Follow-up advisory report on crop protection and local residents

To the Minister for Medical Care and Sport, the Minister of Agriculture, Nature and Food Quality, and the State Secretary for Infrastructure and Water Management

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Health Council of the Netherlands

contents

executive summary

As a follow-up to the Health Council of the Netherlands' 2014 advisory report on the health risks posed by the use of plant protection products to those living in the vicinity of agricultural land, a major exposure study (Research on exposure of residents to pesticides in the Netherlands, or OBO) and a health survey were carried out. At the request of the Minister for Medical Care and Sport, the Minister of Agriculture, Nature and Food Quality, and the State Secretary for Infrastructure and Water Management, the Health Council is once again issuing an advisory report on the current state of knowledge concerning the health risks of exposure to plant protection products.
The members of the government specifically asked whether additional research is needed to gain an insight into these health risks, whether the approval procedure for plant protection products needs to be modified, and whether there is a relationship between the use of plant protection products and Parkinson's disease. A new committee, whose members are experts in the relevant fields, has addressed these questions.

Research indicates that plant protection products do pose health risks

The international epidemiological literature indicates that the use of chemical agents for plant protection can be associated with impaired human health. For instance, links with Parkinson's disease have been found. A link has also been found between prenatal exposure to plant protection products and developmental disorders in children. In such studies, however, the measurements of exposure are often inaccurate. As a result, little is known about the exact level of risk involved, and about which plant protection products are responsible. Experimental animal studies and research into mechanisms of action have produced plausible evidence of links between exposure to plant protection products and Parkinson's disease and developmental disorders in children.

While recent Dutch studies have not yielded any clear evidence of health effects, this has done nothing to allay these concerns. These Dutch epidemiological studies are limited in scope. Furthermore, the weak evidence of effects in some of these studies is in line with findings in other countries. In the Committee's view, the conclusion that exposure to chemical plant protection products poses a health risk is justified. However, the level of risk associated with current Dutch agricultural practice is unclear. What is clear is that, on average, local residents – especially growers and their families – are subjected to greater exposure than those who do not work in agriculture, and who live further away from agricultural land. To what extent this poses a greater health risk to these

population subgroups in the Netherlands remains uncertain.

Approval procedures can never fully eliminate risks

Before they can be used in practice, plant protection products must undergo an extensive approval procedure (based on European legislation), which includes the assessment of health risks. This is based on a conservative exposure estimate and on health-based limit values derived from experimental animal studies. Since 2014, the procedure has included a separate assessment of the risks posed to non-occupational bystanders and to those living in the vicinity of agricultural land. However, an approval procedure can never fully eliminate the risk of health impairment. The procedure is known to suffer from the shortcoming that it does not adequately cover the risks to unborn children and young children. The same applies to neurological disorders that occur later in life, such as Parkinson's disease. Nor can the current procedures accurately assess the risks of exposure to a single substance from several different sources, or those posed by simultaneous exposure to more than one substance.

Enhancing sustainability is progressing slowly, and there is too little emphasis on safe working practices

Various laws and rules set out regulations for the safe use of plant protection products in everyday practice. In addition, information is provided and various government agencies carry out inspections. The government endeavours to reduce our dependence on chemical agents and to replace those that have high acute toxicity with less toxic alternatives.
A recent policy review showed that these efforts to enhance sustainability have not, as yet, been particularly successful. Moreover, it has been found that growers do not consider safe working practices to be a priority. In addition to impacting their own safety and that of their employees and family members, this also poses increased risks to local residents.

Recommendations

Apply the precautionary principle – intensify the pursuit of sustainability

The Committee does not expect further epidemiological health research to clarify the health effects of plant protection products in the near future. This is especially the case for chronic health effects that only manifest themselves in later life. The approval procedure needs to be improved, but that is a complex undertaking and will take a great deal of time. For that reason, the Committee advocates application of the precautionary principle.
In particular, it recommends that efforts to render crop protection more sustainable should be continued and intensified. The guiding principle here is to aim for the lowest possible exposure to chemical plant protection products. Where the use of these substances is unavoidable, the least harmful variant should be selected. Strict compliance with regulations is required.
There is an ongoing need for education and enforcement. It is recommended that both of these strands should be enhanced.

Health research

In the long run, the Committee believes that additional epidemiological health research is likely to generate valuable insights. This is conditional on the researchers' ability to accurately determine people's exposure to chemical plant protection products. For example, the Committee feels that it might be feasible to set up a prospective cohort study into developmental effects in children. That would involve monitoring a group of children for an extended period of time.

Monitoring use and exposure

The Committee recommends that efforts should be made to monitor use and exposure more effectively. This would spotlight the effectiveness of policy aimed at reducing the use of chemical plant protection products. In the longer term, the data obtained could be used to enhance health research.

- The Committee recommends that the plant protection monitor be expanded and transformed into a reliable, uniform, national registration system for the use of chemical plant protection products by growers, at the level of individual agricultural plots.
- The Committee also recommends that a biomonitoring programme be established, to periodically measure human exposure. Such testing would be based on the presence of metabolites in urine, for example. This reveals an individual's total exposure to specific chemicals, from different sources and via various routes. Biomonitoring can also help to make growers more aware of the risks involved. Indeed, if biomonitoring were to be implemented simultaneously in several European states, this would ultimately provide a reliable picture of exposure. It would also reveal any spatial and temporal variation within this overall picture. Furthermore, this body of information could ultimately be used to enhance epidemiological research and to more accurately assess the health risks involved in the Dutch situation.
- The exposure study in the bulb cultivation sector has led to a better understanding of the relative importance of the various routes by which local residents are exposed. It is recommended that checks be carried out to determine whether these findings are representative of other crops. For instance, the fruit growing sector, where plant protection products are sprayed sideways and upwards. Research into the effectiveness of measures to control emission and exposure is also useful.

Improving the approval procedure

The Committee recommends that further international efforts be made to improve the approval procedure. In particular, this should involve the assessment of potential effects on brain development in unborn children and young children, and the risk of neurodegenerative disorders, such as Parkinson's disease. In any approval system for individual products, it is difficult to allow for the risks arising from exposure to substances from different sources

or from combinations of substances.
The Committee takes the view that a pragmatic solution would be to introduce an additional safety factor ('allocation factor'). The purpose of this factor (whose magnitude is yet to be determined) is to reduce the risk of health impairment posed by combined exposure to substances from different sources and routes (work, environment, diet, private use) and to combinations of plant protection products.
The Committee recommends that, within the wider context of the EU, the Netherlands should actively endeavour to introduce a factor of this kind into the approval procedure.

Encourage collaboration
Finally, the Committee recommends that stakeholders should be encouraged to exchange knowledge and views, and to collaborate with one another. Subject to certain conditions, it might be helpful to establish a knowledge platform for this purpose. A platform of this kind could enable the parties involved to cooperate with experts in the implementation of a biomonitoring programme, for example.

01 introduction

1.1 Background

In the Netherlands, many people live close to agricultural land. In rural areas, 30% of the population lives within 250 metres of an agricultural field. That figure is 18% if grasslands are not taken into account.[1] These fields are regularly treated with chemical agents, for the purpose of pest control. The bulb cultivation sector and the fruit growing sector make particularly extensive use of plant protection products. Furthermore, in the latter sector, it is common practice to spray sideways and upwards instead of downwards. According to the National Institute for Public Health and the Environment (RIVM), about 90,000 people live within 50 metres of a field of flower bulbs or fruits.[2] In 2011 and 2014, at the request of the Minister of Infrastructure and the Environment and the Minister of Economic Affairs, Agriculture and Innovation, the Health Council issued advisory reports on the potential health risks posed by the use of plant protection products to those living in the vicinity of agricultural land.[3,4] The Council's main recommendation at the time was that exposure studies should be conducted, as the information these provided could be used to make a more detailed assessment of the risks involved. The Council felt that the time was not yet ripe for an investigation into possible health impairment. It recommended that any decision on this subject should be postponed until the results of the exposure study were available.

