CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

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DISCUSSION PAPER ON MANAGEMENT PRACTICES FOR THE PREVENTION AND REDUCTION OF CONTAMINATION OF FOOD AND FEED WITH PYRROLIZIDINE ALKALOIDS (PAs).

Background

1. A first discussion paper on Pyrrolizidine Alkaloids (PAs) in Food and Feed and Consequences for Human Health (CX/CF 11/5/14)[1] was prepared by an electronic working group, led by the Netherlands, for discussion at the 5th CCCF.

2. At its 5th Session, the Committee noted that there was general agreement with the recommendations of the working group as set out in paragraphs 167-171 of the discussion paper namely:

- to encourage Codex members and observers to develop more analytical reference standards for PA to enable the development and validation of analytical methods;
- to generate more occurrence data on PA contamination in food and feed;
- to request JECFA to identify which PA in food and feed (as carry over from feed to animal products) were of key interest to human health and to perform a full risk assessment based on the available data for the identified PA and/or to identify data gaps if full risk assessment was not possible;
- and to start work on a code of practice for the prevention/reduction of contamination of food with PA including a compilation of existing effective management/mitigation practices to prevent/reduce PAs contamination of food.

3. In view of these considerations, the Committee also agreed with the recommendation of the working group not to start work on an ML for PA in food and feed for the time being.

4. The Committee agreed to re-establish the electronic Working Group on PAs, led by the Netherlands, working in English only and open to all Codex members and observers, to update the discussion paper based on the above considerations, in particular to undertake further compilation of existing management practices and to evaluate the possibility to develop a code of practice for consideration by the next session of the Committee.

5. The electronic working group (eWG) was established and members included: Argentina, Australia, Austria, Belgium, Brazil, Canada, Chile, EFLA, FAO, FoodDrinkEurope, Germany, IADSA, Japan, New Zealand, Norway, Senegal, Switzerland and Thailand (see Annex II). Comments were received from Australia, Austria, Belgium, Brazil, Canada, FAO, FoodDrinkEurope, New Zealand, Norway and Switzerland.

6. A discussion paper was prepared based on Annex VII (Management practices) of the previous discussion paper (CX/CF 11/5/14). The background information is included in Annex I to this document. It should be noted that Annex I is only intended as a compilation of available information, and not as a draft Code of Practice.

Information available to develop a Code of Practice

7. As concluded in the previous discussion paper, management practices can be aimed at

- Measures for the control of spreading of PA-containing plants, which belong to angiosperm families of the Boraginaceae (all genera), Asteraceae (tribes Senecioneae and Eupatorieae) and Fabaceae (genus Crotalaria);
- Measures for reducing exposure to these plants by livestock, as PAs are being carried over from feed to food;
- Practices for reduction of PAs in contaminated feed and food.
- Prevention of contamination of food products (such as salads) with PA
- Creating awareness

1 This document can be downloaded at: ftp://ftp.fao.org/codex/meetings/cccf/cccf5/cf05_14e.pdf.

8. As seen in the compilation in Annex I, most information is available on weed control. For this discussion paper it is emphasized that total eradication of PA containing plants is neither feasible nor ecologically desirable. In addition, livestock will avoid eating these plants under normal circumstances. Animals may eat the plants when feed gets scarce or when PA containing plants are present in dried form in feed. Therefore management on the level of weed control is still recommended. An integrated approach using several methodologies for removal of plants and prevention/reduction of spreading is the most effective.

9. Limited information was found on existing practices for managing exposure of livestock to PA containing plants. It should be noted that cattle and horses will only eat PA-containing plants when food is scarce or when it is present in dried form in feed, so that the principal measure is to keep uncontaminated feed available for the animals. Risk-zoning of available pastures is found to be a possible measure. For bees, it was noted that as these forage at large distances, the removal of beehives from areas with PA containing plants might not be totally feasible. Providing an alternative and more desirable food source than PA-containing plants for bees may help in limiting the amount of PA-containing pollen in honey.

10. Although more information was found on practices for the reduction of PAs in feed and food once contaminated, the exact effectiveness is less clear. Some articles indicate that processing steps such as silage, bagging or storing with composting material will reduce the PA content in feed and food.

