes. Smoking slightly increases the risk of diabetes. The moderate use of alcohol and coffee appears to reduce the risk of diabetes. The lifestyle of groups of immigrant origin is, in some respects, less healthy than that of the native Dutch population (e.g. exercise, obesity), while in other ways it is healthier (e.g. food).

How environmental traits influence risk

The ready availability of food in Western countries is the most influential environmental factor. The social environment is also important. Among those who admit to having diabetes there are many more poorly educated people than people with a background in higher education, by quite a large margin. In the lowest education category, 11.4% of those over the age of 25 have diabetes. The equivalent figure in the highest education category is 3.1%. If educational level can be considered an indicator of people’s socioeconomic status, then this points to the existence of socio-economic health inequalities.

High-risk groups

With regard to individual high-risk groups, it is not possible to say whether their increased risk is due to increased exposure, increased susceptibility, or a combination of both. The disorder is multifactorial in nature, and many factors are closely interlinked. This tends to undermine the meaning of terms such as susceptible and exposed. For this reason, Figure 8 combines all of the identified high-risk groups in a single frame:

- The elderly

- Obese individuals with a great deal of belly fat
- People who are physically inactive
- People who have an unhealthy diet (low in fibre, high in saturated fat)
- Smokers
- Women who have had gestational diabetes
- People with diabetic relatives
- People whose mother had gestational diabetes
- People who had high or low birth weights
- Groups of immigrant origin (mainly Indian-Surinamese)
- People from the lower socioeconomic classes.

Policy measures

The increased risk of diabetes can partly be attributed to people's behaviour and lifestyle. They may consciously opt for a given behaviour or lifestyle, identify themselves with this, or it may be part of the culture to which they belong. This raises the question of how the respective responsibilities of government, industry, and individual members of the public are to be demarcated. This does not mean that the government should adopt a laissez faire stance, but the use of incentives may be preferable to measures that restrict people's freedom. The obvious options are an effective provision of health information and promoting healthy choices that are accessible to everyone. Another is secondary prevention, which is intended to prevent the situation from worsening in those with the initial disease symptoms or early warning signs.

In 2009, in cooperation with the Ministry of Health, Welfare and Sport, the Dutch Diabetes Federation (NDF) drew up the National Action Programme on Diabetes (NAD), which runs from 2009 to 2013.[93] The key objective is the structural implementation of the NDF Care Standard as a guideline for the content, organisation and quality control of programme-based diabetes prevention and care for diabetes patients and for the associated funding system. To this end, five instrumental goals were formulated, aimed at:

- Prevention, health information, early diagnosis, and lifestyle interventions in high-risk groups
- Strengthening the position of the patient, self management, education, patient compliance
- Anchoring the chain approach (multidisciplinary programme-based care)
- Identifying legislative obstacles and reducing them where possible
- Implementing the use of electronic diabetes files.

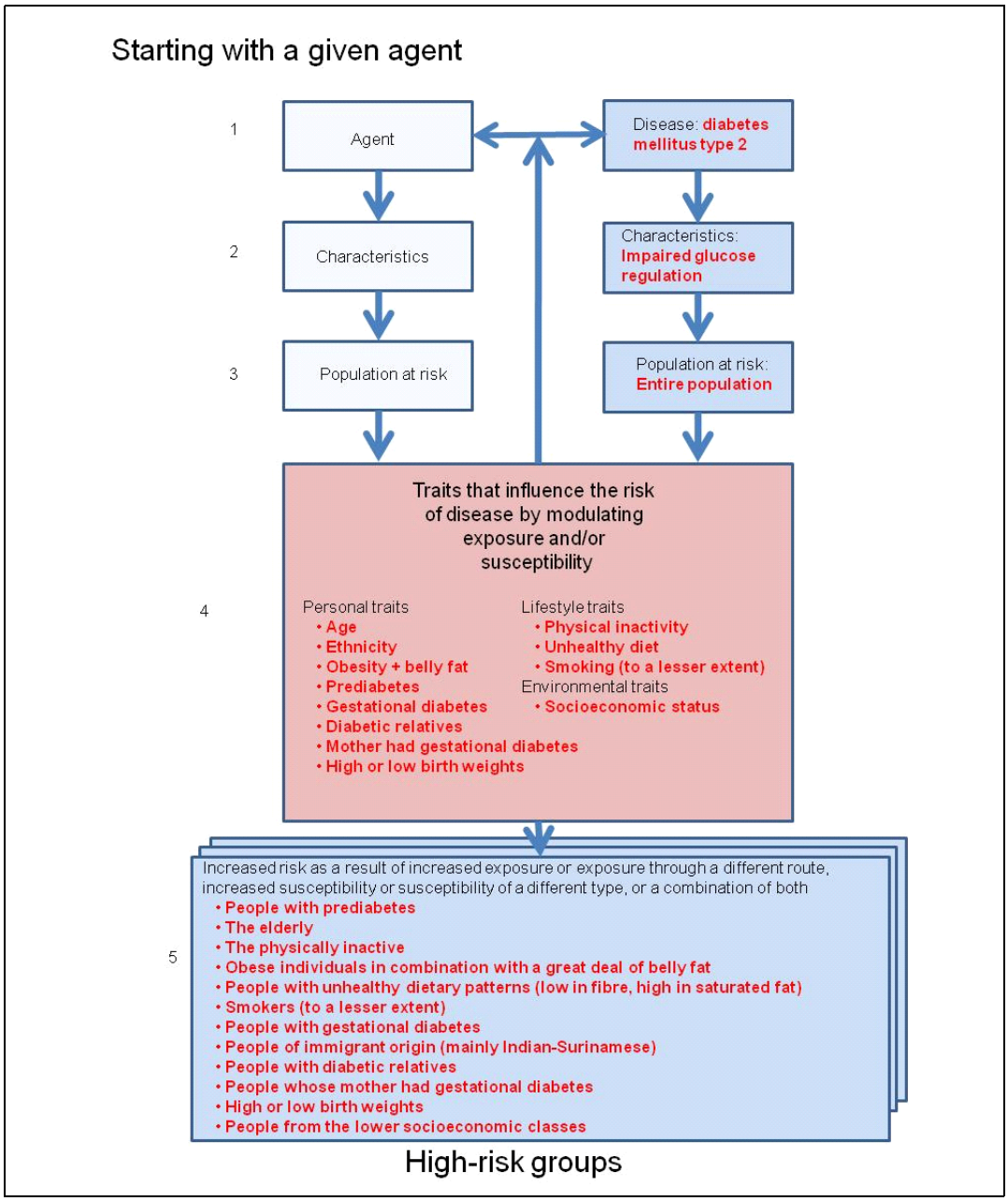

Figure 8 Use of the assessment framework to identify high-risk groups for type 2 diabetes mellitus.

The goals have been translated into an equal number of themes. The first theme is devoted to prevention. It focuses on the design and implementation of an active approach to prevention, with a special focus on the provision of health information about diabetes and early diagnosis. There is also a programme-based range of lifestyle interventions for diabetics, or for those at increased risk of diabetes. In the Netherlands, there are a range of lifestyle interventions. One way to specifically warn people that they may be at increased risk of diabetes is to provide the general public with information about a healthy lifestyle (universal prevention). If people feel that this information applies to them and if – after completing the diabetes Risk Test, for example – they feel that they belong to the high-risk group, their GP can perform additional testing. At that point, people will know whether or not they have diabetes. Another early diagnosis option, the screening of high-risk groups, is yet to be implemented. The programme's objective is to foster research into the usefulness and potential of screening. If individuals are found to have an excessively high fasting glucose level, then steps may need to be taken to improve their lifestyle (indicated prevention). An RIVM inventory of diabetes interventions in the field of prevention and care revealed inconsistencies and deficiencies in terms of supply. For instance, substantial health gains can be achieved for specific high-risk groups such as ethnic minorities and groups from the lower socioeconomic classes, however the range of available interventions is insufficient for this purpose. Moreover, only a handful of interventions are specifically aimed at diabetes prevention. The programme seeks to improve this situation.