The government adopted the Council's recommendations and launched a large-scale, long-term exposure study into the bulb cultivation sector, the Research on exposure of residents to pesticides in the Netherlands (OBO). At the same time, the government wanted research into potential health effects to start immediately. Accordingly, in the summer of 2018, RIVM, Utrecht University, and the Netherlands Institute for Health Services Research (NIVEL) published a health survey.[5] The results of the exposure study were published less than a year later.[1,6] The results of the OBO triggered several additional analyses in the context of the health survey.

1.2 Request for advice

The availability of Dutch research data and the differences in their interpretation by various stakeholders[7] and authorities prompted the government to once again approach the Council for advice concerning the health risks posed by the use of plant protection products to those living in the vicinity of agricultural fields. The Minister for Medical Care and Sport, also acting on behalf of the Minister of Agriculture, Nature and Food Quality and the State Secretary for Infrastructure and Water Management, asked the Council to report on the current state of knowledge concerning the health risks of exposure to plant protection products. Is additional research needed to quantify these risks and, if so, how does this research need to be structured? The Minister also enquired about the extent to which the authorisation policy for plant protection agents needs to be revised, in particular for the protection of vulnerable groups such as children and pregnant women, and with a view to the cumulative effects of several plant protection products. The Minister asked the Council to take

the current policy context into account when preparing this report, and to include the OBO's research results and those of the updated health survey. The full text of this request for advice can be found at www.gezondheidsraad.nl.

Following a general consultation on crop protection in the House of Representatives, the Minister of Agriculture, Nature and Food Quality also requested the Council to explore the possible relationship between Parkinson's disease and the use of plant protection products. This request also relates to the health of growers themselves.

1.3 The Committee

The Health Council's 2011 and 2014 advisory reports were drawn up by the former Committee on 'Crop Protection and Local Residents'. Since then, various members of this committee have been closely involved in the implementation of the exposure study or the health survey. A new Committee on 'Crop Protection and Local Residents' was set up to answer the Ministers' questions. Its members are experts from relevant fields and with a variety of perspectives. The aim is to assess the value of the research results from a fresh and independent viewpoint. A list of this Committee's members can be found at the end of this advisory report. Unless expressly stated otherwise, the phrase 'the Committee' hereinafter in this advisory report refers to this new committee.

1.4 The Committee's mission statement, terminology, and methodology

1.4.1 Mission statement

In addition to answering the government officials' questions, the Committee wanted to respond to recommendations made by the researchers who carried out the health survey and the OBO. It has also tried to meet the information needs of stakeholders as fully as possible. Finally, in the light of the available knowledge and the remaining uncertainties, it wanted to propose various possible courses of action.

In this advisory report, the Committee has confined itself to chemical plant protection products that are used for agricultural purposes. No account has been taken of biological and microbiological plant protection products. With regard to chemical agents, this advisory report does not confine itself solely to products that are sprayed, but also to products that are applied in other ways, such as injection into the soil, spreading as granulates, or fogging. For the sake of convenience, the Committee occasionally uses the terms 'sprayed' fields or 'sprayed' fruit and vegetables, without wishing to exclude other methods of application. The Committee focuses on all types of plant cultivation within the agricultural sector.

The focus was on the exposure experienced by, and any potential effects on, those living in the vicinity of agricultural fields that have been treated with plant protection products. Here too, it is sometimes necessary to

consider the exposure experienced by occupational or private operators and by those who consume sprayed fruit and vegetables. After all, growers and consumers may also be local residents. Thus, a given individual may have been exposed to the same substances from different sources and via different routes. Accordingly, it is important to view the exposure from the adjacent arable field from the perspective of total exposure.

The Committee has limited its focus to the health aspects of the issue. It is aware that there are also ecological, agricultural and economic aspects to consider in the decision-making process.

1.4.2 Terminology

Like its predecessor, the Committee is aware that different stakeholders use different terms for the same chemical products. These different terms reflect the divergent perspectives of the various stakeholders. Farmers and manufacturers see these products as a useful means of protecting valuable crops, in which a great deal of money and effort have been invested. Local residents, on the other hand, see them as poisons that are carried away from farmers' fields on the wind, and that threaten their own health and that of their families. The Committee has no preference concerning these terms or the associated perspectives. For the sake of clarity and consistency, the Committee has chosen to use the term that is used in relevant legislation and, accordingly, in the request for advice as well: 'plant protection products'. The Committee is at pains to point out, however, that by opting for certain terms it in no way wishes to undermine the validity of the other terms and perspectives.

The Committee has used the terms 'plant protection product' and 'local resident' in the same way as in the previous advisory report:

- Plant protection product: an active ingredient or a preparation containing one or more active substances to be used in order to: 1) protect plants or plant products from all harmful organisms or prevent such organisms from inflicting harm; 2) influence the living processes of plants, but without involving any nutrients; 3) store vegetable products; 4) kill unwanted plants or 5) destroy parts of plants or prevent or inhibit the unwanted growth of plants.
- Local residents: persons who live, work or attend school or any another institution adjacent to a field that is or has been treated with a plant protection product (PPP); whose presence is quite incidental and unrelated to work involving PPPs but whose position might lead them to be exposed; who take no action to avoid or control exposure; and who might be in the location for 24 hours per day. The Committee includes farmers and growers themselves, and their families, in the category of 'local residents', inasmuch as they live near treated fields.

1.4.3 Methodology

The Committee has considered what can be added to the Health Council's 2014 advisory report, based on the results of the health survey, the exposure study, and recent scientific publications. The Committee was given access to the preliminary results of additional analyses within the health survey (the most recent version, that of 14 February 2020).[89] The final results will be published later this year. It has also identified the remaining gaps in our knowledge and the extent to which these can be filled by means of additional research.

The epidemiological and toxicological literature on plant protection products is too extensive to study in its entirety and in depth. In addition, part of the research involves confidential commercial information. Thus, to answer the question of whether there is generally a non-negligible risk to the health of local residents and growers, the Committee has opted for a pragmatic approach. Based on a number of recent reviews, it outlines our current understanding of the health effects caused by plant protection products. It then zooms in on the current level of knowledge regarding their relationship to Parkinson's disease and effects on the neurological development of young children. To this end, it has systematically searched the scientific literature for any meta-analyses and systematic reviews on these disorders that have been published since 2013. Finally, it systematically searched for articles published since 2013 about Dutch epidemiological research into the effects of plant protection products on growers, local residents, and the general population. Based on the results of experimental animal studies and mechanistic studies, conclusions have been drawn concerning the plausibility of health effects.

With regard to the approval procedure for plant protection products, the Committee has identified the modifications made since the 2014 advisory report. It has also explored further proposals for modifications that are currently being discussed in a European context. The Committee has addressed the remaining sticking points with regard to approval and potential solutions for the near future.

The Committee held a hearing, at which invited stakeholders were given an opportunity to comment on the new research results, indicate what further information they need, and identify what they see as useful follow-up steps. A list of the hearing's participants, together with a report of their presentations can be found at www.gezondheidsraad.nl. The Committee also consulted various experts, including two researchers involved in the health survey and the OBO. Their names are listed at the back of this advisory report. Finally, the Committee has consulted the Health Council's permanent Committee on Ethics and Law. A draft version of the advisory report has been reviewed by the Health Council's standing committee, and its comments have been incorporated into the final version.

1.5 Reading guide

In Section 2, the Committee discusses the known health risks of plant protection products. Next, in Section 3, it explores the approval procedure for chemical plant protection products. In Section 4, it examines the use of such products in practice. In Section 5, the Committee formulates its recommendations.

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health risks posed by the use of chemical plant protection products

In the international literature, links have been found between exposure to plant protection products and Parkinson's disease, as well as to developmental disorders in children. While recent Dutch studies have not yielded any clear evidence of health effects, this has done little to allay these concerns. This is due to the limited scope of these studies, some of which produced some evidence of effects, albeit weak. What is clear is that, on average, local residents – especially growers and their families – are subjected to greater exposure than those who do not work in agriculture and who live further away from agricultural fields. Whether or not this poses a greater health risk to these population subgroups in the Netherlands remains uncertain.