11. Sieving or filtering could also be a means to reduce PA content, although PA content in honey products such as mead does not seem to decrease despite several processing steps. Also, regular honey filtration is not effective against the transfer of PAs from bee pollen into honey and above all, it is inconsistent with the Codex Standard (12-1981) for honey which does not allow the removal of pollen from honey. Blending and diluting have been proven to be effective measures in borage oil and honey, however this may also not be allowed according to (possible future) national or regional legislation. One member suggested that a recommendation could be discussed not to produce unifloral honeys of PA-containing plants. More information about the effective removal of PAs from feed and food is needed. Consequently, for now it is a better option to prevent/reduce PAs from coming into feed and food.

12. The eWG recognized that non-agricultural management practices such as consumer education, dietary advice or labelling could potentially reduce PA exposure. These matters were not considered in detail by the eWG, as its focus was more on agricultural practices to develop a Code of Practice. Nevertheless the eWG agreed that it could be discussed by CCCF that such non-agricultural management practices could be developed further in a future Code of Practice.

13. It should be noted that any risk management methodology needs to be thoroughly assessed by each country to ensure that it is appropriate and practical for their country-specific conditions. The eWG discussed the possibility for evaluation of the available management measures (either by the eWG or the competent authorities) before considering them for practice, but it was also recognized that methods/results for such an evaluation were hard to find. There are no precise figures which indicate how effective the management measures are, so this could not be evaluated in this discussion paper but it would be worthwhile determining if more information could be obtained on this point prior to finalizing a Code of Practice. The eWG suggests a Code of Practice could include a methodology (e.g. a score card) which parties could use to evaluate if a particular measure is relevant/effective for their own situation. Also a case study for such an evaluation could be included in a future Code of Practice.

Conclusions and recommendations

14. As concluded in the preceding discussion paper (CX/CF 11/5/14), the eWG acknowledges that there are a number of data gaps and uncertainties regarding the risk of PAs to humans, including:

- the relative toxicity of different PAs;
- the major PA contributors in the human diet in different geographical areas;
- the extent to which animal consumption of PAs contributes to human health effects;
- the overall risk to humans from PAs;
- the efficacy of different management practices.

15. Nonetheless, due to the potential health-threatening effects that can be caused by ingestion of these toxins in feed or food, the eWG concludes that it is desirable to reduce exposure of both humans and animals to PAs as much as possible. Therefore, it recommends that CCCF starts new work on a ‘Code of Practice for the prevention and reduction of contamination of food and feed with pyrrolizidine alkaloids’, but notes that in the absence of adequate characterisation of human risk at this stage, it would represent a precautionary approach and guidance for further work on developing measures of effectiveness. The eWG concludes that the development of such a Code of Practice is feasible as there is some useful information available, especially for weed control.

16. As such, the eWG recommends that:

- the Code of Practice includes 'Management practices for weed removal/reduction';
- the topics 'Management practices to reduce exposure of animals to PAs', 'Management practices to reduce exposure of food-producing animals to PA-containing plants – livestock and bees' and 'Management practices to reduce presence of PAs in commodities – raw and processed' in principle should be included in the proposed Code of Practice, but that there is currently too little information available on existing practices and their efficacy to fully support this. The eWG recommends that it is discussed by CCCF whether this information could be gathered during the development of a Code of Practice or as a separate activity;
- non-agricultural management methods such as education, dietary advice or labelling, could potentially reduce PA exposure, and that it is discussed by CCCF if these could be developed further in a future CoP;
- the development of a methodology which parties could use to evaluate if a particular measure is relevant/effective for their own situation is explored by CCCF. The eWG recommends that it is discussed by CCCF whether this development could be done as part of the work on a Code of Practice or as a separate activity.

ANNEX I

MANAGEMENT PRACTICES FOR PREVENTION OR REDUCTION OF CONTAMINATION OF FOOD OR FEED WITH PYRROLIZIDINE ALKALOIDS (PAs)

1. INTRODUCTION

Pyrrolizidine alkaloids (PAs) are natural toxins occurring in a wide variety of plants. PAs are probably the most widely distributed natural toxins that can affect wildlife, livestock and humans (WHO, 1988; FAO, 2010). There is currently insufficient information on the levels of PAs in different foods to estimate human dietary exposure and its significance to human health. Nonetheless, due to the potential health-threatening effects that can be caused by ingestion of these toxins in feed or food, it is desirable to reduce exposure of both humans and animals to PAs as much as possible. Therefore, this Annex summarizes management or mitigation practices aimed at preventing or reducing the occurrence of PAs in feed and food.