6.3 Cervical cancer [94,95]

Characteristics

Cervical cancer is a malignant or invasive abnormality of surface tissue at the junction of the external orifice of the uterus and the cervix. A stubbornly persistent human papilloma virus (HPV) infection is the cause of the disease.[96] HPV infection is common in both men and women. The virus is transmitted by sexual contact.

More than 160 types of HPV have been identified. Not all of these cause cervical cancer. At least fourteen HPV types are carcinogenic. These are designated hrHPV (high-risk HPV).[97] Two of these, HPV-16 and HPV-18 are responsible for the majority of HPV-related cancers, most of which involve cervical cancer. Seventy percent of all cases of cervical cancer are caused by these two types of HPV.

Research shows that approximately 80% of the entire population have, at some time, had an hrHPV infection. The virus is most common in young people. HPV infections are usually relatively short-lived, and symptom free. Prevalence and point prevalence (the number of people infected with hrHPV at any given time) among women initially increase with age. It peaks at approx. 21% between the ages of 18 and 24, then gradually falls until the 45th year, after which it stays below a level of 3%.[98]

Persistent hrHPV infections in women can develop into transforming infections, producing abnormalities in the epithelium at the junction of the external orifice of the uterus and the cervix. At this early stage, the underlying tissue is unchanged. Without medical intervention, only 1% of these "premalignant" anomalies will develop into cervical cancer. The interval between the earliest beginnings and the ultimate development of cervical cancer can be as much as 10-15 years.

The number of women with cervical cancer in the Netherlands has been estimated at about 5,400. Each year approximately 700 women are diagnosed with cervical cancer, mainly in the 30-60 age group. Based on tissue testing, cervical cancer can be broadly divided into two types: squamous cell carcinomas (almost 80% of all new cases) and adenocarcinomas (20%). Symptoms do not appear until the later stages. These involve bleeding, excessive discharge, and pain during intercourse. Each year, between 200 and 250 women die of cervical cancer.

Population at risk

All women

Traits that might influence the risk of disease by modifying exposure or susceptibility

How personal traits influence risk

Cervical cancer is caused by stubbornly persistent human papilloma virus (HPV) infections. Persistent infections sometimes lead to the development of cervical cancer precursors. Cancer precursors can either undergo progression or regression. The risk of progression (or the likelihood of regression) depends on the severity of the abnormality in question. Little is known about the factors that determine the persistence of infections, the development of precursors, or progression. A woman's age does not seem to be of major importance in this

regard. The most likely explanation is that these factors are influenced by the quality of the immune system. The course of an infection is probably decided by the collective effect of various factors associated with the virus and the host. As yet, however, little is known about the nature of these factors and their collective effect.

How lifestyle traits influence risk

Sex at an early age increases the risk of cervical cancer, as the developing cervix is more susceptible to infections. Condom use reduces the risk of HPV transmission by 70%.[99] Condom use also results in fewer abnormalities in a chronic HPV infection, and more often to a complete cure ("clearance") of HPV infection. Even where abnormalities do occur, the precursors of cervical cancer show a greater tendency to regress. Use of the contraceptive pill for periods in excess of five years is probably a risk factor for the development of cervical cancer. Smoking may tend to increase the level of risk involved by impairing local immunity. Having multiple sexual partners increases the risk of cervical cancer. Sexually transmitted diseases (STDs) have the same effect, although nothing is known about the mechanism involved. This may be associated with sexual behaviour, but it is also possible that STDs either increase the risk of acquiring HPV infections or cause them to persist for longer. Alternatively, the key effect might involve a combination of these factors.[100]

High-risk groups

Resulting from increased exposure or exposure through a different route:
- No use of condoms
- Having multiple sexual partners.

Resulting from increased susceptibility or a different type of susceptibility:
- Sex at an early age, as the cervix is more susceptible at that time
- Smoking increases the risk of cervical cancer by impairing the body's ability to clear HPV infections
- Use of medication that adversely affects the immune system.

Resulting from a combination of both (or unclear):
- Women in the 30-40 age group
- Use of oral contraceptives for periods in excess of five years
- STDs.

Policy measures

Population screening for cervical cancer has been carried out in the Netherlands since 1996. Once every five years, women between the ages of 30 and 60 are invited for a smear test. The smear test can detect cervical cancer (and, more especially, its precursors) before any symptoms have appeared. Mortality from cervical cancer can be prevented by the treatment of early-stage cancer, abnormalities, and possible precursors. In 2008, among the group of women to whom invitations were sent, 66% actually participated in the screening-programme. It should be noted that some of the women did not respond to the invitation as they had already had a smear test, on medical grounds, outside the context of the screening programme. Another reason for non-attendance was that the women in question had had a hysterectomy. Since the introduction of population screening, there has been a substantial decline in mortality from cervical cancer.

The fact that cervical cancer is caused by some types of human papilloma virus was only discovered at the end of the 20th century. Vaccines recently became available, since when it has been possible to vaccinate women and girls against the disease. Vaccination against human papilloma virus infections at least provides protection against the high-risk virus types, HPV-16 and HPV-18. Vaccination is certainly useful before individuals become sexually active. This is because such individuals are very unlikely to have previously acquired an HPV infection. Effective protection requires three separate vaccinations against HPV, spread over a period of six months. The Health Council has recommended that all 12-year-old girls should be vaccinated against HPV infections. It has also recommended a one-off, “catch-up” campaign to vaccinate girls aged from 13 to 16.[94] Vaccination was included in the National Immunisation Programme in 2010.

In reaching this decision, a range of factors were carefully weighed against one another. First and foremost, the reduced burden of disease and mortality from cervical cancer has to outweigh any potential, unknown adverse effects of the vaccine in the long term. This was why the Health Council strongly recommended follow-up for all vaccinated individuals. Secondly, in terms of cost-effectiveness, it must comply with the government’s criterion of € 20,000 per QALY. Finally, there must be a clear line of demarcation between the government’s responsibilities and those of individual members of the public. Of relevance here is the knowledge that the risk of cervical cancer is associated with sexual behaviour. It is legitimate to ask whether the active provision of vaccination by the government can be justified, if individuals themselves are