What is clear, however, is that an increasing number of disorders exhibit positive associations with exposure to plant protection products and biocides. These findings are supported, to varying degrees, by the results of experimental animal studies and mechanistic studies. These include various forms of cancer, neurodegenerative diseases such as Parkinson's disease, amyotrophic lateral sclerosis (ALS) and Alzheimer's disease, respiratory, reproductive, developmental and metabolic diseases, and congenital abnormalities.[9-12] In the current advisory report, the Committee is limiting itself to those health effects that are of particular interest to the ministers and stakeholders – Parkinson's disease and nervous system damage in young children.

2.1 International literature on the health effects of plant protection products

There are no exact details concerning the level of health impairment associated with the use of chemical plant protection products. Severe acute poisonings are rare in industrialised countries. There, the main concerns are associated with the potential health effects that result from long-term exposure to low concentrations of these products.[8] These are difficult to assess, as it is often difficult to determine the exposure experienced in the relevant period – which, in some cases, may be many years before the first symptoms of disease appear.[9] In addition, the focus on certain health effects (such as immunotoxicity, endocrine disruption, and developmental neurotoxicity) is a relatively recent phenomenon.

2.1.1 Parkinson's disease

The relationship between plant protection products and Parkinson's disease is the subject of a substantial body of international research. The Committee has found a variety of meta-analyses and systematic reviews on this topic.[13-23] These publications all demonstrate a statistically significant increased risk of Parkinson's disease associated with exposure to plant protection products (generally up to a factor of 2). Nevertheless, experts feel that the case for a causal relationship has yet to be proven.[24] This is partly due to the substantial degree of heterogeneity displayed by the results of individual studies. It seems that this is due, to some extent, to the varying and often imprecise ways in which exposure has been measured.[14] It is almost always estimated on the basis of a person's

profession, the crops grown, the nature and area of crops in the vicinity of the home, or answers to questionnaires about the use of products by people themselves or by others around them. This fails to take account of certain relevant factors, such as whether or not personal protective equipment is worn, compliance with the instructions for safe use, pest pressure (scale of the infestation), wind direction, and the amount of time people spend away from home. One way to strengthen the evidence for causation is to study exposure-response relationships (does the risk increase in step with exposure?). However, this is something of a challenge, given the lack of reliable exposure data.[25]

The characterisation of exposure usually focuses on plant protection products in general or on large groups of products, such as insecticides, herbicides, or fungicides. Exactly which products cause the health impairment in question remains unclear. Accordingly, the epidemiological evidence for the involvement of specific, individual agents is much less consistent and convincing.[24,26,27] Nevertheless, certain agents are particularly suspect. These are the herbicides paraquat and 2,4-D, as well as the insecticides rotenone, dieldrin and chlorpyrifos and the dithiocarbamate group of fungicides (maneb, zineb, ziram).[24,28,29] There are indications that combined exposure to paraquat and dithio-carbamates poses a particularly high risk.[30-32] Experimental animal studies and in vitro research have also revealed a certain mechanistic plausibility.[26,33]

Various meta-analyses of occupational exposure to plant protection products all indicate an increased risk of Parkinson's disease.[13,14,16,19] In France, this disease has been officially recognised as an occupational disease among growers.[34] A similar step is currently being considered in Germany.[35] Research has shown that implementing hygiene measures at work, such as wearing protective gloves, can reduce people's risk of Parkinson's disease.[36]

No separate meta-analyses have been carried out of studies that focus purely on exposure from the environment. However, meta-analyses into both occupational and environmental exposure paint much the same picture as purely occupational meta-analyses. Some studies (individual studies), but not all, suggest the existence of a positive relationship with exposure to plant protection products from the living environment.[31,32,3738] Those who are exposed to plant protection products both at work and at home appear to be most at risk of developing Parkinson's disease.[32]

It should be remembered that Parkinson's disease only manifests itself later in life. The associations being unearthed by current epidemiological research reflect past exposures to outdated agents, some of which are no longer commercially available.[34] A recent US study revealed an association between the risk of premature death from Parkinson's disease and environmental exposure to the herbicide glyphosate.[39] Glyphosate is a herbicide that is still widely used in the EU and elsewhere. A few

descriptions of individual medical cases would appear to support an association of this kind.[40-42]

In addition, epidemiological research indicates that occupational exposure to plant protection products may be linked to other neurodegenerative disorders, especially ALS and Alzheimer's disease.[43-47] A relationship has also been found between long-term occupational exposure to low concentrations of organophosphate insecticides and milder neurological symptoms related to memory, concentration, psychomotor skills, behaviour, and depth perception.[48]

2.1.2 Developmental effects in children

Several recent reviews have summarised the results of research into the potential effects of chemical plant protection products, especially insecticides, on the developing nervous system of the unborn child and those of young children.[49-54] Due to the enormous diversity of research methods used, no meta-analyses were performed.[51,52] These publications consistently show that prenatal exposure to certain organochlorine compounds and organophosphates is associated with adverse effects on children's cognitive abilities, social-emotional development, behaviour, reaction times, or motor skills. Changes in brain structure have also been observed.[55] There is less consistent evidence that postnatal exposure might have an adverse effect on development.[52,54] These effects usually only become apparent from a child's second year of life onwards.

Low levels of insecticides, including pyrethroids, also appear to play a part in the development of attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD).[56-58] One study found a link between the risk of ASD and exposure to the herbicide glyphosate.[58,59] Most of these studies have been conducted in the US, but the results of various Belgian[60], French[61,62] and Danish[57] studies also point in the same direction. While experts do not consider the available epidemiological data to be conclusive evidence, they do feel that there is cause for concern and that further research is needed.[52,56] Here too, the measurement of exposure is often a weak point.

Experimental animal studies and mechanistic studies support the results of the abovementioned epidemiological research.[53,56] However, there is a debate about the extent to which observations in experimental animal studies can be extrapolated to humans who experience low-level exposure[63], and whether there are any effects in humans at exposure levels below those that were deemed to be safe at the time of approval (see next section)[50].

Recently, in the United States, paediatricians have urged that agricultural uses of the organophosphate chlorpyrifos (one of the most suspect agents in this regard) be terminated.[64] Indoor use is already prohibited. In Europe, the European Food Safety Authority (EFSA) recently determined that products based on this substance no longer meet the approval criteria.[65]

With effect from 16 April 2020, their use will no longer be permitted in the EU. The same goes for products based on the related substance chlorpyrifos-methyl.

2.2 Research into health effects in the Netherlands

Findings from other countries cannot be automatically extrapolated to the Dutch situation. Agricultural practices (crops, the plant protection products used, spraying techniques), land use, housing, and climate can vary greatly from one country to another. To a large extent, these determine the risks posed to local residents. That is why research carried out here in the Netherlands is so important.

2.2.1 Notifications of concerns, health problems, poisonings and diseases

Various Dutch authorities submit reports every one or two years concerning notifications of health problems related to circumstances at work or in the living environment.

Every two years, RIVM publishes a summary of notifications from members of the public to the municipal health services, concerning environmental health problems. Notifications of concerns about environmental factors are recorded as health problems as well. Over the period from 2017 to 2018, the municipal health services received more than 7,000 notifications. Fifty-seven of these were related to ‘pesticides’. As in previous periods, that constitutes less than 1% of the total number of notifications. Fifty-two of these 7,000 notifications were cluster notifications involving concerns about a large number of cases of a particular disease (mostly cancer) in a particular area. In three of these cases, the individual submitting the notification indicated that pesticides were the probable cause.[66]

In cases involving acute poisoning in humans and animals, medical professionals can consult the National Poisons Information Centre (NVIC). In its 2018 annual review, the NVIC reported that 1,619 exposure notifications (3% of the total number of notifications) were related to ‘pesticides and disinfectants’.[67] Most of these notifications concerned exposure to disinfectants (690 cases). A total of 383 cases concerned insecticides (mainly pyrethroids), while 115 cases concerned herbicides (mainly glyphosate). The figures were comparable to those of previous years. However, the number of notifications of exposure to cyano pyrethroids had increased from 45 in 2017 to 78 in 2018. This was linked to a box tree moth infestation in 2018. Most pesticides contain low concentrations of cyano pyrethroids, so the associated health effects in humans are usually limited to local irritation problems involving the mouth, throat, skin or respiratory system, and to gastrointestinal complaints. Most of the notifications submitted to the NVIC probably involve the use of substances by private individuals.