In this Annex, different management practices for the prevention or reduction of contamination of food or feed with PAs are presented. It should be noted that this Annex is only intended as a compilation of available information, and not as a draft Code of Practice.

Furthermore, it should be noted that any risk management methodology needs to be thoroughly assessed by each country to ensure that it is appropriate and practical for their country-specific conditions. Methodologies or results for such an assessment have not been identified for this discussion paper; these would need to be developed.

A principal control measure is weed control in combination with Good Agronomical Practices (see also CoP on Good Animal Feeding, CAC/RCP 54-2004) (FAO, 2010). For this discussion paper it is emphasized that total eradication of PA-containing plants is neither feasible nor ecologically desirable as they may be important for the insect population in the area. In addition, livestock will avoid eating these plants under normal circumstances. Animals may eat the plants when feed gets scarce or when PA containing plants are present in dried form in feed. Therefore management on the level of weed control is still recommended and is included below.

2. PRACTICES FOR WEED CONTROL

The most effective way to control PA-containing plants is to follow a combination of agricultural, mechanical and chemical methods (integrated weed management) to assure an infestation will be minimized. A short description of each of these methods including their advantages and disadvantages can be found below.

The use of an integrated weed management plan is more effective and has other environmental and economical benefits. It will reduce the use and reliance of herbicides, thereby lowering the chance on herbicide resistance, and allow weed management in most environments (Naughton *et al.*, 2006).

In addition, it must be recognized that the different PA-containing plants may react in a different way to certain management measures. Therefore, it is always important to keep the ecology of the specific plant in mind. The management practices discussed below may be effective for some PA-containing plants but not for others. Additionally, influences of weather or climate must also be taken into account.

2.1 REMOVAL AND REDUCTION OF PA-CONTAINING PLANTS

2.1.1 Mechanical

For the control of PA-containing plants, one may use mechanical methods such as (hand) pulling, mowing and slashing. Effective manual control requires removal of the crown and all larger roots. Therefore, this may be only effective for seedlings and rosettes in contrast to bigger plants, which normally develop deep roots. In addition, effective hand pulling is useful for small infestations but is not cost-effective for large ones (Thorne *et al.*, 2005). Another issue is that disturbance of the soil may lead to more germination since buried seeds will be exposed to (sun) light.

Wheat fields, millet fields, etc., should be weeded prior to planting and periodically during the first six weeks of the growth cycle. A final weeding about two weeks before harvest significantly reduces the possibility of contamination of the harvest with toxic seeds. In legume crops, mechanical or manual weeding may be the only option (FAO, 2010). Attention should be paid to areas bordering the crop or pasture, as these may constitute a continuous reservoir for the weed infestation (North West Weeds, 2007, cited by FAO, 2010).

Another form of mechanical removal is slashing or mowing. Mowing and cutting can be easily applied for large-scale restorations, but are not always effective in killing the plants and may even encourage them to re-shoot. For example, tansy ragwort (*Jacobaea vulgaris*) has got the ability to grow back in a few weeks and might switch to vegetative reproduction forming multiple crowns extending their lifespan (van der Meijden & van der Waals-Kooi, 1979; Wardle, 1987 cited by Leiss, 2010). Also Paterson's curse (*Echium plantagineum*) is not killed by slashing but slashing will delay and suppress flowering and weaken the plant by forcing the plant to regrow and use up its energy reserves. Consequently, slashing or mowing may need to be executed on a very regular basis and applied in combination with other control measures as part of an integrated weed management plan. For example, one can combine high mowing frequencies with the use of additional nitrogen. This leads to the promotion of fast growing grass species, which resist frequent defoliation and are strong competitors. In this way germination and establishment of, for example, tansy ragwort is strongly impaired (Crawley & Nachapong, 1985 cited by Leiss, 2010).