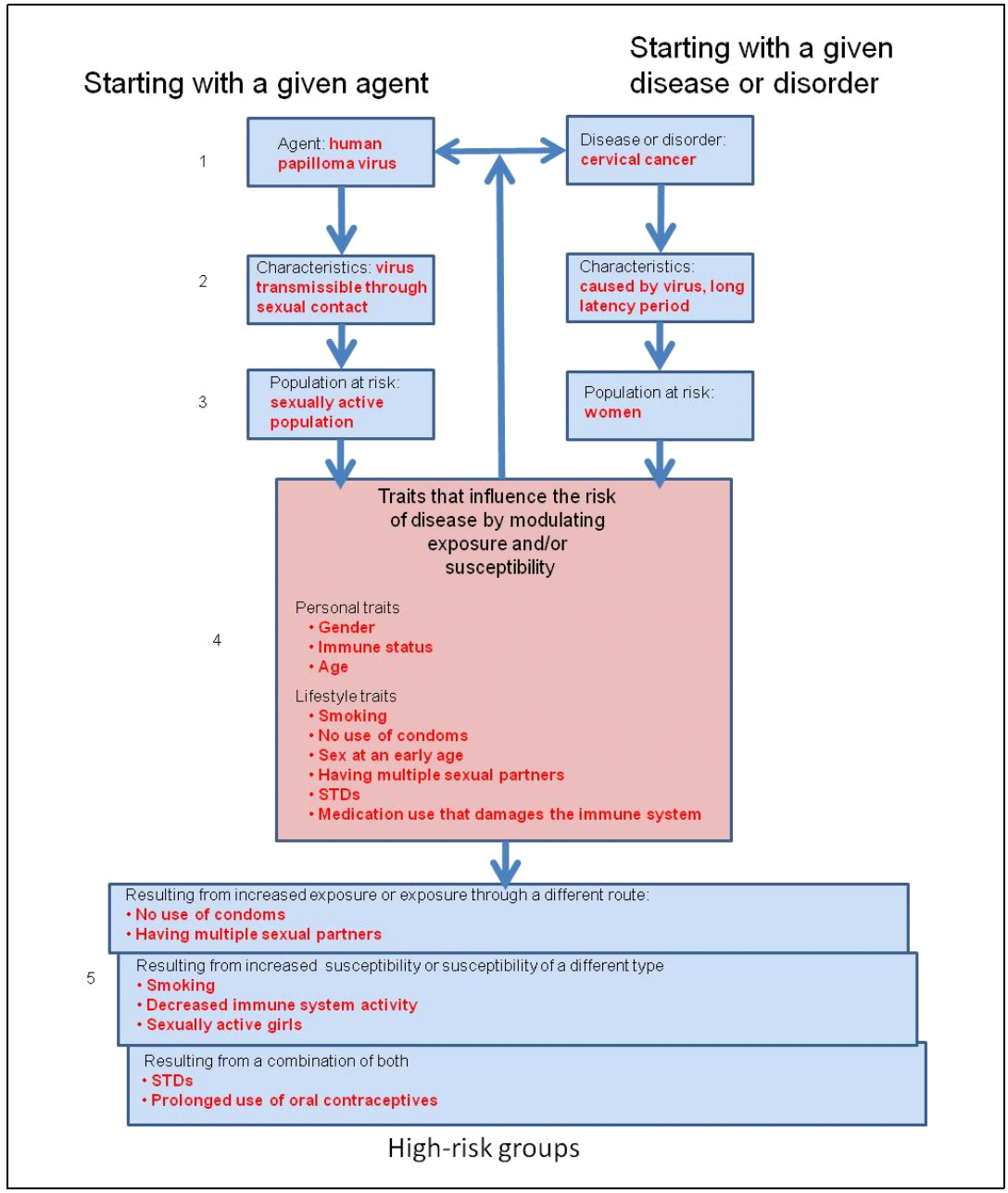

Figure 9 Use of the assessment framework to identify high-risk groups for cervical cancer.

capable of limiting their risk of the disease. One complicating factor in this regard is the limited mental competence of the target group. There are two reasons for the government to take an active role in this matter. Firstly, individuals are exposed to the risk of HPV infection at a relatively early age, and secondly, adolescents take little account of long-term risks. However, this issue of limited mental competence also complicates, in equal measure, the decision of target-group members about whether or not to opt for vaccination.

The Health Council recently recommended that smear-test screening should be enhanced by first testing smears for the presence of hrHPV. If the virus is detected, then a cytological evaluation can be carried out. The Council has called for a greater role for GPs in the process of inviting women to attend for screening. This would help to increase the number of women participating, especially those from ethnic minorities and women of low socioeconomic status. In addition, the Health Council recommends that women who do not respond should be sent a home test kit. Model-based calculations show that this would prevent 330 cases of cervical cancer each year, cutting the number of deaths by 175. As yet, these recommendations have not led to any political decisions. It can be noted here that enhanced screening will reduce the cost-effectiveness of the vaccination programme. Conversely, the vaccination programme will reduce the cost-effectiveness of screening.

6.4 Bisphenol A [101]

Characteristics

The chemical 2,2-bis (4-hydroxyphenyl) propane, or bisphenol A, is used in the manufacture of some plastics (polycarbonate, and epoxy resin), and as an anti-oxidant in others (PVC). Polycarbonate is used in the manufacture of products such as babies' bottles, reusable water bottles, plates, mugs, and storage canisters. One of the many uses of epoxy resins is as the inner lining of food tins or drinks cans. Trace amounts of bisphenol A can migrate from these materials into these food products. In the EU, these materials have been legally approved for use as "food contact materials", which are subject to a migration limit of 0.6 mg/kg food.

Bisphenol A has undergone extensive toxicological testing. The compound has been shown to have endocrine disrupting properties. It can also give rise to epigenetic effects. As a result, the substance is capable of disrupting the ontogenetic development of humans and animals. In the course of *in vitro* studies, studies in experimental animals, and epidemiological studies, exposure

to bisphenol A has been linked to a variety of diseases and disorders that may result from this same disruptive effect. These include prostate cancer, breast cancer, early menarche, diabetes, obesity, and cardiovascular diseases. However, these links have yet to be confirmed.

Population at risk

From a toxicological perspective, the population at risk corresponds to the entire population. This is because everyone is exposed and can potentially suffer health impairment if the exposure in question is high enough. In the United States, this substance was found in the urine of over 92% of the 2,500 individuals examined (aged six and above).[102]

From a disease perspective, the nature of the population at risk depends on the disorder (or disorders) under consideration. For most disorders, the population at risk will correspond to the entire population. In terms of health impairment resulting from disrupted development, the population at risk consists of developing children.

Traits that might influence the risk of disease by modifying exposure or susceptibility

How personal traits influence risk

Age has an enormous influence. Young children in the prenatal and postnatal phases are at particular risk. They have a higher dietary exposure, due to their greater intake of food per kg of body weight. In addition, they use more bisphenol-A-releasing products, especially babies' bottles. To make matters worse, these generally have to be heated as well, which aids the release of this substance. Very young children are also more susceptible. This group's detoxifying enzymes are still not fully effective. Accordingly, model-based calculations show that the concentration of free bisphenol A in their blood can be three times higher than in adults with the same oral exposure per kg of body weight. Finally, their bodies are undergoing all sorts of developmental processes that are susceptible to disruption. In addition to age, genetic factors are involved. There are inter-individual differences in the degree to which enzymes involved in the conversion of bisphenol A are expressed. Furthermore, some of the enzymes involved are polymorphic. This means that there are a variety of different forms, some of which are more active than others.