The Netherlands Center for Occupational Diseases (NCvB) receives very few notifications concerning people who develop occupational diseases as a result of their use of plant protection products. In its 2017 report, the NCvB stated that ten out of twelve questions about reproductive disorders that were submitted to the helpdesk concerned exposure to chemical substances 'such as solvents and pesticides'.[68] In the 2015 report, two out of fifteen diagnoses of chronic toxic encephalopathy (CTE), also referred to as organic psychosyndrome (OPS) or painters' disease, were attributed to exposure to neurotoxic pesticides and eleven to solvents.[69]

The individuals concerned included bulb growers. This disease is characterised by memory problems, concentration problems, fatigue and increased irritability. That year, the helpdesk received two questions about the reproductive risks posed by plant protection products.

The Netherlands Organisation for Applied Scientific Research's (TNO) 2018 Arbobalans (Health & Safety Balance) shows that agricultural workers run the greatest risk of developing a self-reported, substance-related occupational disease.[70] In 2016, the number of new cases per year (incidence) was four in every thousand employees (0.4%), twice the average for all labour sectors. It should be noted that these figures are based on the Netherlands Working Conditions Survey (NEA), which is conducted among employees. This takes no account of the burden of disease that only manifests itself after retirement.

2.2.2 Epidemiological research

Since the previous Health Council advisory report on crop protection and local residents was published in 2014, a number of scientific articles have been published about Dutch epidemiological research into the relationship between health and exposure to plant protection products. Most of these articles involve research into the effects of occupational exposure. Two of them concern research into potential health effects in those living in the vicinity of agricultural fields.[71,72] Several articles describe research into health effects among the population of Rotterdam.[73-76]

Health effects in adults

Three studies focused on Parkinson's disease. Brouwer (2015) found an association between occupational exposure to chemical plant protection products at the start of the study (1986) and death from Parkinson's disease in subsequent years.[77] However, the authors were cautious about drawing conclusions from this finding, as no association was found with the duration of exposure or with cumulative exposure. Van der Mark (2014) investigated the relationship between occupational exposure and Parkinson's disease.[78] Farmers who had developed this disease were found to have experienced a higher exposure to the fungicide benomyl than those of their peers who did not have the disease. The researchers found no associations with other products. However, they did point out that while the risks associated with the highest exposure to other plant protection products were not significant, they were consistently higher.

Brouwer (2017) estimated the lifetime exposure of residents of agricultural areas, based on the distance of their homes from agricultural land and on the types of crop being grown.[71] This study found no relationship between exposure to previously suspect agents and the risk of Parkinson's disease. A hypothesis-generating analysis found that exposure to a cluster of 21 substances was associated with a risk of developing this disease. This concerned various plant protection products used in the cultivation of grain and potatoes. High correlations between these agents made it impossible to identify the specific individual agents responsible for the observed association, and the researchers do not rule out chance findings.

Two studies into the relationship between occupational exposure to plant protection products and another disease, ALS, yielded conflicting results. One study based on data from ALS patients in Italy, Ireland and the Netherlands, found that exposure to all plant protection products (herbicides, insecticides and fungicides) was associated with a risk of developing this disease.[79] However, the second study found no such association.[80] Another study found that the higher the occupational exposure to plant protection products at the start of the study, the lower the risk of dying from dementia (1986).[81]

In two separate studies, De Jong (2014a,b) investigated the relationship between occupational exposure and pulmonary function. In both studies, she found an association between exposure to plant protection products and diminished pulmonary function.[82,83]

Effects on children (and the unborn child)

The Generation R study in Rotterdam measured the concentrations of metabolites in the urine of pregnant women, as a measure of their exposure to organophosphates. Metabolite concentrations were related to reduced foetal growth at mid-pregnancy, but not to the infant's length and weight at birth.[73] Indications of an association between organophosphate metabolites and nonverbal IQ at age 6 were inconsistent.[74] Nor were any associations with ADHD and autism found.[75] Finally, no association was found with thyroid hormone concentrations, which play a part in foetal brain development.[76] The concentrations of metabolites found in this Rotterdam population were substantially higher than those in other countries. Based on previous research[84], the authors suggest that this could result from high levels of fruit consumption.

In Flanders, relatively high concentrations of the metabolites of another group of insecticides, the pyrethroids, were recently found in the urine of young people aged 14 to 15.[85] These concentrations were higher than those found in the United States, Canada and Denmark. Evidence from epidemiological research carried out abroad suggests that these levels may produce health effects.[86,87]

Spinder (2017) investigated the relationship between maternal occupational exposure to substances such as solvents, plant protection products, metals and dust, and cases of cleft lip/palate in a registry of congenital disorders (Eurocat) in the Northern Netherlands.[88] In babies born between 1997 and 2013, the risk of cleft lip/palate was found to be higher if the mother had experienced occupational exposure to chemical plant protection products. However, only a few children with the disorder had mothers who had been exposed to plant protection products. This led the researchers in question to conclude that larger-scale studies are needed to confirm the results.

In the PIAMA study, Bukalasa (2018) estimated children's exposure based on the distance of their homes from agricultural land, the types of crop being grown, and the use of agents.[72] In young people, no relationship was found between their exposure to plant protection products and cases of asthma.

The health survey and the OBO

In 2018, RIVM, the Institute for Risk Assessment Sciences (IRAS) and NIVEL conducted an exploratory and hypothesis-generating study into human health in relation to the proximity of agricultural crops.[5] In most of the disorders studied, it was found that those living near agricultural fields enjoyed better health than those who lived further away. However, higher rates of mortality from respiratory complaints were consistently found in the vicinity of maize cultivation. A potential link to the use of chemical plant protection products was not investigated. Other cultivation-related factors, such as fine particulate matter, might also be involved. Less clear links with other types of crop (higher birth weight near spring barley, eye irritation near fruit growing areas, Parkinson's disease near fruit growing areas, leukaemia near areas of crop rotation involving grain-beet-potatoes) do not seem robust, based on the preliminary results of supplementary health survey analyses.[89] The study did not explore any potential effects, in the form of autism and ADHD, on children or on the unborn child.

A consortium of Dutch research institutes recently conducted an exposure study among those living in the vicinity of bulb fields (OBO). The aim was to obtain a better understanding of local residents' environmental exposure to chemical plant protection products and of the exposure routes involved.[6] Traces of the plant protection products used on the bulb fields were found in the open air around nearby houses, as well as in house dust. These products were also found in the urine of residents – both adults and children. However, that was also the case with those who lived more than 500 metres away. Yet local residents were found to be more exposed than people living at a greater distance. The highest exposures were found among growers and their families. The traces of plant protection products in people's urine may result from the use of these products on the nearby bulb fields. However, the analyses of air and

house dust samples indicated that environmental exposure was responsible for only a small percentage of the total exposure. The two most commonly occurring agents in these urine samples were the sprout inhibitor chlorpropham and the fungicide tebuconazole, which are also used on food crops. Indeed, the fungicide is also used as a wood preservative (biocide). Accordingly, it is suspected that other sources, such as diet, have made a significant contribution to exposure.

The OBO was not a health study, as the researchers themselves were keen to make clear. Nevertheless, they did draw tentative comparisons between the levels of five agents in the urine of local residents and the corresponding health-based limit values, which had been determined by experimental animal studies when the agents were first approved. In all cases, exposure was found to be below these limit values. It should be noted that this concerns only five agents in a single crop, and that the conditions under which the study took place were not worst-case conditions. Moreover, the limit values are based on experimental animal studies and have not – of course – been validated in the OBO. Accordingly, based on this study alone, it is not possible to draw any conclusions concerning the health risks (or the absence thereof) to local residents.