The timing of applying mechanical methods is also important. Cutting or slashing tansy ragwort at the start or end of anthesis, for example, reduced the number of flower heads by 87% in one study (Siegrist-Maag *et al.*, 2008 cited by Leiss, 2010). It is therefore recommended to do the first mowing when 50% of the plants start anthesis, and the second mowing when half of the re-established plants start anthesis again. However, fireweed (*Senecio madagascariensis*) should not be slashed in late spring or when more than 25% of the plants are flowering, since the mature plant, that otherwise might have died, may go into re-shooting (Weed Management Unit, 2009).

2.1.2 Chemical

Chemical spraying with appropriate herbicides may be an effective way of controlling weed, especially when other methods are not feasible. For some weeds, the use of a surfactant will help to increase the effectiveness. Also, the use of herbicides should be done in combination with other control methods to increase effectiveness. For most PA-containing plants, the most effective time to spray herbicides is when the plants are actively growing and commencing flowering, i.e. in the spring before bloom and in the autumn, applied to the new rosettes. Weeds should, however, not be sprayed when the plants are stressed either through lack of water, too much water, disease, insect or mechanical damage, as spray effectiveness will diminish (Peirce, 2009). In addition, the use of non-selective herbicides may damage the crop and pasture species and surrounding crops, pastures and environment. Therefore, it is better to use selective herbicides or use non-selective herbicides only for spray topping the weed (Naughton *et al.*, 2006). Another disadvantage is that some weeds can develop resistance against a particular herbicide overtime (Thorne *et al.*, 2005).

Herbicides that can be used, depending on the specific PA-containing plant, are 2,4-D, dicamba, metsulfuron, 2-methyl-4-chlorophenoxyacetic acid (MCPA), glyphosate and triclopyr or a combination (Weed Management Unit, 2009; Dellow *et al.*, 2008; Naughton *et al.*, 2006). For ragwort species, the effectiveness of several chemical management interventions have been analyzed (Roberts & Pullin, 2007). Application of the herbicides 2,4-D, Asulam, Clopyralid, and MCPA is effective at reducing ragwort densities. However, when considering individual species, 2,4-D and MCPA are only effective against tansy ragwort, while Asulam was only effective against marsh ragwort (*Senecio aquaticus*)[2]. Furthermore, because tansy ragwort has a large proportion of biomass in the crown and root system below ground level, it is a challenge to get an effective amount into the crowns and roots. For the best results herbicides should be applied when the plants are not under stress (e.g. from drought or extreme temperatures) (McLaren & Faithfull, 2004). Furthermore, the effective concentration will be reduced when rain falls within 5 hours of application, as is observed with 2,4-D and MCPA (Coles, 1967 cited by Roberts & Pullin, 2007; Forbes *et al.*, 1980 cited by Roberts & Pullin, 2007).

2.1.3 Biological

Insects

Biological control involves the use of natural enemies of a plant to control the spread of those plants. It may be an economical and effective method. However, efficacy must have been established and the natural enemy must not present an environmental problem itself (Myers, 2000). For example, after the natural enemy has reduced its natural food source to levels below those able to sustain its population, the natural enemy could start on a non-target plant as a substitute. Furthermore, good biocontrol is only feasible for a number of species as costs associated with finding, screening and testing potential agents can be very high. Successful biological control requires extensive development and establishment phases and costs. Often, natural enemies must be introduced into an exotic environment as weeds may be imported from other parts of the world and become established. These difficulties are demonstrated by the outcomes of a worldwide review of biological control of weeds, in which it was calculated that 63% of the agents released became established, but only 24% of the releases were considered effective in controlling their weed host (Ensbey, 2009). A few examples for insects illustrating successful biological control are given below.

