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Case studies on genetically modified organisms (GMOs): Potential risk scenarios and associated health indicators

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ABSTRACT

Within the frame of the EU-funded MARLON project, background data were reviewed to explore the possibility of measuring health indicators during post-market monitoring for potential effects of feeds, particularly genetically modified (GM) feeds, on livestock animal health, if applicable. Four case studies (CSs) of potential health effects on livestock were framed and the current knowledge of a possible effect of GM feed was reviewed. Concerning allergenicity (CS-1), there are no case-reports of allergic reactions or immunotoxic effects resulting from GM feed consumption as compared with non-GM feed. The likelihood of horizontal gene transfer (HGT; CS-2) of GMO-related DNA to different species is not different from that for other DNA and is unlikely to raise health concerns. Concerning mycotoxins (CS-3), insect-resistant GM maize may reduce fumonisins contamination as a health benefit, yet other *Fusarium* toxins and aflatoxins show inconclusive results. For nutritionally altered crops (CS-4), the genetic modifications applied lead to compositional changes which require special considerations of their nutritional impacts.

No health indicators were thus identified except for possible beneficial impacts of reduced mycotoxins and nutritional enhancement. More generally, veterinary health data should ideally be linked with animal exposure information so as to be able to establish cause-effect relationships.

1. Introduction

1.1. Marlon project

Within the EU-funded MARLON project, which ran from 2012-until 2015, we explored the possibility to develop a methodology for post market monitoring (PMM) of specific potential health impacts of the consumption of genetically modified (GM) crop-derived feeds by livestock animals. Under EU legislation, case-specific monitoring may be required, on a case-by-case basis, by the European authorities as one of the conditions of marketing approval for such crops. Whilst such crops have to undergo a rigorous pre-market assessment, post-market monitoring could serve to verify assumptions or to address any questions arisen during the previous assessment. Up to now the requirement for post-market monitoring of GM feed impacts has not been imposed by the EU authorities for any GM feed yet. With the aim to assist applicants, risk assessors, decision makers, and veterinary health professionals with any potential future requirement for the post-market monitoring of a given GM feed, the MARLON project aimed to identify the gaps and to develop a generally applicable tool and methodology as it could not be known on beforehand for which crop species, which target livestock species and what health

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effect the monitoring would be asked for. In the development of a generically applicable monitoring methodology, two basic questions are asked, namely: 1) which effects are already known to be associated with the consumption of GM feeds by livestock; and 2) which indicators of a potential health impact can be used to monitor for such effects of feeds in a post-market monitoring program. This review examines four scenarios of potential health effects and attempts to define health indicators in the frame of four case studies: allergenicity (CS-1), horizontal gene transfer (CS-2); mycotoxins (CS-3); and second-generation nutritionally altered crops (CS-4).

1.2. GM crops

Generally, soybean is the most important animal feed in the European Union (EU). Soybean and other commodity crops such as maize, oilseed rape (canola) and cotton, have been genetically modified for agronomic input traits, such as insect resistance and/or herbicide tolerance (first-generation GM products). These plants are both used in monogastric and ruminant diets as energy and protein source. They are used as fresh or ensiled whole crop forage (i.e. maize and lucerne), as a specific crop component (i.e. maize grain), or as co-products (i.e. oilseed meals or maize stover). In 2015, twenty-eight countries planted 179.7 million hectares of GM crops worldwide, but most of these crops were grown in just five countries: the United States, Brazil, Argentina, India and Canada (ISAAA, 2015). From these countries, GM crops are exported to Europe, whereas the latter is quite self-sufficient when it comes to maize. Most of Europe's maize production is used in animal feed. Maize is the only GM crop cultivated in the EU with 107,749 ha sown in Spain in 2015 and the remainder (9121 ha) in Czech Republic (997ha), Romania (2.5ha), Portugal (8,017ha), and Slovakia (104ha) (Monsanto, 2016).