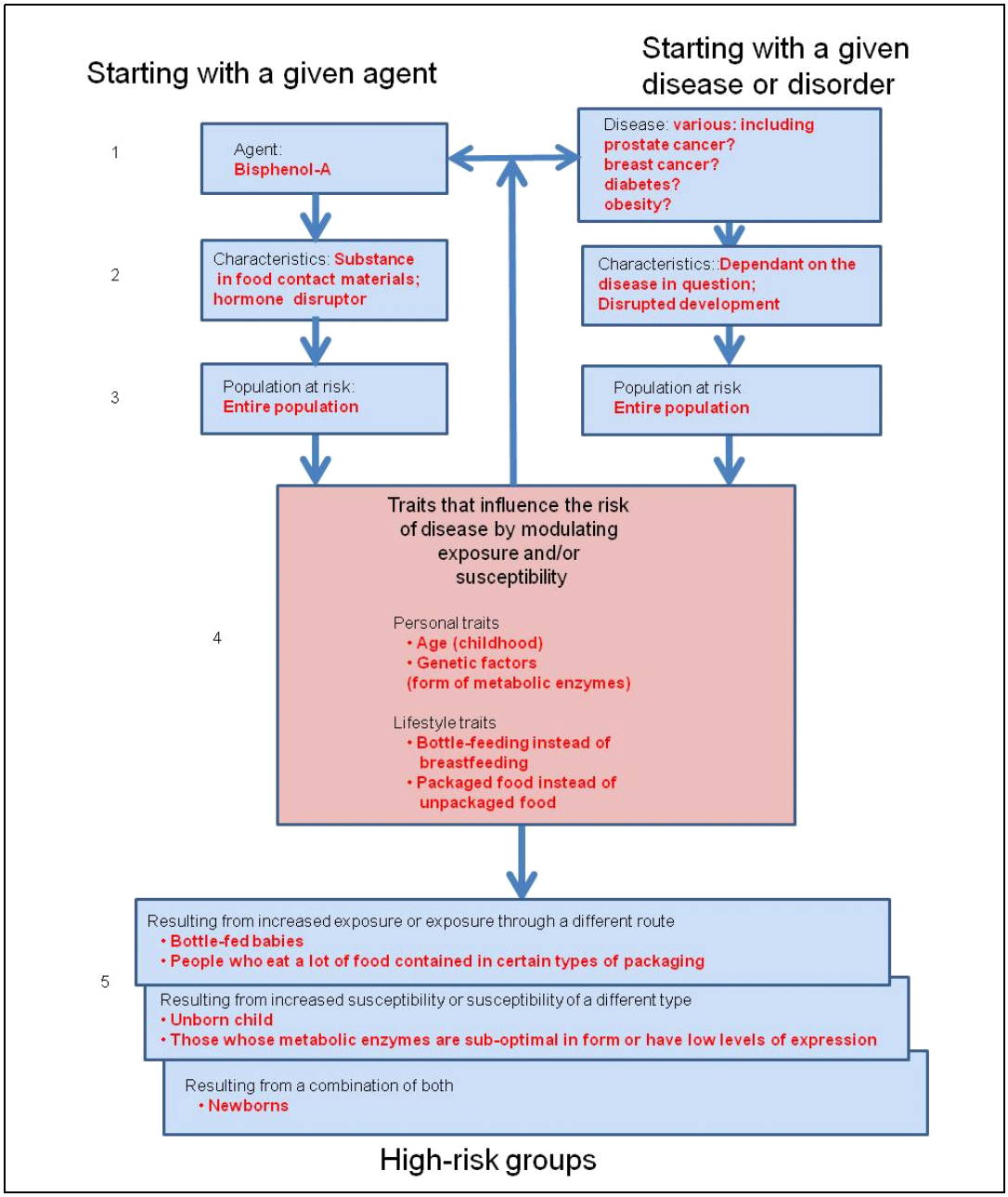

Figure 10 Use of the assessment framework to identify high-risk groups for bisphenol A.

How lifestyle traits influence risk

The use of bottle feeding rather than breastfeeding increases a newborn's exposure. Exposure is also boosted by the frequent use of tinned food or food packaged in polycarbonate.

High-risk groups

Resulting from increased exposure or exposure through a different route:
- Bottle-fed babies
- People who eat a lot of tinned food or food packaged in polycarbonate.

Resulting from increased susceptibility or a different type of susceptibility:
- Unborn child
- Those with a low level of expression of the enzymes involved in the breakdown and excretion of the substance (or with less active forms of such enzymes).

Resulting from a combination of both:
- Newborns.

Policy measures

Given the uncertainties involved, and invoking the precautionary principle, the European Commission recently decided that, with effect from 1 March 2011, polycarbonate may no longer be used in the manufacture of babies' bottles for infants. Moreover, with effect from 1 June 2011, such bottles may no longer be sold.[103] This measure applies to all Member States of the European Union which, of course, includes the Netherlands.

In the next Chapter (which is also the final Chapter), the Committee will explore the value of the assessment framework and the decision framework in terms of identifying, and reaching decisions about, high-risk groups in various policy domains. It will also put forward some policy recommendations.

Chapter 7

Significance of the assessment framework and decision framework for current policy in various domains

In this final Chapter, the Committee discusses the added value of the assessment framework and the decision framework. It also examines dealings with high-risk groups in a way which, while broad-based, makes no claims to be fully comprehensive. The domains involved are environmental policy, working conditions policy, consumer policy, and public health policy. The Committee also indicates what can be added, on the basis of the frameworks presented here.

7.1 Added value of the assessment framework and decision framework when dealing with high-risk groups

The Committee feels that the added value of the assessment framework and the decision framework lies in the structured approach used to identify high-risk groups and to make decisions that will affect them. As discussed in Chapter 4, the assessment framework for identifying high-risk groups deliberately focuses on two approaches in particular. Many policy domains usually adopt a single starting point, either an agent or a disease. The schedule can raise awareness of the other route, or better yet, for a combination of routes. In this way it can also foster cooperation between different disciplines. Furthermore, the assessment framework requires a systematic check of the effects of any relevant personal, lifestyle, and environmental traits that, either separately or in combination, can affect the level of risk in terms of health impairment or disease. This reduces the risk that relevant factors might be overlooked. It could also generate more highly

refined characterisations of high-risk groups than is currently the case. In this way it becomes clear that the greatest increase in risks results from a cumulative effect of adverse personal, lifestyle, and/or environmental factors. One added advantage of this systematic approach is that it uncovers gaps in the requisite knowledge which, in turn, can shape the course of future research.

The decision framework discussed in Chapter 5 serves to illustrate a number of issues, such as the health issues at stake, and how health and disease are distributed across the population. It also indicates what can be said about this, in terms of fairness and the allocation of responsibility. Other highlighted issues include possible courses of action, the effectiveness of individual options, and the costs (in the broadest sense of the word) associated with each of these options. In this way, the framework clarifies the considerations involved and explicitly highlights choices that might otherwise remain implicit. Accordingly, it promotes transparency and provides information for decision-making. This facilitates the process of risk governance by which policymakers reach decisions, during or after consultation with stakeholders.

Both frameworks provide a generic approach applicable to all policy domains that are, in some way, engaged in prevention. The frameworks facilitate a consistent approach to high-risk groups across the various domains while, at the same time, providing sufficient scope for specific choices to be made within individual policy domains.

7.2 Dealing with high-risk groups in various policy domains

In the following subsections, the Committee conducts an exploration of dealings with high-risk groups in the domains of environmental policy, working conditions policy, consumer policy, and public health policy. In this connection, it points out that the lines of demarcation between these domains are by no means always sharp. It addresses both the identification of high-risk groups (a process in which experts take the lead), and the process of decision-making by policymakers. Completeness is not a priority. It is more a question of using examples to briefly show how policy domains can benefit from the proposed approach, what individual domains can learn from one another, and where there are any gaps or blind spots. During the discussion, the Committee regularly refers to the possible courses of action set out in section 5.2. For the sake of convenience, it has presented them again in the box below.

Possible courses of action when dealing with high-risk groups

- Deliberately make allowance for some or all high-risk groups:
  - through the implementation of generic measures that are geared to such groups;
  - through measures (which may be supplementary in nature) specifically targeting some or all high-risk groups.
- Consciously take no account of some or all high-risk groups; generic measures that deliberately offer suboptimal protection (or none at all) to some or all high-risk groups.