The natural enemies *Longitarsus jacobaeae* (ragwort flea beetle) and a combination of *Longitarsus jacobaeae* and *Tyria jacobaeae* (cinnabar moth) appear to have the potential to reduce tansy ragwort densities. The combination of flea beetles and the cinnabar moth was found to reduce tansy ragwort with an average of 99.5%. The application of *Tyria jacobaeae* alone does not appear to significantly reduce tansy ragwort densities, but does reduce the number of capitula per plant, seeds per capitula, viability of seeds, and dry weight of the plants (Roberts & Pullin, 2007). *Cochylis atricapitana*, a ragwort stem and crown boring moth from Europe, was released as a biocontrol agent in Australia and New Zealand. As a result, a 40% reduction in plant height of flowering plants and a significant reduction in both size and survival of rosettes have been observed (McLaren *et al.*, 2000; Gourlay, 2007a). Another biocontrol agent used is the ragwort plume moth (*Platyptillia isodactyla*), which has as common host marsh ragwort. This plume moth has been released in Australia in 1999 and in New Zealand in 2006. Marsh ragwort densities were reduced by 60-80% (Gourlay, 2007b). In Australia, biological control of blue heliotrope (*Heliotropium amplexicaule*) has been trialed. Blue heliotrope is an introduced weed in Australia of South American origin and target biological control agents were sourced from similar origin with selection based on host specificity (Briese & Walker, 2002). In 2001, the blue heliotrope leaf-beetle (*Deuterocampta quadrijuga*) was first released. At high densities, leaf-beetles can completely defoliate the plant, with both the larvae and adults feeding on the leaves (Dellow *et al.*, 2008).

Currently, for most of the PA-containing plants no effective biological control agent is available. For example, for common heliotrope (*Heliotropium europaeum*) two agents have been released in Australia being a rust fungus (*Uromyces heliotropii Sred*) and a flea beetle (*Longitarsus albineus Foundras*), but the first had no measurable impact and the latter failed to establish under difficult conditions (Dellow *et al.*, 2004).

Livestock

Grazing management by PA resistant livestock can be applied quite effectively against PA-containing plants, since it may weaken the plants and prevent prolific seeding. The best stocks to use for grazing management are sheep, especially non-pregnant, non-lactating Merino sheep, or goats. The sheep rumen has a great capacity to degrade most of the PAs in the plant, making them relatively resistant (Dellow *et al.*, 2008; Anjos, 2010; McLaren & Faithfull, 2004). Grazing management is very useful against PA-containing plants that are palatable and non-toxic to these Merino sheep. It can be applied on low-level, widespread infestations. Disadvantages are that enough grazing animals must be available when needed; water and fencing or herding to control movement must be set up; and the timing, intensity and duration of grazing must be closely monitored and managed to prevent overgrazing (Thorne *et al.*, 2005). Overgrazing may lead to loss of the competitive nature of the pasture or of native plants or might even lead to weeds to return and spread over the bare soil. Overgrazing may also lead to livestock poisoning, as such it is recommendable to stop grazing during flowering of (a number of) PA-containing plants as their PA-production is then very high (Naughton *et al.*, 2006). This is underlined by Suter *et al.* (2007), as continuous grazing was found to lead to a significantly higher risk of infestations with ragwort species.

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2 Asulam is no longer approved at EU level, however it is still registered in some EU countries (Austria, Belgium, Czech Republic, Spain, France, Ireland, Italy, Luxembourg, Netherlands, Poland, Portugal, Slovakia, United Kingdom).

Antimethanogenic therapy in livestock may also provide a means to increase ruminant resistance to PA toxicity. The relative resistance of ruminants to hepatotoxic PAs compared to monogastric species is due to rumen bacteria that rapidly convert PA-*N*-oxides to the corresponding free bases and subsequent action of other rumen bacteria, such as *Peptostreptococcus heliotrinreducans*, (*Peptococcus heliotrinreducans*) that use free hydrogen in the rumen to hydrolyse the C9 ester linkages of PAs to yield non-toxic aliphatic acids and 1-methylenepyrrolizidine derivatives (Dick *et al*., 1963; Lanigan 1970; Lanigan 1971; Lanigan 1976). The latter are further reduced in the rumen to the corresponding 1-methylpyrrolizidines which are also non-toxic (Lanigan & Smith 1970).

The level of *P. heliotrinreducans* varies considerably in ruminants living in different environments. Animals with no previous exposure to PAs are very susceptible to poisoning while animals with prior exposure to weeds containing PAs show enhanced rumen detoxifying activity, suggesting that *P. heliotrinreducans* levels in the rumen increase on exposure to PAs. This helps to explain the observed wide variation in susceptibility of ruminants to PAs and the increasing resistance to their toxic effects when ruminants have had prior exposure to low levels of these natural toxicants (Peterson *et al*., 1992).

