Regulatory Toxicology and Pharmacology xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

Development of a risk management tool for prioritizing chemical hazard-food pairs and demonstration for selected mycotoxins

Alessia Stornetta [a], Barbara E. Engeli [b], Jürg A. Zarn [b], Gérard Gremaud [c], Shana J. Sturla [a,*]

[a] Swiss Federal Institute of Technology Zürich, Department of Health Sciences and Technology, Institute of Food Nutrition and Health, Schmelzbergstrasse 9, 8092 Zürich, Switzerland
[b] Federal Food Safety and Veterinary Office FSVO, 8004 Zürich, Switzerland
[c] Federal Food Safety and Veterinary Office FSVO, 3097 Liebefeld, Switzerland

ARTICLE INFO

Article history:
Received 20 September 2014
Available online xxxx

Keywords:
Food safety
Hazard
Mycotoxin
Prioritization
Ranking
Risk management
Tool

ABSTRACT

We developed a simple tool for ranking chemical hazard-food pairs to assist policy makers and risk managers selecting the hazard-food pairs that deserve more attention and need to be monitored during food safety inspections. The tool is based on the derivation of a "Priority Index" (PI) that results from the ratio of the potency of the hazard and the consumer exposure. The potency corresponds to a toxicity reference value of the hazard, whereas the exposure results from the combination of the concentration of the hazard in the food, and the food consumption. Tool's assumptions and limitations are demonstrated and discussed by ranking a dataset of 13 mycotoxins in 26 food items routinely analyzed in Switzerland. The presented ranking of mycotoxin-food pairs has to be considered as relative due to scarce exposure data availability, and uncertainties in toxicity reference values. However, this representative example allows demonstrating the simplicity and the ability of the PI tool to prioritize chemical hazard-food pairs.

1. Introduction

The high number of foodborne hazards drives the need for risk-prioritization tools that allow risk managers to plan time- and cost-effective food safety inspections. Ranking of food safety issues allows the identification of factors most likely to cause significant public health problems, and it is viewed as the starting point for risk-based priority setting and allocation of resources focused on the development of strategies for addressing them (Davies, 1996; Ross and Sumner, 2002; EFSA, 2012). Ranking tools for prioritizing foodborne hazards differ in their purpose (prioritization of chemical vs. biological hazards), degree of complexity (number of variables), level of quantification, and approach to model construction (derivation of different risk metrics) (EFSA, 2012). There is no agreed methodology to perform a ranking; rather, the hazard-food pair being considered and the purpose of the ranking guide the selection of the most appropriate ranking tool.

Various ranking tools aiming at the prioritization of both chemical and biological hazards in food exist (Table 1). Currently used tools mainly focus on the prioritization of biological, but not chemical, hazards (Table 1). Most of these ranking tools rely on the calculation of a numerical score from the weights chosen for each input variable (Ross and Sumner, 2002; McNab, 2003; Anderson et al., 2011; Muehlemann, 2013). This technique consists in assigning each input variable value to a category of weights depending on the range in which the value can be found (e.g., a weight of 1, 2, or 3 will be assigned according to a low, middle, or high substance range of toxicity). Although the use of weight categories instead of real values may be an advantage in the case of missing or unknown data, a disadvantage of using this approach is that it decreases the discrimination power of the final result, not allowing for example to distinguish between those hazards and foods bearing the same characteristics (e.g., if both hazards have distinct but low-range toxicity values) and receiving, therefore, the same weight. Other prioritizing tools rely on the derivation of risk metrics such as the quality-adjusted life year (QALY) (Batz et al., 2004) or the (pseudo) disability-adjusted life year (pDALY or DALY) (Newsome et al., 2009; Ruzante et al., 2010; Chen et al., 2013). Although these risk metrics allow one to measure disease

Abbreviations: ADI, acceptable daily intake; AF, aflatoxins; AFB1, aflatoxin B1; AFB2, aflatoxin B2; AFG1, aflatoxin G1; AFG2, aflatoxin G2; BMD, benchmark dose; BMDL, BMD lower limit; DALY, disability-adjusted life year; DON, deoxynivalenol; F, fumonisins; FB1, fumonisin B1; FB2, fumonisin B2; LO(A)EL, lowest observable (adverse) effect level; NO(A)EL, no observed (adverse) effect level; OTA, ochratoxin A; pDALY, annual pseudo-disability adjusted life year; QALY, quality-adjusted life year; TeA, tenuazonic acid; ZEA, zearalenone.

* Corresponding author. Fax: +41 44 632 11 23.
E-mail addresses: alessia.stornetta@hest.ethz.ch (A. Stornetta), barbara.engeli@blv.admin.ch (B.E. Engeli), juerg.zarn@blv.admin.ch (J.A. Zarn), gerard.gremaud@blv.admin.ch (G. Gremaud), sturlas@ethz.ch (S.J. Sturla).

http://dx.doi.org/10.1016/j.yrtph.2015.04.014
0273-2300/

Table 1
Selected ranking tools for prioritizing hazard-food pairs.