7.2.1 *Environmental policy*

A few years ago, to facilitate decision-making in environmental policy, RIVM drew up the Beoordelingskader Gezondheid en Milieu (AFH&E; Assessment Framework for Health and Environment) (see Annex C).[9] The institute has since tested the AFH&E on issues ranging from power lines, mobile phone base stations, Legionella, radon in the indoor environment, fine particulates, and noise from road traffic.[9,104] In previous advisory reports, the Health Council found this tool to be useful for organising all the information in the "Characterisation" stage. It was also found to provide an ordered basis for the "Assess and decide" stage (see Figure 3 on page 31).[17,105] In future, it may perhaps be possible to tailor the AFH&E to decision-making in other policy domains.[24,106] Point II3 in the AFH&E raises the issue of who exactly is affected by health effects. The term "high-risk groups" is added, in brackets. The Committee feels that this question can be effectively answered using the assessment framework for identifying high-risk groups that it has presented. It takes the view that a single disconnected question in the AFH&E about high-risk groups cannot adequately guarantee that high-risk groups will be sufficiently well identified for the purposes of decision-making. The Committee recommends that questions about high-risk groups be much more closely interlinked with the other questions in the AFH&E. This applies both to the questions about the extent and severity of health impairment, and those relating to the intervention options with their associated costs and benefits. This can be achieved by incorporating the assessment framework and the decision framework described in this advisory report into the AFH&E. In Annex C the Committee shows how this could be achieved.

With regard to question I6 of the AFH&E, referred to as Maximum Permissible Risk Level (MPRL), the Commission notes it has now been politically established that, from the standpoint of cost effectiveness and the need for customisation in practice, varying levels of safety will have to be accepted.[24] That means that the outcome of all considerations may sometimes result in policy that takes no account of some (or any) high-risk groups. Such is the case with the policy on overhead power lines and childhood leukaemia, at least in existing situations. [9,107] Nevertheless, in new situations, the appropriate authorities ensure that buildings and overhead power lines are not erected too close to each other. So, in this case, a conscious decision was taken to tailor generic measures to a specific high-risk group.

AFH&E plays no part in environmental policy on substances and chemical products, such as plant protection products and biocides. These are subject to comprehensive, statutory and European-style authorisation or registration procedures for ensuring safety. These are usually based on experimental animal studies, which must then be extrapolated to humans in practical situations. The mandatory toxicological dossier created for the purposes of the assessment should theoretically compensate for possible gender-specific or age-specific health effects, particularly disruptions of the development of the unborn child or young children. In 2004, however, the Health Council determined that it is not possible to entirely eliminate the risk that specific adverse effects on the unborn child or young children (resulting from exposure to the residues of plant protection products) might be overlooked. The effects in question involved the developing nervous system, the developing immune system, and the hormone balance.[10] Work is currently under way, at international level, to address this issue.

Other traits that can affect people's susceptibility to substances include ageing, genetic characteristics, health status and lifestyle. However, our limited understanding of these areas means that studies with a specific focus on such traits are few and far between. These traits can produce substantial variation in terms of susceptibility. Efforts have been made to compensate for this by applying uncertainty factors to a "no effect" level (NOEL; No Observed Effect Level) derived from the toxicological dossier. Using this approach, researchers are attempting to derive a safe level of exposure for the entire population, i.e. including the high-risk groups. It is often assumed that the factors used are sufficient to compensate for virtually all of the variation in susceptibility within the population. However, there is limited evidence to support this view.[32] In particular, age, genetic factors[108,109] and severe pre-existing disease[110] may, in some cases, produce even greater differences in susceptibility.

Under the terms of REACH (legislation regulating the authorisation of chemicals within the EU), requirements concerning the scope of the toxicological studies to be carried out depend on the production or import volumes in question. The underlying concept is that a decline in the amounts of a substance that are manufactured or imported will result in proportional reductions in exposure and, therefore, risk. While that is indeed the case for the population as a whole, the situation may be different for certain subgroups. Small groups of workers involved in manufacturing or processing the substance in question, or small groups of consumers or patients who use products containing this substance, can indeed suffer high levels of exposure. Such groups might include pregnant women, infants or the chronically ill, for example.[111] This criterion derives from the implicit choice not to take possible high-risk groups into account when low production volumes and low import volumes are involved. However, manufacturers are free to take the initiative and submit data on groups of this kind. The Committee favours transparency in this regard.

In addition to data on susceptibility, details of exposure are needed when assessing the risks associated with a given substance. When collecting this data (either by measurement or through the use of model-based calculations), an attempt is usually made to consider personal, lifestyle, and environmental influences.[112] However, this is often made more difficult by the lack of exposure data on subgroups within the population.

7.2.2 *Working conditions policy*

Workers can be exposed to physical, chemical, or biological agents to a greater or lesser degree, depending on the nature of their work. Numerous occupational hygiene regulations have been drawn up, as excessively high levels of exposure can be harmful to health. Various exposure standards also apply. These all take account of high-risk groups, to a greater or lesser extent. For the purpose of illustration, the Committee provides an explanation of how this is regulated in terms of chemical substances.

In the workplace, limit values (previously known as MAC values) govern workers' exposure to substances that can potentially pose a danger to health. These limit values are designed to protect workers and their offspring against health impairment, even those who are exposed throughout their working life. The limit values are basically geared to the resilience of healthy workers.[113] However, the underlying assumption – that only healthy people work – is not in keeping with recent government policy geared towards boosting the employment rate. In the near future, those with occupational disabilities will be expected to

work, in keeping with their ability.[114] Older people are expected to work for longer. [115] The goal is “sustainable employability” until the age of retirement.[116] As a result of these measures, people with chronic disorders will probably come to make up a larger part of the workforce than is presently the case. To some extent, they will be given adapted work, but an increased susceptibility due to greater age, illness, or use of medication may escape notice.

Limit values for substances in the workplace (aside from those substances for which no safe exposure level can be determined, such as genotoxic carcinogens) are derived from health-based recommended exposure limits. These, in turn, are based on published toxicological data from experimental animal studies and/or epidemiological studies. In theory, when deriving these values, both sexes are taken into account, as well as the unborn child (as pregnant women are part of the workforce). The values are not geared to children, however, as they are not part of the workforce. No consideration is usually given to their potential exposure to chemical substances through breastfeeding. As with environmental policy, no other personal, lifestyle, or environmental factors are specifically taken into account. Efforts have been made to compensate for the variations in susceptibility resulting from these factors by applying an uncertainty factor to a “no effect” level of exposure derived from the toxicological data. This usually involves the use of a smaller factor than is the case with environmental policy. The reason for this is that there is less variation in susceptibility within the workforce than in the population as a whole.[117] Accordingly, here too, the general aim is to attune the limit value to the most susceptible group. As with environmental policy, it is not known whether this compensates for the full range of variation in susceptibility (such as that due to genetic factors).

If epidemiological data is available when a health-based recommended exposure limit is being derived for a given substance, then separate data is sometimes available on the susceptibility of smokers and non-smokers to the substance in question. The main reason for collecting this information is not so much the protection of smokers, however, but rather to correct for smoking as a confounding factor. That often leads to situations in which no account is taken of smokers’ increased susceptibility when setting limit values.

7.2.3 Consumer policy (food and non-food)

Food policy focuses both on the safety of food and on its health-promoting qualities. Comprehensive, statutory and European-style authorisation or standard setting procedures are in place to ensure the safety of given levels of plant protection product residues, food additives, and chemical contaminants. This is

in keeping with the Committee's previous comments when discussing environmental policy with regard to chemical substances. Here too, the general goal in standard setting and authorisation is to arrange things in such a way that high-risk groups are also protected. As with environmental policy, the possibility that plant protection product residues may affect the development of the unborn child or children cannot be entirely ruled out.[10] Perhaps as a result of this uncertainty, additional, more stringent rules have been introduced specially for commercial baby foods.

The established Acceptable Daily Intakes (ADIs), on which safety assessments are based, generally relate to healthy individuals.[110,118,124] This means that seriously ill people are implicitly excluded.