2.1.4 Other

Other eradication methods include soil solarization, flaming (burning) and use of boiling water. These methods may be destructive for other plant species than the target species. In established pastures burning may even have a more detrimental effect on the pasture than on the weed. Therefore, applying these methods must be done after good planning taking into account possible risks to the environment. For tansy ragwort, flaming killed 93% in the seeding stage whereby the burned plants did not retain their viability (Wardle, 1987 cited by Leiss, 2010). Burning Paterson's curse on the other hand will kill many seeds but will also stimulate others to germinate (Naughton *et al.*, 2006).

Another option for reducing PA-containing plant material is reducing the PA content of remaining plants by cultivation methods. The total PA concentration in roots and shoots is influenced by both soil moisture and nutrient availability (Kirk *et al.*, 2010; Hol *et al.*, 2003). In the roots, increasing soil moisture led to higher concentrations of PAs. PA concentrations are expected to be higher when nutrient availability is low. Higher PA concentrations were found in plants grown in sand without nutrients than with nutrients. Decreasing PA concentrations seems to result from a diluting effect as plant biomass increases with increasing nutrient supply (Hol *et al.*, 2003). These findings suggest that increasing soil moisture and nutrient supply will reduce the PA concentrations in the weed. According to Hol *et al.* (2003), it is however unclear whether the same effect may be expected in flowering plants. Brown & Molyneux (1996) did not find an effect of nutrient deficiency on PA concentrations. Both the flower head biomass and total amount of PAs increased with nutrient supply, while the PA concentrations remained constant. However, Brown and Molyneux only looked at the total PA amount in the flower heads and not in other parts of the plant. Therefore, it might be that a change in distribution to the flower heads occurred to compensate for the dilution effect.

2.2 CONTROL OF PA-CONTAINING PLANT RELEASE AND SPREAD

Preventing PA-containing plants spreading is one of the most important practices to consider since it tackles the problem at the source and lowers the cost which could be incurred for other management practices. Early detection of the PA-containing plant is therefore vital. Once such a plant is detected, immediate action is required to prevent spreading of the plants. To achieve an early detection, good education of the farmers and local population is crucial. (FAO, 2010).

2.2.1 Control movement of plants/seeds over borders/agricultural zones

Several steps can be taken to reduce the chance that seeds of PA-containing plants will enter pastures or agricultural land. Planting of high quality, weed-free crops or grass seeds is essential (Weed Identification and Control Handbook Idaho). There may be national or regional laws and directives introduced assuring that suppliers must deliver seed for planting that is not contaminated (e.g. certified seed) (Naughton *et al.*, 2006). This also applies to hay and other fodder that is used to feed livestock (McLaren & Faithfull, 2004).

2.2.2 Control plant seed movement on animals

Another point is to quarantine livestock that have grazed in infested areas as seed could be carried on the hooves and coats, and in the digestive tracts of livestock. These quarantine areas must be inspected regularly for the presence of any PA-containing weed on the land (McLaren & Faithfull, 2004).

2.2.3 Control plant seed movement on vehicles and agricultural machinery

It is also important to clean vehicles, machinery and equipment when used in infested areas to prevent introduction of the weed to other pastures or land by spread of seeds. In addition, weed-free buffer zones between infested and un-infested lands will help to contain the infestation (McLaren & Faithfull, 2004).

2.2.4 Identification of alternative plant sources to reduce undesirable growth

Vigorous perennials will contribute to successful weed control in the long term, as these plants will suppress the introduction and growth of PA-containing weeds. This can be achieved by 1) sowing winter pasture species; 2) allowing a stand over of summer pasture feed; and 3) growing combinations of winter and summer pastures (Weed Management Unit, 2009). According to Suter *et al*. (2007) for example, swards with a high percentage of uncovered soil (>25%) carried a 40-fold higher risk of occurrence of ragwort (*Senecio*) species than swards with less than 25% uncovered soil. Sound crop rotations can also minimize weed problems, since it will help to build up soil fertility and structure to produce increasing yields. Increased fertility in its turn will reduce the impact of weeds, and rotating crops can reduce the seeding and germination of weeds (Weed Management Unit, 2009). Good agronomic practice, such as appropriate sowing time and depth, adequate fertility and moisture at sowing, is important to ensure good pasture management (Naughton *et al.*, 2006). Pasture management must also often be accompanied, mainly in the establishment phase, by other forms of weed control, such as herbicides and mechanical means (Ensbey, 2009).