2.3 Conclusion

The Committee concludes that the international scientific literature indicates links between exposure to plant protection products and the risks of Parkinson's disease and developmental disorders in young children. There is no evidence that severe (inadvertent) acute poisonings caused by chemical plant protection products occur frequently in the Netherlands. Nor are there any clear indications that long-term exposure to lower concentrations in the Netherlands leads to substantial health effects, such as Parkinson's disease or impairment of the neurological development of the unborn child and young children. Nevertheless, national epidemiological research cannot allay the latter concerns, given that it is limited in scope, that exposure to chemical plant protection products can often only be broadly determined (in retrospect), that some studies in the Netherlands provide weak evidence of effects, and that there is clearer evidence of health impairment in neighbouring countries. Thus, for the time being, the extent to which growers, their families and local residents in the Netherlands experience a higher health risk due to exposure (or extra exposure) to chemical plant protection products in the course of their work or from the living environment remains unclear.

03
the approval of chemical plant protection products

A comprehensive and meticulous approval procedure (based on the EU model) is used to ensure that only effective and safe plant protection products are made commercially available. While this procedure is continuously being modified and upgraded, it can never entirely eliminate the risk of health impairment with absolute certainty.
Recent improvements include an assessment of the risks to those living in the vicinity of agricultural fields, the identification of endocrine disruptors, research into the formation of metabolites in the human body, and residue definitions for biomonitoring. The remaining sticking points include the identification of effects on the unborn child and young children, and of neurodegenerative effects. Little or no account is taken of the risks posed by exposure to a substance from different sources and via different routes, or by exposure to several different substances at once. One way to mitigate this problem is to introduce an ‘allocation factor’.

3.1 The procedure

Plant protection products are usually mixtures of substances (known as ‘formulations’). In addition to one or more active ingredients (which generally kill the target pest), they usually contain various additives. Member States may only approve plant protection products whose active ingredients are on a European Union (EU) positive list. Inclusion in this list is based on a comprehensive dossier that manufacturers are required to supply. The national approval boards continue to be responsible for the approval of formulated commercial products (plant protection products). In the Netherlands, that would be the Board for the Authorisation of Plant Protection Products and Biocides (Ctgb). The EU is divided into three zones – north, central and south. If a plant protection product is approved by one country then, in principle, it must also be approved by every other country in the same zone. Exceptions to this rule are permitted, provided that this can be justified by special national circumstances. The active substances on the positive list (and, thus, the approved plant protection products as well) are reassessed at least once every ten years. This is because the test protocols used in the approval procedure are regularly updated in line with the latest findings. If previously unsuspected harmful effects come to light in the course of everyday practice, the approval is reviewed as soon as possible.

An assessment of the risks to human health is a major component of the approval procedure. The risk assessment is aimed at all those who might come into contact with a product, either while it is being used or at some later stage. If the crops involved are intended for human consumption, then the risks to consumers are also assessed. This is because minute traces of plant protection product (residues) can remain in the crop. Differences between men and women are taken into account. The risks posed to the unborn child are also assessed. When assessing the risk to consumers, a separate examination is also made of the risk to children (including young children).

The Ctgb's assessment involves estimating the exposure experienced by these groups of people under 'realistic worst-case conditions'. It makes use of computer models based on the use of the product, as proposed by the manufacturer. The estimated exposure is compared to health-based limit values. These limit values are derived from the results of experimental animal studies, as toxicological experiments on humans are precluded on ethical grounds. If the calculated exposure for all groups remains below the health-based limit values, the product in question is eligible for approval. For a more detailed description of the assessment, the Committee refers the reader to the Health Council's 2014 advisory report (subsection 3.2.1 and Annex H).[4]

3.2 Recent improvements

However meticulous the approval procedure may be, it can never offer an absolute guarantee that every single product that is made commercially available will be totally safe. Since it is impossible to prove a negative, it is not possible to prove that there will be no harmful effects if the product is used in accordance with the instructions for use. There is always a possibility that little or no account has been taken of specific aspects or circumstances. Exposure calculations and – to an even greater extent – health-based limit values are inevitably subject to uncertainties. Thus, it happens regularly that, as a result of new discoveries, products that are already commercially available do not have their approval extended. Some recent examples are herbicides and sprout inhibitors based on chlorpropham and insecticides based on chlorpyrifos and chlorpyrifos-methyl. In an international context, efforts are continually being made to further refine the approval procedure, based on new scientific knowledge and on experience gained in everyday practice. However, this work is very complex and time consuming.

One relatively recent addition to the procedure is an assessment of the health risks posed to local residents. This had been requested by the Health Council, in its 2014 advisory report. Since 2014, a clear-cut risk assessment has been carried out for local residents. This initially involved the use of German and British calculation methods. Since 2016, the EFSA's OPEX model (which has been adopted in Europe) has been used.[90] This model also uses a worst-case scenario, and is based on a daily exposure:

a. to spray drift during application (where the local resident is two metres away from the crop and is exposed via his respiratory system and entire skin surface);
b. via evaporation (this is based on exposure for 24 hours per day);
c. through skin contact with contaminated surfaces, such as lawns (for two hours per day);
d. when entering the crop after spraying (this is based on entering the treated crop for 15 minutes per day with intensive contact between the crop and the skin).

The total exposure via all these routes is summed to give a calculated daily exposure. The risk assessment is then based on daily exposure to this calculated amount, throughout the spraying season and over a period of several years.

The OBO has shown that house dust can be an additional exposure route for local residents. The research data has been submitted to EFSA, to enable it to decide whether it wants to include this additional exposure route in the OPEX model. Incidentally, it is anticipated that local residents will not generally suffer any substantial exposure to plant protection products from the fields via house dust. As a rule, the intake of house dust does not exceed 100 mg per day in young children and 50 mg per day in adults. Furthermore, the levels of plant protection products in house dust are in the order of magnitude of nanograms per gram. Health-based limit values are in the order of magnitude of milligrams per kilogram of body weight per day.[90,91]

In 2014, the Health Council recommended that details of the methods used to measure plant protection products and their conversion products in human blood and urine should be routinely included in the dossiers that manufacturers submit for approval. This is necessary to enable human biomonitoring. The range of plant protection products selected for investigation in the OBO was severely limited, due to the limited availability of analytical methods. The Council also recommended that the Netherlands should launch a debate within the EU about whether the approval dossier provides adequate guarantees concerning the details of a product's kinetics (its fate in the human body: absorption, distribution, conversion and excretion). This information is necessary for the proper interpretation of biomonitoring data. These data are also necessary to derive toxicity data for other exposure routes, based on experimental animal studies involving oral exposure. Experimental animal studies into dermal exposure – and particularly into inhalation exposure – are not always available.

In the EU, new requirements have recently been added to the approval procedure in this regard. From now on, applicants must carry out research into the metabolites that can form in the human body. In addition, a residue definition must be established for biomonitoring, for which an analytical method must be available (body tissues and fluids).
The requirement applies to newly approved active substances. In the case of substances that have already been approved, this information must be submitted during the regular re-evaluation.

In 2018, the European Commission issued a Regulation (EU Regulation 2018/605) setting out scientific criteria for the identification of endocrine disruptors. The EFSA, the ECHA (*European Chemicals Agency*) and the JCR (*Joint Research Centre*) have jointly drawn up a manual for the application of these criteria in the approval of plant protection products

and biocides.[92] If an active substance is identified as an endocrine disruptor, then products based on this substance are not (or no longer) eligible for approval. However, it is still possible to grant exceptions – on the grounds that a product is indispensable for agriculture – for example.

3.3 Wishes regarding improvements

The approval procedure takes limited account of any effects on the unborn child. In 2012, the Health Council recommended that the *Extended One-generation Reproductive Toxicity Study* be used for this purpose. It did so because, compared to a previous test, this test measures more parameters that are capable of shedding light on potential effects on the development of the nervous system, the immune system and the hormonal system (provided that the correct analyses (or cohort analyses) are performed to this end.[93] However, manufacturers can still use the old test. Furthermore, follow-up tests, such as the *Developmental Neurotoxicity Study*, are rarely performed.

As long ago as 2013, the EFSA ruled that the detection of effects on the developing nervous system needs to be improved.[94] At an international level, intensive efforts are being made to develop methods for improving the detection of effects on the developing nervous system based on a battery of in vivo tests in non-mammalian species, in vitro tests (cell cultures), and in silico tests (computer models).[95-100] However, this has yet to result in any tangible modifications to the approval procedure.