Before a genetically modified organism (GMO) can be marketed or grown in the EU, it must be authorized under Regulation (EC) 1829/2003 (the 'GM Food and Feed Regulation') amended by the implementing Regulation (EC) 503/2013. The authorization procedure includes a scientific assessment by the Panel on Genetically Modified Organisms of the European Food Safety Authority (EFSA). The EFSA Panel assesses the safety of the GMO and the food or feed derived from it. The safety assessment follows a comparative approach, i.e. the food and feed are compared with their non GM counterparts in order to identify differences reflecting intended or unintended effects of the genetic modification which subsequently are assessed with respect to their potential impact on the environment, safety for humans and animals, (EFSA, 2011a). A scientific opinion is expressed by the Panel which is taken into account by the risk manager (e.g. the Commission and member states competent authorities to grant authorization for the GMO use in the EU.

Currently (http://ec.europa.eu/food/dyna/gm_register/index_en.cfm - 10/01/2017), in the EU, 77 GM plants/products with a possible use in feed: 43 events of maize, 11 events of cotton, 15 events of soy bean, 4 events of oilseed rape, a sugar beet, a potato and two micro-organisms have temporary or full authorisations, granted under the GM Food and Feed Regulation (Table 1). Apart from the micro-organisms and the withdrawn potato, these products are GM crops varieties of which most were produced to exhibit resistance to certain herbicides, insect pests or both (first generation GM products). All of these GM varieties have been authorized for import and processing. Two of the maize varieties have also been licensed for cultivation, but only one is being grown commercially on a limited basis in Europe. There are also currently GM plants developed with significant intended alterations in agronomic properties (drought resistance, salt tolerance etc), and in composition to enhance the nutritional properties for health or growth benefits (second generation GM products). A few of these products have been recently authorized to be marketed in the EU: maize MON87460 modified for improving water use efficiency; Soybean DP-305423 with modified seed fatty acid content, specifically with high oleic acid and low linolenic acid contents, and soybean MON 87769 which contains stearidonic acid (SDA; 18:4), as an alternative source of an omega-3 fatty acid to help meet the needed dietary intake of long-chain omega-3 fatty acids.

1.3. Post Market Monitoring (PMM) of food and feed derived from GM plants

GMOs are authorized only if considered safe for human and animal health and the environment. Nevertheless, their routine surveillance has been considered necessary as precaution in those cases when there are residual uncertainties deriving from the pre market safety assessment and to detect unforeseen effects. Towards this end, all applications for releasing them into the environment or marketing GMOs as food, feed and derived products, must propose a PMM for each specific GMO for which a marketing application has been filed. This plan is part of the EU authorization decision and the applicant must implement it and regularly report on it to the EU authorities. The objective to be achieved and the general principles to be followed to design the monitoring plan are described in the annex VII of the Directive 2001/18/EC: “The objective of a monitoring plan is to: i)confirm that any assumption regarding the occurrence and impact of potential adverse effects of the GMO or its use in the environmental.risk assessment (e.r.a.) are correct, and ii) identify the occurrence of adverse effects of the GMO or its use on human health or the environment which were not anticipated in the e.r.a.” The first type of monitoring activities is also referred to as “case-specific” given that it focuses on a specifically identified issue identified during pre-market risk assessment (e.g. the development of pest insect resistance to an insect-resistant crop) whilst the second type is referred to as “general surveillance”.

Applications concerning food/feed uses and import and processing do not require scientific information on possible environmental effects associated with the cultivation of the plant given that this outside the scope of the application. The program of the environmental PMM will depend on the level of the release and exposure on the environment. In fact, the EFSA guidelines differentiate between general surveillance plans when GM is for cultivation and when applications are intended for import/processing.

In the latter case, general surveillance plans need to consider the modified characteristics specific to the GM plants in question, their intended use and the receiving environment. In the case of non-viable GM material (e.g. derived products not containing any living GMOs) and according to Directive 2001/18/EC, the applicant does not have to provide any environmental monitoring plan (including general surveillance). In the case of imported GM products containing viable propagating material, general surveillance plans should consider that, appropriate management systems to restrict environmental exposure if substantial loss, spillage from the establishment is possible.

Case-specific Post Market Monitoring should be required for food and feed derived from GM plants only in specific cases, such as for foods with altered nutritional composition and modified nutritional value and/or with specific health claims. In the particular case of various vegetable oils with modified fatty acid composition, the PMM thus requested had to complement the thorough pre-market risk assessment with further information on the intake of the product by consumers. Given that pre-market risk assessment studies have some attendant uncertainties regarding coverage of the breadth of prospective consumers’ health status

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