Agricultural methods are helpful to improve the growth and establishment of desirable, native plants so they can resist weed invasion. The above-mentioned pasture management is an example of an agricultural control measure. Furthermore, water and nutrient management or mulching are measures that can also be applied. For example, fertilization of pastures with superphosphate or urea promoting a dense pasture sward reduced densities of tansy ragwort (*Jacobaea vulgaris*) (Thompson & Saunders, 1986 cited by Leiss, 2010). High nitrogen application, i.e. doubling nitrogen from 50 to 100 kg per hectare per year, reduced the occurrence of tansy ragwort (*Jacobaea vulgaris*) fivefold and that of marsh ragwort (*Senecio aquaticus*) threefold (Suter *et al.*, 2007; Suter & Lüscher, 2008 cited by Leiss, 2010).

Agricultural control methods are useful for large restoration projects and help to (re-)establish native plant communities on disturbed or depleted areas. On the other hand, seeds from locally adapted plants for ground cover (see pasture management above) are not always available and there are costs of fertilizers and irrigation equipment to consider (Thorne *et al.*, 2005).

2.2.5 Legislation and regulation for undesired plants and seed in food/feed

There may be (local) regulations that encourage farmers to control undesirable plants.

3. PRACTICES TO REDUCE EXPOSURE OF FOOD-PRODUCING ANIMALS TO PA-CONTAINING PLANTS

3.1 LIVESTOCK

It should be noted that cattle and horses will in general avoid eating PA-containing plants, and will only start grazing on these when other food becomes scarce. The best management measure would be ensuring sufficient feed for the animals and in all cases recently transported hungry or thirsty animals should not be placed in pastures contaminated by PA-containing plants (Riet-Correa and Medeiros, 2001). However, in some situations this may not be feasible and other measures may become relevant. In some cases when infestation is severe, it may be necessary to remove livestock from the affected pastures.

Since this will mean a big impact on farming practices, prioritization of control measures could be done using the system as proposed by Neumann *et al.* (2009). Based on distance of tansy ragwort (*Jacobaea vulgaris*) to a field or pasture, three risk zones are identified. When the risk is classified as high (0-50 metres), immediate action on controlling ragwort (*Senecio*) species is recommended. At medium risk (50-100 metres), a control policy should ensure that changes from medium to high risk are anticipated and effectively dealt with. No immediate actions would be required at low risk (>100 metres).

3.2 BEES

Placing bee hives not too close to PA-containing plants may not be a sufficient control option to prevent PAs from entering the food chain via honey. Honey bees may operate in a radius of more than 3 km around the bee hive, covering an area of many km^2. Moreover, some PA-containing plants, e.g. Viper's Bugloss (*Echium vulgare*), play an important role as food source for honey bees which may need replacing if taken away, in order to prevent a decrease in honey production. Thus, the access to PA plants has to be lowered, but at the same time it is necessary to provide another food source, which is ideally flowering at the same time as the PA-containing plant. If the new food source is of higher quality for the honey bees than the PA-containing plant, this could also have a positive effect on PA concentrations found in honey as the honey bees will preferably visit the more attractive plant (FoodDrinkEurope, 2011, personal communication).

4. PRACTICES TO REDUCE PRESENCE OF PAS IN RAW COMMODITIES

4.1 WITHHOLD AFFECTED ANIMALS/CROPS FROM FOOD/FEED CHAIN

Once contamination has been observed, it is an option to withhold the animals or crops from the food chain. Affected products may be cleaned from parts or seeds of PA-plants before they can be used for animal or human consumption.

4.2 FILTERING/SIEVING

Seeds

The provisions in the Codex Standards for cereals and pulses (CODEX STAN 153-1985 CODEX STAN 171-1989, CODEX STAN 172-1989, CODEX STAN 199-1995, CODEX STAN 201-1995) for the presence of toxic seeds should be applied before the crop is milled or distributed for human consumption. The test method contained in the ISO standard is easily applied and does not require elaborate laboratory equipment or extensive training of operators. In some cases, sieving can be used to separate the PA-bearing weed seeds on the basis of size (FAO, 2010).

It is worth noting, however, that the removal of toxic seeds by sieving will assist in reducing the level of PAs in contaminated cereals and pulses but will not ensure that they are free of PA contamination. PA-bearing dust remains associated with contaminated cereals and pulses following complete removal of contaminating PA seeds by sieving (ANZFA, 2001; Edgar, 2003).