Another problem is that the aetiology (causes) of disorders such as autism, ADHD, and cognitive impairment in children is poorly understood. This makes it difficult to determine which tests are needed to identify chemicals that might trigger such disorders. The same applies to neurological disorders that occur later in life, such as Parkinson's disease.

Another limitation of the approval procedure is that it focuses purely on individual products. There is no aggregate risk assessment.[101] People can come into contact with the same active substance in different plant protection products and via various exposure routes. Consumers will do so through their diet, while professional operators or workers make occupational use of such products. Others will be involved as bystanders or local residents, or make personal use of these products in the home and garden. The risks are assessed separately for each of these different situations. No consideration is given to the possibility that all of these cases might involve the same individual. In addition, those substances that are the active ingredients in plant protection products may also be present in other products, such as biocides, veterinary medicines, medicinal products, and cosmetics. These products are subject to different legal regimes and their safety is assessed separately.[102]

In the approval procedure, the risks posed by combinations of active substances are only assessed if these substances are contained in a single plant protection product, or where there is an intention to mix plant

protection products together in a single spray tank. Cumulative risk assessment is not part of the procedure. Cumulative risks occur in situations where people are exposed, virtually simultaneously, to several plant protection products containing active substances with the same mechanism of action and/or effect. Even in cases where exposure to each individual active substance remains below the health-based limit value, the combined effect of all active substances can still be strong enough to produce harmful effects. Accordingly, an approval procedure based on the assessment of individual plant protection products can lead to an underestimation of the actual risks involved. Indeed, the Council for the Environment and Infrastructure recently drew attention to this very problem.[103] The EU regulation concerning the placing of plant protection products on the market requires exposure to more than one product to be taken into account. The complex methodology required for this purpose is currently under development. The initial work is primarily being aimed at dietary exposure, in other words the exposure experienced by consumers. One challenge here is to adapt decision-making procedures for the approval of individual substances to take account of the risks posed by combinations of substances. In fact, substances or products other than plant protection products with the same mechanism of action or effect should also be included in the risk assessment.[102,104]

The most comprehensive toxicological research is directed at the active substances in plant protection products. Very little toxicological research focuses on formulated products. Its main purpose is to determine the product's classification (e.g. 'harmful if swallowed'). Another research topic is the extent to which the product can be absorbed through the skin. The toxicity of the additives is not addressed. Nor is any research being carried out to determine the additives' potential to boost the toxicity of the active substance. That could involve mechanisms such as promoting absorption into the body or inhibiting conversion and excretion. This could lead to a situation in which the limit values of the active substance result in an underestimation of the mixture's toxicity. Indeed, research has shown that formulated products are generally substantially more toxic than the active substance alone.[105] However, it might not be acceptable to subject all formulated products (more than 1,000 in the Netherlands alone) to the same extensive toxicological analysis as the active substances (about 260 in the Netherlands). After all, that would involve additional costs for the manufacturer and the use of additional experimental animals.

According to the Committee, the introduction of an 'allocation factor' could help to resolve the problem that exposure to a given active substance can take place from different sources and via different routes. This could also be useful in situations that often involve exposure to several active substances with the same mechanism of action or effect. Any such allocation factor would need to ensure that each plant protection product only accounts for a limited percentage of the health-based limit value via each exposure route (work, environment, private use, diet).

That would then leave some room for exposure via other routes and to other substances. Various other advisory bodies have recently proposed the same solution.[103,106] It is not ideal, because the scientific basis for determining how big this factor should be, is limited. It is also a political choice, one that is shaped by the desired level of caution and by the degree of uncertainty concerning health risks that one is prepared to accept in the light of other societal interests. However, this is a very pragmatic approach and it does overcome at least part of the problem.

04 chemical crop protection in practice

Extensive regulatory frameworks, education and inspections by various government agencies are designed to ensure that chemical plant protection products are used safely in practice. The government is endeavouring to reduce agriculture's dependence on chemical agents and to replace those that have high acute toxicity with less toxic alternatives. A recent policy review showed that this pursuit of greater sustainability has not, as yet, been particularly successful. Moreover, it has become apparent that growers themselves do not give sufficient priority to occupational safety. In addition to impacting their own safety and that of their employees and family members, this also poses increased risks to local residents.

4.1 Rules for safe use

The Plant Protection Products and Biocides Act (Wgb) regulates many aspects that are designed to promote the effective and safe use of plant protection products in practice.

- The professional operators of plant protection products must be in possession of a certificate of professional competence.
- The statutory instructions for use that are printed on the packaging of plant protection products list the applications for which the product is intended and the way in which the product should be used.
  The packaging also carries information about hazards to human health and the environment and about the measures to be taken to counter them (such as the use of gloves or respiratory protection, or re-entry intervals for workers in treated crops).
- Spraying equipment must be regularly checked and the use of emission-reducing nozzles is mandatory.
- Growers are required to draw up a crop protection plan and to keep a log (plant protection monitor, including spray registration) that includes details of exactly which products have been used, when, in what quantities, and on which agricultural fields. This data must be retained for at least three years, for inspection purposes.
- The storage of plant protection products and the disposal of residual products and empty packaging are subject to certain safety requirements.

In addition to the Plant Protection Products and Biocides Act (Wgb), agricultural holdings are subject to the Working Conditions Act.
This makes it mandatory for agricultural holdings that have employees to carry out a risk inventory and evaluation (RI&E). That is a summary of an agricultural holding's occupational safety risks, and an action plan for minimising those risks. In an agricultural holding, dealing with plant protection products is part of a risk inventory and evaluation. Because the Working Conditions Act is fairly general, many sectors have drawn up their own Health and Safety Catalogue, setting out further instructions for safe working practices. Source control measures (reducing the amounts of plant protection products used, and switching to less hazardous products) and technical provisions (automatic filling and mixing systems, sealed

cabins) are preferred over the use of personal protective equipment (gloves, face mask). Sector organisations and the Health and Safety Service for the agricultural and green sectors (Stigas) provide occupational safety information to employers and employees. Employers are required to offer periodic health checks (PMOs) to their employees. Stigas recommends that any employees who work with plant protection products should have annual health checks. Finally, agricultural holdings also have to deal with a range of environmental legislation. Compliance is monitored by the Inspectorate SZW, the Netherlands Food and Consumer Product Safety Authority (NVWA), and the Human Environment and Transport Inspectorate (ILT).

4.2 Enhancing environmental sustainability

Even though the approval procedures and the use of plant protection products are properly regulated, these products are still hazardous substances. That is why the Dutch government is endeavouring to achieve sustainability, in terms of a crop protection system that safeguards food production by effectively controlling diseases and pests, while at the same time minimising any risks to human health, nature and the environment.

To achieve this sustainability, above and beyond the safety measures already outlined, it is necessary to embed chemical crop protection in 'Integrated Pest Management' (IPM). This broad approach initially involves measures designed to prevent diseases and pest infestations, such as site optimisation, crop rotation and the use of crop varieties with increased resistance to pests and disease. If they do appear, then a range of control measures can be used. These can be mechanical (e.g. weeding), physical (e.g. steaming or burning) or biological (e.g. using the natural predators of pests) are given priority. Wherever possible, the use of chemical crop protection is limited. If these products do have to be used, then growers can opt to use those that are least harmful to the environment. They can obtain guidance in this regard from the 'Environmental Yardstick' (see www.milieumeetlat.nl).

To encourage IPM, the government has concluded a covenant with the stakeholders involved and has drawn up various policy documents with quantitative policy goals. This is in line with the EU Directive on the Sustainable Use of Pesticides, which obliges Member States to draw up a national action plan for sustainable crop protection, with effect from 2012, and to submit this to the European Commission. The most recent policy document on sustainable plant protection provides a basis for policy from 2013 to 2023.[107] This is the first specific focus on the risks to those living in the vicinity of fields on which plant protection activities involving the use of chemical agents are carried out.

In April 2019, the Minister of Agriculture, Nature and Food Quality, also acting on behalf of the State Secretary for Infrastructure and Water

Management, and in consultation with various stakeholders, sent details of a vision for the future of crop protection to the House of Representatives of the Netherlands, in addition to the Second Policy Document on Sustainable Plant Protection.[108] That vision is designed to disrupt current thinking and practice in the area of crop protection, by focusing on resilient plants and cultivation systems and on stronger links between agriculture, horticulture and nature. One aim is to reduce the use of chemical plant protection products over the next ten years. Another is to reduce emissions to the environment and the levels of residues on products almost to zero by 2030, thereby enabling those living in the vicinity of agricultural and horticultural holdings to feel that their living environment is safe. Work on an implementation programme is underway.