Unlike the policy on chemical substances, policy in the area of microbial safety (e.g. *Salmonella*, *Listeria*) has a greater focus on high-risk groups, such as pregnant women, young children, the elderly, and those in poor health. This is because incidence data clearly indicate that these groups are often at increased risk of infection, or that they suffer more severe effects.

Health promotion in the area of nutrition is embodied in the Guidelines for a Healthy Diet and in dietary reference intakes.[125] This identifies nutrients that should ideally be taken daily, giving details of the quantities involved. The goal is to avoid both deficiencies and excess. While the Guidelines apply to healthy individuals, they also form an excellent starting point for patients. Nevertheless, the question of whether additional measures are needed for the latter group is a matter for the medical profession. In the Guidelines, dietary reference intakes are always broken down by age and gender. In many cases there are separate standards for pregnant women, and for women who are breastfeeding infants. In setting these standards an attempt has been made to identify any factors that might give rise to additional requirements. In the case of vitamin D, for example, this has led to a separate, higher standard for dark-skinned people, and for those who spend most of their time indoors, or who wear concealing clothing. If a given disease is known to be directly related to the deficiency of a single nutrient then this is used as the basis for the standard in question. Accordingly, the guideline for vitamin K intake by all infants has been geared to the prevention of bleeding in a small group of children with impaired fat absorption. These children have a greater requirement for vitamin K. This is an example of a generic measure which has been geared to a high-risk group. Obviously, the Guideline has been designed to ensure that healthy children do not ingest a detrimental excess of this vitamin.

Extra folic acid intake during the first weeks of pregnancy is known to cut the risk of a neural tube defect (spina bifida) in babies.[126] The current Dutch policy

of prescribing folic acid tablets to all women who are trying to become pregnant can also be seen as measure targeting the entire population at risk. This focus on the entire population at risk is driven by a poor understanding of risk-enhancing factors in that particular group. One problem with this approach is the poor accessibility of part of the population at risk. The fortification of all bread, bread-replacement products, or flour with folic acid (as in some other countries) is a generic (or even more generic) measure that can overcome that problem. One potential drawback, however, is that there is some evidence that high doses of folic acid may promote the development of cancer, especially in those with undetected precursors of the disease.

The safety of non-food products is guaranteed by the Commodities Act. In theory, this is geared to the target group for whom the products are intended. This is especially true for children, and relates to both chemical and physical/ mechanical safety (e.g. small components breaking off). The range of potential policy interventions include a ban, imposing requirements on labelling (e.g. age indications), instruction leaflets, or manuals. Icons can clarify matters for illiterates and for people who do not speak the language. In some cases, allowance is made for the possibility that products could come into the possession of groups other than the target group, which could be potentially dangerous. One example of this is the use of child-friendly closures on bottles containing chemicals.

7.2.4 Public health policy

The area of public health policy involves a wide range of measures relating to health promotion. In recent years, the government has tackled the obesity epidemic by using public information campaigns that encourage people to adopt a more healthy diet and take more exercise. Rather than specifically targeting obese individuals, these campaigns were aimed at the general population. To date, these campaigns have only had a modest impact. Indeed, the number of obese children and adults is still increasing.

Public information campaigns on safe sex are another example. These mainly target high-risk groups (young people, homosexuals). The government's deterrent policy on smoking largely targets young people. This is because smokers are a major high-risk group for many different health problems, and because they tend to take up the habit before the age of twenty. In practical terms, the policy takes the form of public information campaigns for young people and their parents, and teaching materials for schools.

Within infectious disease policy, both the identification of high-risk groups, and decision-making on such groups have an important part to play. To some extent, the identification of high-risk groups is felt to be less problematic: Registration systems, sentinel practices or notification requirements are used, depending on the disorder in question. These routinely record basic patient data such as gender, age and place of residence. The incidence data will show, almost automatically, if either of the sexes, a specific age group, or the residents of a particular region are at an increased risk of a given disease. Other personal traits, such as health status, lifestyle traits, and environmental traits are regularly used for identification purposes. When it comes to less obvious traits, such as genetic factors, epidemiological studies are needed to highlight the high-risk groups involved.

The measures taken often involve the use of vaccines that specifically target high-risk groups. For instance, there are the vaccinations against seasonal influenza (for the elderly and those in poor health), Q fever (heart patients living in the vicinity of infected goat farms) and Swine Flu from Mexico (young children and those with cardiac and respiratory disorders). For individuals with compromised or vulnerable immune systems, such as newborns, the chronically ill, and the elderly, one alternative to vaccination is cocooning. Here, rather than vaccinating the individuals to be protected, those with whom they come into contact on a daily basis are vaccinated.[119,120]

In the past, the preferred way of dealing with hepatitis B was to restrict vaccination to high-risk groups.[121,122] These groups consisted of the children of mothers who were carriers of the hepatitis B virus, certain patient groups, and behavioural risk groups, as well as medical and paramedical staff. Infants whose parents were from medium-endemic or high-endemic countries were added to this group at a later date. However, some of these groups have proved difficult to reach, and a significant proportion of the burden of disease occurred outside the high-risk groups. As a result, the decision was recently taken to instigate a general vaccination campaign, within the context of the National Immunisation Programme (NIP).

In the case of other infectious diseases, which can theoretically affect anyone and which involve few, if any, additional risk factors, everyone is vaccinated through the NIP. That is already the case with ten childhood diseases. One fringe benefit (provided that there is a sufficiently high level of participation in the programme), is that those who are unwilling to be vaccinated are, to some extent, protected by group immunity. Recently, vaccination against cervical cancer was also incorporated into the NIP. Vaccination is being restricted to girls, as group immunity is not an objective in this case.

Population screening is another area of public health policy that focuses on high-risk groups. Government-organised population screening usually targets a single, specific disease. It is also intended for a defined category of the population, based purely on age and gender (universal screening).[123] These include population screening for breast cancer (once every two years for women aged from 50 to 75) and cervical cancer (the “smear test”, currently once every five years in women aged from 30 to 60). Other forms of screening simultaneously target a range of diseases or risk factors. Take, for instance, screening for metabolic diseases and cystic fibrosis in newborns (the Guthrie test or “heel prick”). These types of screening can be classed as strategies targeting the entire population (including high-risk groups), unless the use of gender and age-based pre-selection is considered to be a high-risk group approach. Cascade screening (selective screening or risk profiling) is a purely high-risk group approach. It primarily involves a search for high-risk groups within an unspecified – or previously specified – target group. This approach is based on risk factors, questionnaires, and – in some cases – additional testing. Such pre-selection can either be disease-specific or it can focus on a range of different disorders that have some risk factors in common.

Selective screening sounds appealing: if the final screening group can simply be limited to a high-risk group, then fewer people will ultimately be exposed to the screening test, and there will be a greater chance of detecting disease. Furthermore, there will be a more favourable relationship between the intended and unintended effects of screening, while the staff costs and material costs involved will be less than in the case of universal screening.[123]

Nevertheless, selective screening has not really taken off in practice. Risk factors other than age and gender are not generally very useful in distinguishing between those who are eligible for screening and those who are not. While risk factors do indeed increase the relative risk, the absolute risk remains low. It is not possible to curtail the final screening group to such an extent that the benefits outweigh the disadvantages of not offering screening to those outside the high-risk groups. Too many cases of disease occur outside the known high-risk groups. From the outset, the option of selective screening has featured in decisions on whether or not to introduce screening programmes for given diseases. To date, however, without success.[123] Nevertheless, it is anticipated that the practice of selective screening will be expanded.[79] A study into the usefulness of screening for type 2 diabetes is currently under way in the Rijnmond region. As part of this study, a high-risk group of individuals who are eligible for diabetes screening is being selected.[79] The chosen selection method

involves sending measuring tapes to everyone over the age of forty and asking them to measure their waist size.