Honey

Bee pollen is the major source for the PA content found in honey. PA content is directly proportional to the absolute amount of PA pollen. The PA transfer from pollen to honey is rather quick and therefore regular honey filtration is not an option to reduce free PA content of honey. Filtration would reduce though the amount of hidden/pollen-bound PAs (Kempf *et al*., 2011). However, filtering of honey is not consistent with the Codex Standard (12-1981) for honey which does not allow the removal of pollen from honey.

Knowledge of bee biology might help to limit the amount of pollen that gets into honey by the use of different hive structures. Furthermore, alternative extraction methods could be used that reduce the pollen content in honey. A shift in general perception might be necessary for this purpose, as currently the presence of pollen in honey is considered to give health benefits (Boppré, 2011).

4.3 DESTRUCTION OF WEED SEEDS & PLANT MATERIAL

Removed PA-containing plant material (see section 2) or seeds (see section 4.2) should be destroyed in such a manner to avoid spreading of the plants.

4.4 DECOMPOSITION

Silage may be an option for reduction of PAs in contaminated feed, e.g. tansy ragwort. It was demonstrated that composting the plant in black bin bags in the direct sunlight in the field lead to a breakdown of PAs within four weeks and a complete loss within 10 weeks (Crews *et al.*, 2009). It is also possible to place tansy ragwort plants in a digester. Accordingly, Wiedenfeld (2011) compared the amount of PAs in hay and silage from tansy ragwort. The data show that in the case of hay no reduction of the PA level compared with dried plants can be observed. Contrary to this, the results for silage show a decrease in PA level down to 10%. It can be assumed that this is due to an enzymatic decomposition. Bagging samples of tansy ragwort and inoculating and covering it with composting material, lead to a reduction the PA concentration to levels below detection limits within four weeks (Hough *et al.*, 2010). However, from this information it is unclear if the resulting metabolites could be a health concern.

4.5 EXISTING LEGISLATION AND REGULATIONS FOR THE CONTROL OF PAS IN FEED/FOOD

There may be national or regional laws and directives introduced assuring that suppliers must deliver seed for planting that is not contaminated (e.g. certified seed) (Naughton *et al.*, 2006). This also applies to hay and other fodder that is used to feed livestock (McLaren & Faithfull, 2004).

5. PRACTICES TO REDUCE PA CONTAMINATION BY FURTHER PROCESSING OF COMMODITIES

5.1 REFINING OF OIL

After spiking borage oil with 100 ppb crotaline, several refining steps were shown to be able to reduce the content of crotaline in the oil significantly (Wretensjö & Karlberg, 2003). During bleaching, the crotaline content was reduced by a factor of more than 100 and after deodorization about half as much. During these steps, pigment components, such as chlorophyll and carotenoids, other unwanted components, such as metals, sulfur compounds and peroxides, and flavoring compounds are removed. A smaller decrease was found during alkali refining, but this was expected as this initiating step is mainly focused on removal of acid components.

It has been shown that no pyrrolizidine alkaloids are present in crude borage oil at levels above the 100 ppb limit. The PA content in crude borage oil, if any, is reduced by a factor of about 30,000 by the refining process. This implies that the PA content at a parts per billion level would be reduced to a parts per trillion level (Mierendorff, 1995; Parvais *et al*., 1994).

5.2 PROCESSING OF HONEY AND MEAD

The production process might influence the amount of PAs in honey. For example, blending different honey types with different amounts of pollen has an apparent effect when comparing PA patterns, concentrations and abundances in raw and retail honey (Dübecke et al., 2011). Conversely, the PA concentration in mead (one sample) was found to be about four-fold higher than the highest value found by the same method of analysis for regular honey. This was surprising because candy and mead have undergone some technological treatments (dilution, heating and/or fermentation) and still show PA values that are well above the average of regular retail honey. This means that PA contamination of the used raw material (honey) can be carried on to the final product and significant amounts of PAs can be present (Kempf *et al*., 2011).

5.3 Quality Assurance of inputs and Good Manufacturing Practice

The quality of inputs during processing of feed/food can be assured by using only certified material and processing according to GMP.

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