4.3 Room for improvement

Last year saw the publication of the interim evaluation of the Second Policy Document on Sustainable Plant Protection, entitled 'Healthy growth, sustainable harvest'.[109-111] This shows that efforts made by the agricultural sector, customers and government agencies in many areas are starting to bear fruit. Nevertheless, only the interim goals for food safety have been achieved, unlike those for IPM, water quality, biodiversity and occupational safety. The Committee has summarised those findings that are most relevant to human health.

4.3.1 Use of chemical plant protection products

The evaluation shows that there has been little tangible progress towards resilient cultivation systems and the increased use of natural pest control agents. The routine use of biological control is restricted to greenhouse horticulture and the fruit growing sector. There is still a high level of dependence on chemical plant protection products. Sales fell from 10 to 9 million kilograms of active substance in the period from 1990 to 2016. However, consumption per hectare has increased somewhat, as crops which need relatively intensive spraying such as flower bulbs are grown more often. Nor has there been a shift to products that pose a relatively low risk to the environment or to human health. There is no incentive to do so and low-risk agents are not always available.

Growers say that they feel there is a shortage of effective non-chemical measures. IPM also requires a great deal of knowledge on the part of growers. The main sources of such knowledge are often the suppliers of plant protection products themselves. Given their vested interest in the sale of plant protection products, this raises the question of whether their advice provides a fully balanced view of all aspects of IPM.

4.3.2 Food safety

The evaluation shows that, since 2010, there have been proportionally fewer breaches of the standards for residue levels in fruit and vegetables (unprocessed). This means that the goals of the policy document entitled

'Healthy growth, sustainable harvest' have been achieved.[109,110] This is especially applicable to products of non-Dutch origin (approximately 1-4%). The percentage of instances in which Dutch products were in breach of a standard was already low (less than 1%). In the case of products from outside the European Union, the number of instances involving a breach of standards varies from one year to another. Accordingly, there is a continuing need for monitoring by the NVWA.
In addition to the government, buyers such as supermarket chains have also played an important part in improving food safety. Under pressure from public opinion, they have imposed stricter requirements on the levels of residues that the food they sell is legally permitted to contain. They also randomly check their products for residues of plant protection products.

Calculations based on measured residue levels show that infants and young children have a slight risk of being exposed to levels that exceed the limit values for acute toxicity.[110] More data is needed on the consumption patterns of non-Western Dutch citizens to reliably assess whether the residue levels found could pose a threat to the health of these groups.[110]

4.3.3 Occupational safety

Unlike food safety research, occupational safety research is not based on measurements, but on surveys conducted among agricultural employers. It has become apparent that, when it comes to plant protection products, growers still do not give sufficient priority to safe working practices.[109,111] Despite the availability of less hazardous plant protection products, growers still use products that have high acute toxicity, the so-called 'skull and crossbones' agents. The lack of a good overview makes the less risky alternatives that are currently available difficult to find. As a result, the first measure in the occupational hygiene strategy scale – mitigating risks at source – has not been successful.

The evaluation shows that a quarter of growers fail to inform their employees about the risks of chemical crop protection. They seem to assume that this is not necessary if spraying takes place outside their employees' working hours. But working in sprayed crops or in the vicinity of spraying activities (this is prohibited but it does occur nevertheless) and handling empty packaging can also be risky. A failure to provide sufficient information mainly poses risks to employees who are not themselves involved in spraying activities. They are less aware than others that they should not enter the crop too soon after it has been sprayed, and that they may need to use personal protective equipment. Some additional complications are that employees who work in the crop are often seasonal workers, do not speak Dutch, or are less than 16 years of age. This is less important for those who are directly involved in spraying activities. They possess a certificate of professional competence and are, therefore, better aware of the risks. The government itself is not very active in this regard.

Since 2013, the Inspectorate SZW (ISZW) has carried out very few inspections related to the safe use of plant protection products.[111]

Most growers (about 90 percent) claim to have drawn up a risk inventory and evaluation. However, few if any holdings have carried out assessments of the exposure to plant protection products experienced by operators and other workers. Assessments of this kind are needed because each approval only applies to an individual product, while in practice several products are used simultaneously or in sequence.
In practice, the risk inventory and evaluation are mainly seen as a mandatory paper exercise, so it rarely leads to the implementation of measures to improve occupational safety. Very few health checks (PMOs) are performed.

Three of the six Health and Safety Catalogues used in the arable farming and horticultural sectors make no mention of crop protection. Furthermore, in those cases where this topic does feature in a catalogue, fewer than 20% of employers are aware of it.

Finally, only a fraction of the empty packages and excess plant protection products are disposed of via the *Stichting opruiming restanten landbouwbestrijdingsmiddelen* (Foundation for the disposal of excess agricultural pesticide products), which was founded specifically for this purpose. This is due to a failure to provide proper information, and to a lack of official locations when these can be handed in free of charge.

The survey achieved a response rate of 45 percent. It is conceivable that, on average, those who completed the survey had implemented better occupational safety measures than those who did not participate. Thus, according to the authors of the evaluation report, the survey may still be giving an overly rosy picture of occupational safety.[111]
Prompted by the results obtained in the OBO, the interim evaluation also briefly focuses on local residents.[109] However, the Committee has already covered this aspect in Section 2.

05 advise

There are indications in the international literature that exposure to chemical plant protection products does entail some health risks. While Dutch epidemiological studies have not yielded any clear evidence of health effects, this has done little to allay these concerns. The extent to which growers, their families and those living in the vicinity of agricultural fields run health risks as a result of exposure is unclear. Within the near future, any additional health research will not help to clarify this matter. The approval procedure needs to be improved, but that is a complex undertaking and will take a great deal of time. Accordingly, based on the precautionary principle, the Committee recommends that efforts to make crop protection more sustainable and to reduce dependence on chemical agents be redoubled. It also recommends that progress should be tracked by monitoring the use of chemical agents and people's exposure to them. In the long run, the data gathered may also pave the way for better health research.

5.1 The health risks posed by plant protection products

In the previous sections, the Committee revealed that the international epidemiological literature identifies links between exposure to chemical plant protection products and the occurrence of diseases. These include Parkinson's disease and cognitive effects in young children. The results of experimental animal studies and mechanistic studies indicate a certain degree of plausibility of such effects. Recent epidemiological health research in the Netherlands has provided no clear evidence of health impairment. However, it was limited in scope and quality, so it has done little to allay these concerns. Growers and other professional users of chemical plant protection products, as well as those who work on agricultural holdings, are known to experience higher exposure than people who have no contact with these products in the context of their occupation. Furthermore, it has been found that those living in the vicinity of agricultural fields and the family members of growers are generally more exposed than people who live further away from agricultural fields. Sources other than people's work and living environments can also contribute to their total exposure. These include their diet and private use in and around the home. In the Netherlands, the extent to which growers and local residents experience extra health risks in the course of their work or from the living environment is unclear.

5.2 Intensifying the pursuit of sustainability

Several years ago, the Health Council defined the precautionary principle as a strategy for dealing with uncertainties in a careful way.[112] At the time, the Dutch government embraced this viewpoint. In its first advisory report on crop protection and local residents, the Council indicated that this strategy could be appropriately implemented by adopting the need to avoid exposure (rather than the health risks involved) as the guiding principle and by implementing cost-effective measures. It also felt that proportional, more expensive measures were also worthy of

consideration.[4] The Committee feels that the recommendations made by the Council at that time are still applicable.

Based on the precautionary principle, the Committee recommends that the government and the agricultural sector should robustly implement and intensify the plans to make agriculture more sustainable, as recently set out in the 2030 Vision for the Future of Crop Protection.[108] Measures implemented at source are always preferable. Reduced dependence on chemical agents and cutting down on their use will directly result in lower exposure, not only for growers and workers in treated crops, but also for local residents and consumers. By extension, this will lead to a reduction of potential health risks for the entire population.