7.3 Conclusion

In many domains, a highly structured and systematic approach is used when assessing the risks of disease or health impairment, and when deciding on possible steps to mitigate the risk involved. Where human diversity is involved, however, there is sometimes a lack of clarity about the extent to which assessment and decision-making take account of certain high-risk groups, and about whether or not these processes are underpinned by conscious choices. Usually the most obvious, potential high-risk groups are considered. This concerns both sexes, and some or all age-based groups (especially the unborn child or young children). The explicit inclusion of other factors peculiar to individuals in assessment and decision-making, such as an individual's genetic (or epigenetic) profile or physical condition, as well as lifestyle factors and environmental factors that could affect risk, occurs only sporadically. This is especially true of policy domains that focus on health protection, such as environmental policy, working conditions policy, and consumer policy. Here, there is no focus on a particular disorder or disease. Potential high-risk groups must be estimated in advance on the basis of data from experimental animal studies. This makes a systematic approach, such as the one proposed by the Committee, even more important. Conversely, public health (which mainly deals with disease prevention and health promotion) does generally focus on a particular disease. The incidence data obtained in this way will, almost automatically, highlight at least some of the high-risk groups.

Health protection is mainly focused on healthy individuals, the philosophy being: "those who are healthy now must stay healthy in future". This explains why scant consideration is given to the possible influence of pre-existing disease on health risks resulting from environmental factors. It is wrongly assumed that only healthy people work. Those who suffer from some diseases and disorders (such as diabetes, asthma or kidney disease) are often able to continue working, and government policy is designed to help them do so.

The authorisation policy for plant protection products, thus also acceptable residue levels in food, are geared to the resilience of healthy individuals. This raises the question of what this means for members of the public with severe metabolic diseases, for example, or for those with liver or kidney disorders.

The elderly too, as a potential high-risk group, are much less evident in the area of health protection than in the area of disease prevention. This could give

rise to a suggestion that the elderly show increased susceptibility to microorganisms but not to substances. As people age, it is not only their immune systems that become less effective. Systems for the detoxification and excretion of harmful substances are similarly affected. The frameworks presented by the Committee are intended to raise questions like these, and to help answer them.

In terms of health protection, overlooking or deliberately ignoring high-risk groups can increase the burden of disease. Conversely, a very strong focus on high-risk groups (especially where generic measures are involved) may have an adverse effect on efficiency. The opposite appears to be true in the case of disease prevention and health promotion. While overlooking high-risk groups reduces efficiency, an overly strong focus on them can also result in an additional burden of disease outside such groups.

We still know relatively little about human diversity, and especially about its impact on health risks. What we do know is mainly restricted to the average member of the public, " Mr Average", to use Rose's term. Information needed to take certain groups (factors) into account is often found to be lacking. The Committee takes the view that this should be reason enough to launch a research effort. The assessment framework presented here provides the structure needed to highlight such gaps in our knowledge.

The Committee concludes its advisory report by noting that the identification and decision-making processes relating to high-risk groups are dynamic and iterative in nature. One reason for this is that new knowledge can cast fresh light on high-risk groups. Another is that, in a society that is constantly changing, normative views about the weighing of costs and benefits, the just and fair distribution of advantages and drawbacks across communities, and the allocation of responsibilities to government bodies, businesses and individuals are similarly not set in stone. These two frameworks presented by the Committee can assist in gathering and organising any available information and in clarifying the pros and cons involved. This does not make the deliberations themselves any easier, however. The Committee feels that the most appropriate approach would involve a process of governance, in which the government reaches a decision either during – or following – consultations with stakeholders. However, an in-depth consideration of how this should be organised is beyond the scope of the present advisory report.

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Annexes

Annex **A**

The request for advice

On 10 June 2005, the President of the Health Council received a request from the Minister of Health, Welfare and Sport for an advisory report on a decision framework for high-risk groups. The Minister wrote (letter VGP/P&L 2581995):

Both politically and socially, there is an increasing focus on specific policies for separate high-risk groups with a potentially higher degree of vulnerability. The goal of health policy is to protect all members of the public, including specific high-risk groups who may be more susceptible (those in poor health, children, pregnant women, the elderly), or who may have different dietary habits or lifestyles (e.g. members of ethnic minorities). This is considered separately for each policy domain.

Based on environmental and consumer policy, the Ministry of Health Welfare and Sport and the Ministry of Housing, Spatial Planning and the Environment (VROM) want to achieve a more consistent approach to the protection of public health (including potential high-risk groups) across the range of policy dossiers. The above high-risk groups make up a large part of society, so it is of great social importance that the policy should take them into account. A uniform approach would be most helpful in this regard.

The State Secretary for the Environment and I would like to ask you to draw up an assessment framework that can be used to develop a reasoned argument for classifying a particular group within society as a high-risk group. To this end, it is also necessary to define exactly what is meant by a the term “high-risk group”.

The Health Council is also asked to draw up a decision framework, for use when a specific policy domain needs to take a given high-risk group into account.

We have the following specific questions on this matter:

Feasibility: Do we currently have the scientific knowledge required to establish such a uniform assessment framework, for assessing the validity of high-risk groups? Is it possible to create a decision framework that uses a uniform approach to determine whether any specific high-risk groups need to be taken into account when drawing up policies or measures?

What type of assessment framework would be needed to determine whether specific high-risk groups exist? What criteria or factors are involved? These could include factors such as exposure, the occurrence of health effects, or estimates thereof, additional factors (physical or behavioural) capable of boosting exposure, risk or susceptibility in specific groups. The framework would also have to allow for the accumulation of multiple stressors. What high-risk groups can be defined?

What aspects/considerations/criteria are important if a decision framework is to determine when policy domains need to give greater consideration to one or more specific high-risk groups. What type of decision framework would be needed to determine this, in a uniform way, across a range of different policy domains?

With regard to environmental and consumer policy, can you identify any relevant policy domains that, according to the general decision framework that you have created, need to take specific risk groups into account? The objective here is to ensure that future policy will provide protection to every member of the public, including these special high-risk groups. Will you also use the assessment framework to identify the specific high-risk groups that would be involved in these policy domains? Given the wide scope of the current request, the Health Council is asked to apply the assessment and decision framework to some specific cases that are of relevance in terms of environmental policy and health policy.

In the advisory report, could you give details of how the policy approach should be geared to allow for specific high-risk groups? Please give a general indication of the consequences in areas such as risk assessment, standard setting, dealing with situations that are in breach of standards, and communications aimed at specific high-risk groups.

The current request is clearly related to the “Health and Environment” assessment framework, to your 2004 advisory report on “Pesticides in food: assessing the risk to children” and to the “Coping rationally with risks” memorandum. Furthermore, in 2005, RIVM drew up an advisory report in

which it listed national and international trends in the risk assessment for children with regard to chemical substances.

Please incorporate relevant aspects of the above subjects when drawing up the advisory report. In view of the importance of this subject, I would be grateful if you would issue your advisory report no later than mid-2006.