In situations that require the continued use of chemical agents, it is important to give preference to agents that pose the lowest risks to people and the environment, wherever possible. In this connection, there must be strict compliance with the legal instructions for use, of course, and there must be a strong focus on the safety aspects involved. To this end, the education and motivation of growers are of great importance.
It is recommended that the government and agricultural organisations invest even more in this area. The health check (PMO) is also a suitable tool for this purpose. Enforcement by the inspectorates of the relevant ministries (NVWA, ILT, ISZW) also needs to be strengthened.[113]

5.3 The usefulness of additional research

Health research

In the Netherlands, epidemiological research into health effects will not help to clarify matters within the near future. In the longer term, however, it can provide valuable insights, provided that exposure to plant protection products can be properly characterised. For example, the Committee feels that it might be useful to set up a prospective cohort study into developmental effects in children. That would involve monitoring children for an extended period of time. It recommends that efforts should be made to seek collaborative ventures with European partners. This would facilitate the creation of a larger and better study, one that would produce more meaningful results.

Monitoring use and human exposure

According to the Committee, it would be particularly worthwhile to monitor the use of chemical plant protection products. The use of the plant protection monitor has been mandatory for several years now. It requires growers to provide a range of information, including which chemical plant protection products they have used, when, and in which crops.
The Committee recommends that this monitor be expanded and transformed into a reliable, uniform, national registration system for the use of chemical plant protection products at the level of individual agricultural fields. The Committee also recommends that human exposure be monitored periodically, at least, for an extended period of time, by means

of biomonitoring. In doing so, it is in line with the previous recommendation made by the Council and by other advisory bodies, which have recently championed monitoring (and biomonitoring).[103,114] This research serves several purposes:

- *Monitoring the effectiveness of the policy that is being pursued*
  This is the main goal. The registration of use directly reveals the extent to which the pursuit of reduced dependency is succeeding, while at the same time offering opportunities for policy adjustment. Biomonitoring reveals the extent to which measures are mitigating the exposure experienced by growers, workers in treated crops, local residents, and consumers.
- *Testing assumptions inherent to the approval procedure and detecting instances of incorrect use*
  The results of biomonitoring reveal the total body burden of a substance, or a series of related substances, from all exposure sources and via all exposure routes.[115] If the results of biomonitoring are compared to exposure estimates and health-based recommended exposure limits from the approval procedure, this can reveal shortcomings in the approval system which is focussing on individual products, or in the Ctgb's exposure estimates. Alternatively, this may reveal uses that deviate from the instructions for use and therefore result in high-risk situations that require further investigation.
- *Encouraging a focus on safety*
  Biomonitoring can help to raise awareness among growers about potential health risks, starting with themselves and their family members. In this way, it will encourage them to focus on safety. Local residents will also benefit from this. Launching a biomonitoring programme shows local residents and citizens in general that good care is being taken of their health.
- *Prelude to better epidemiological health research*
  If the usage data gathered at the level of individual agricultural fields are made publicly available, or at least to independent researchers, this will improve the prospects for good-quality epidemiological research into potential health effects. The use of biomonitoring data can open up even more options. A biomonitoring programme could be set up in the vicinity of different crops and in regions with high and low levels of agricultural activity. Over time, this will provide a reliable picture of human exposure and of how it varies from one place to another and over time. The usefulness of the results would be maximised by establishing links with biomonitoring programmes in other European countries. In addition, a comparison of Dutch exposure data with the results of epidemiological research elsewhere in the world provides insight into the health risks in the Netherlands. Ultimately, epidemiological research may make it possible to verify whether the approval procedure's health-based limit values actually offer sufficient protection.

The Netherlands has already acquired quite some expertise in biomonitoring through the OBO, and by participation in various EU projects.[115] Accordingly, the Committee feels that the Netherlands will very likely be able to set up a programme that meets all of the requirements for meaningful research into internal exposure.[4] A Flemish human biomonitoring programme, which has been running for eighteen years, focuses on numerous chemical substances, including plant protection products. This could serve as a source of inspiration.[116] It is recommended that stakeholders could be involved in setting up, organising and maintaining a biomonitoring programme of this kind, to ensure that it matches their needs as closely as possible. Furthermore, the lessons learned about stakeholder participation in the context of the OBO are also quite useful.

Additional environmental research

The OBO has provided a great deal of insight into the importance of different exposure routes for local residents in areas of bulb cultivation. This was an important verification of the Ctgb's exposure estimates in the approval process. The Committee recommends that further research be carried out to determine whether the findings in the bulb cultivation sector are representative of those in other crops. This is especially important for the fruit growing sector. Not only does it use relatively large quantities of plant protection products, but these are sprayed sideways and upwards. The Committee anticipates that, with a modest research effort, this representativeness could be determined in greater detail for other crops, by analysing house dust, for example.

Various measures, such as low-drift spray nozzles, windbreak plants, no-spray zones and keeping windows closed, can limit emissions to the environment and/or the exposure experienced by local residents. However, little is known about the effectiveness of such measures under different conditions. Further research is needed to determine the optimum approach.

5.4 Improving the approval procedure

While the Committee feels that the approval procedure needs further improvement, it does recognise that this would be a very complex and time-consuming process. Moreover, an approval procedure can never entirely eliminate the risk of health impairment with absolute certainty. Rather, it should be seen as the first in a series of provisions that collectively ensure safety.

For several years now, the approval procedure has assessed the risks to local residents separately. This is based on unfavourable conditions that lead to high exposure. Yet exposure via house dust can be discounted here. This method does take sufficient account of the distance to residential structures and population centres. The OBO has confirmed, albeit for a single crop and a limited number of products, that the Ctgb's

exposure estimate does offer sufficient protection. Rather, the uncertainty is associated with the derivation of health-based limit values, according to the Committee, which are necessarily based entirely on experimental animal studies, at least for newly approved plant protection products. Moreover, the design of some of these studies is not optimal.

The Committee considers it important that further efforts be made, in an international context, to improve the approval procedure. It also feels that, given its extensive expertise, the Netherlands should play an active part in this endeavour. Priority should be given to improving the assessment of potential effects on the development of the unborn child and young children. The same applies to assessments of the risk of neuro-degenerative disorders, such as Parkinson's disease.

Work is underway to develop methods for aggregate and cumulative risk assessment. To date, however, this has focused mainly on dietary exposure. The Committee does not expect these methods to be incorporated into the approval procedure in the foreseeable future. It takes the view that the most pragmatic way to solve this problem would be to introduce an 'allocation factor', the magnitude of which is yet to be determined. Any such allocation factor would need to ensure that each plant protection product accounts for only a limited part of the health-based limit value via each exposure route (work, environment, private use, diet). That would then leave some room for exposure via other routes and to other substances. The Committee recommends that, within the wider context of the European Union, the Netherlands should actively endeavour to introduce a factor of this kind into the authorisation policy.

5.5 Promoting the exchange of knowledge, dialogue, and collaboration

RIVM has advocated the establishment of a Knowledge Platform on Crop Protection and Health.[1] This should make existing scientific and policy information accessible and comprehensible to a wide audience, while supporting growers and other professionals in the responsible use of chemical plant protection products, and contributing to a social dialogue between stakeholders – such as local residents, agricultural organisations and the producers of plant protection products – on such matters as the interpretation of scientific data, the ideal level of protection, and effective ways of achieving that level of protection. The Committee supports that recommendation. A platform can help to build trust by facilitating the exchange of information and perspectives.

The Committee would like to point out, however, that the design and maintenance of a platform of this kind must be subject to certain quality conditions. Various aspects must be established in advance. These include the platform's goals, the resources that the platform would use to achieve these goals, who would manage the platform, the nature of the stakeholders' input, and the rules to which the creation and addition of

documentation and published information would be subject. Existing knowledge platforms in other fields, such as the Knowledge Platform on Electromagnetic Fields and Health, could serve as examples.
The platform could also be a suitable place for stakeholders and experts to jointly consider a meaningful design and implementation of the biomonitoring programme proposed by the Committee. This would represent a useful follow-up phase to the joint research that started with the OBO.[7]

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