Yours sincerely,

The Minister of Health, Welfare and Sport
(signed)
H. Hoogervorst

Annex **B**

The Committee

- Prof. W.R.F. Notten, *Chairman*
  Professor of Health Management, Institute of Health Policy and Management, Erasmus University, Rotterdam
- Dr. R.A. Bausch-Goldbohm
  Epidemiologist, TNO, Leiden
- Prof. F.W.A. Brom (until 02/20/2008)
  Professor of Ethics in the Life Sciences, Wageningen University and Rathenau Institute, The Hague
- Dr. M.N. Pieters
  Risk assessor, Director of Public Health and Care, National Institute of Public Health and the Environment, Bilthoven
- Prof. P.J.J. Sauer
  Emeritus Professor of Paediatrics, University Medical Center, Groningen
- Prof. F.J. van Schooten
  Professor of Genetic Toxicology, University Medical Center, Maastricht
- Prof. K. Stronks
  Professor of Social Medicine, Academic Medical Center, Amsterdam
- T. van Teunenbroek, *observer*
  Ministry of Infrastructure and the Environment, The Hague
- Dr. M.F. Verweij (from 28/07/2009)
  Ethicist, Ethics Institute, Utrecht University

- Dr. M.E.J. van der Weiden, *observer*
  Ministry of Health, Welfare and Sport, The Hague
- Dr. P.J.J.M. Weterings
  Toxicologist, Weterings Consultancy BV, Rosmalen
- Prof. F.A. de Wolff (until 13/09/2010)
  Emeritus Professor of Clinical and Forensic Toxicology, Leiden University Medical Center, Leiden
- Dr. H.F.G. van Dijk, *Scientific secretary*
  Health Council of the Netherlands, The Hague

The Health Council and interests

Members of Health Council Committees are appointed in a personal capacity because of their special expertise in the matters to be addressed. Nonetheless, it is precisely because of this expertise that they may also have interests. This in itself does not necessarily present an obstacle for membership of a Health Council Committee. Transparency regarding possible conflicts of interest is nonetheless important, both for the chairperson and members of a Committee and for the President of the Health Council. On being invited to join a Committee, members are asked to submit a form detailing the functions they hold and any other material and immaterial interests which could be relevant for the Committee's work. It is the responsibility of the President of the Health Council to assess whether the interests indicated constitute grounds for non-appointment. An advisorship will then sometimes make it possible to exploit the expertise of the specialist involved. During the inaugural meeting the declarations issued are discussed, so that all members of the Committee are aware of each other's possible interests.

Annex **C**

Modified Health and Environment Assessment Framework

The Health & Environment Assessment Framework developed by RIVM[9] and the Health & Environment Assessment Framework modified by the Committee.

The Health & Environment Assessment Framework developed by RIVM.[9]

I Scope of health impairment	II Severity of health impairment	III Assigning values to the effects or risks	IV Intervention: opportunities or necessity	V Costs and benefits
I1. How many individuals are exposed?	II1. Which diseases or symptoms are involved, what is known about the effects of this type of exposure?	III1. Does the risk threaten people's sense of security?	IV1. Do standards or requirements (European or otherwise) necessitate intervention?	V1. What are the costs of retaining current policies unchanged?
I2. How many individuals become ill or develop symptoms?	II2. What health effects do the residents or victims themselves attribute to the exposure in question?	III2. Is the risk voluntary and/or manageable?	IV2. Is intervention possible? • at source or at the recipient • at European, national, regional, local level • economic, technical, spatial, subsidies, legal, information provision	V2. Are there any details of the likely budget for such measures?
I3. Is this figure likely to change in the future?	II3. Who (high-risk groups?) is suffering these health effects?	III3. Are there any other reasons why some consider the risk involved to be unacceptable?	IV3. Which bodies are responsible for intervention measures? Which ones are advocated?	V3. What would risk reduction or risk avoidance measures cost?
I4. Does the risk exceed the accepted Maximum Permissible Risk Level?	II4. How often do health effects occur (regularly, occasionally, constantly)?		IV4. How effective are these in theory, with regard to exposure reduction or disease prevention?	V4. How does that compare to other forms of health gains?
I5. How firm is the relationship between exposure and health effects?	II5. Is treatment possible?		IV5. How effective are they in practice, how soon can results be expected, how great is the pressure to falsify results, is enforcement possible?	V5. Will the measures have any desirable effects in other policy domains?
I6. Of the total number of cases of disease, how many can be attributed to this exposure?			IV6. Is there any current or anticipated social or political pressure?	V6. Will the measures have any adverse effects in other policy domains?

First part of the Health & Environment Assessment Framework[9] supplemented with questions for decision-making on high-risk groups (amendments and additions are shown in italics).

I. Scope of health impairment	II. Severity of health effects
I1. How many individuals will be exposed *or will be at risk of exposure?* • *Are there any subgroups that have higher levels of exposure or that are exposed via another route or that are at greater risk of exposure?* • *How large are these subgroups?*	II1. Which diseases or symptoms are involved, what is known about the effects of this type of exposure? • *Do the diseases or symptoms affect high-risk groups in a different way or to a different degree?*
I2. Are there any subgroups with increased susceptibility or with a different type of susceptibility? • *How large are these subgroups?*	II2. What health effects do the residents or victims themselves attribute to the exposure in question?
I3. *How many people are at risk of developing symptoms or becoming ill?* • *Do those at risk belong to certain subgroups?* • *How large are these high-risk groups?*	II3. *[Now question I4.]*
I4. How many individuals *actually* become ill or develop symptoms? • *Do those who actually become ill or develop symptoms belong to certain high-risk groups? [This is actually question II3 of the original AFH&E]* • *How large are these high-risk groups?*	II4. How often do health effects occur (regularly, occasionally, constantly)? • *Does this vary from one high-risk group to another?*
I5. *Are these figures likely* to change in future?	II5. Is treatment possible? • *Does this vary from one high-risk group to another?*
I6. Does the risk exceed the accepted Maximum Permissible Risk Level? • *for the entire exposed population?* • *for the various high-risk groups?*	
I7. How firm is the relationship between exposure and health effects?	
I8. Of the total number of cases of disease, how many can be attributed to this exposure? • *within the entire population?* • *within the various high-risk groups?*	

Second part of the Health & Environment Assessment Framework[9] supplemented with questions for decision-making on high-risk groups (amendments and additions are shown in italics).

III. Assigning values to the effects or risks	IV. Intervention: opportunities or necessity	V. Costs and benefits
III1. Does the risk threaten people's sense of security? • *Does this differ for high-risk groups in particular?*	IV1. Do standards or requirements (European or otherwise) necessitate intervention?	V1. What are the costs of retaining current policies, unchanged?
III2. Is the *cause* of the risk in question *natural, other individuals, or people themselves* (voluntary), is it manageable?	IV2. Is intervention possible? • at source or at the recipient • *in the area of exposure or susceptibility* • at European, national, regional, local level • economic, technical, spatial, subsidies, legal, information provision	V2. Are there any details of the likely budget for such measures?
III3. Are there any other reasons why some consider the risk involved to be unacceptable? • *Do some consider the higher risk for high-risk groups to be unfair?*	IV3. Which bodies are responsible for intervention measures? Which ones are advocated? • *generic measures, not geared to high-risk groups?* • *generic measures geared to high-risk groups?* • *specific measures targeting high-risk groups?*	V3. What would various risk reduction or risk avoidance measures cost?
	IV4. How effective are these in theory, with regard to exposure reduction or disease prevention, *also for high-risk groups in particular?*	V4. How does that compare to other forms of health gains?
	IV5. How effective are these in practice, *also for high-risk groups in particular?* • *are the individuals in high-risk groups identifiable and accessible?* • How soon can results be expected, how great is the pressure to falsify results, is enforcement possible?	V5. Will the measures have any desirable effects in other policy domains?
	IV6. Is there any current or anticipated social or political pressure?	V6. Will the measures have any adverse effects • *on health, or on any other interests of high-risk groups?* • *on health, or on any other interests of other individuals?* • *for the autonomy of high-risk groups or other individuals?* • *in connection with drawbacks associated with the individual identification of members of high-risk groups?* • in other policy domains?