Tool	Hazard[a]		Risk metrics	Approach[b]		References
	B	C		BU	TD	
Risk Ranger	x		Numerical score	x		Ross and Sumner (2002)
Food Safety Universe Database	x		Numerical score	x		McNab (2003)
Foodborne Illness Risk Ranking Model (FIRRM)	x		Cost of illness and QALY[c] loss		x	Batz et al. (2004)
Multi-Factorial Risk Prioritization Framework for Foodborne Pathogens	x		DALY[d] and cost of illness		x	Ruzante et al. (2010)
sQMRA Tool	x		Relative risk		x	Evers and Chardon (2010)
Risk Ranking Tool for Fresh Produce	x		Numerical score		x	(Anderson et al. (2011)
iRisk	x	x	pDALY[d]	x		(Newsome et al. (2009), Chen et al. (2013)
Practitioner Framework for the Evaluation and Prioritization of Food and Feed Safety Hazards	x	x	Numerical score	x		Muehlemann (2013)
Risk Quotient (RQ)		x	Relative risk	x		Mengelers (2013a,b)
Priority Index (PI)		x	Relative risk	x		

[a] Biological (B) or chemical (C) hazards.
[b] Bottom-up (BU) vs. top-down (TD) approach regarding whether the tool relies on toxicant data (BU) or on health outcomes (TD).
[c] The quality-adjusted life year (QALY) is a measure of disease burden that includes the quality and the quantity of the life lived (National Institute for Health and Care Excellence, 2015).
[d] The disability-adjusted life year (DALY) or pseudo-disability adjusted life year (pDALY) are measures of disease burden that include mortality and morbidity (World Health Organization, 2012–2015).

burden and may be useful in prioritizing and comparing both chemical and biological hazards in food, such is the case for iRisk, the complexity of these approaches require specialized experience in their use and interpretation of results. Another metric used previously to prioritize hazards in food is the derivation of a relative risk (Evers and Chardon, 2010; Mengelers, 2013a,b), which may be of advantage for increase the discrimination between hazard-food pairs due to the use of empirical data versus weight categories and its derivation is generally more simple that other risk metrics such as QALY or DALY.

The goal of this study was to develop a simple tool for the ranking of chemical hazard-food combinations that relies on empirical data, instead of weight categories, and considers health-related characteristics. Thus, we describe herein the development of a priority index (PI) that incorporates a toxicological reference value for a chemical hazard, its concentration in food commodities, and consumption of the food it is in. The tool allows distinction among different hazard-food pairs, as well as among the same hazard in different foods and the same food item contaminated with different hazards. As a demonstration of how the tool may be applied with available data, we evaluated a group of mycotoxins routinely analyzed in food items by the cantonal laboratories in Switzerland. The results of this work are expected to help risk managers to identify and prioritize hazard-food pairs to be included into food inspection programs.

2. Methods

2.1. Model variables

2.1.1. Toxicity (T)

Toxicity reference values used herein were European Food Safety Authority (EFSA)- and World Health Organization (WHO)-animal study-derived benchmark dose lower limits (BMDLs), no observed adverse effect levels (NOAELs), or no observed effect levels (NOELs) from toxicity studies ranging in duration from 3 to 104 weeks (Table 2). In the case that multiple values were available for a given chemical hazard, the lowest toxicity value was used as *T* for deriving a PI. NO(A)EL and BMDL are commonly accepted toxicological values used as a basis of risk assessment and are the most directly and widely accessible for commodities of interest. Toxicological values that account for clinical symptoms such as DALY and QALY may also be the basis of risk ranking, however, these values are not as widely accepted, available, or simple to utilize without specialized knowledge as NOAEL and related values. Similar to the derivation of the acceptable daily intake (ADI), if neither NO(A)EL nor BMDL values were available lowest observed adverse effect level (LOAEL) or lowest observed effect level (LOEL) values were used. Typically, a correction factor of 3 is applied to arrive at a value more comparable to a NOAEL if the ADI is derived from a LO(A)EL rather than NO(A)EL (World Health Organization, 2009). To verify whether the use of a LO(A)EL instead of a NO(A)EL resulted in a relevant change in the final ranking of the mycotoxin data and therefore needed to be adjusted by a correction factor, we lowered the toxicity values by a factor of 2 or 3. We found that the final result (PI) varies by only 1 order of magnitude (Table A.1), whereas the complete range of PI values in the mycotoxin dataset varies by 6 orders of magnitude (Table 3). This magnitude of deviation was considered to not have a major impact on the final ranking position, and no correction factor was applied therefore to the available LO(A)EL value. However, this trend may be specific for the representative mycotoxin dataset and cannot therefore be generalized to other chemical hazards, for which the application of a correction factor needs to be verified case by case. For chemical hazards of unknown potency that were lacking any available toxicological reference value (BMDL, NO(A)EL, or LO(A)EL) the toxicity reference value was set to be equivalent to that of a known hazard with similar structure (Table 2 and Fig. 1). For example, no toxicity reference values were available for the aflatoxins B2, G1, G2 or the sum of aflatoxins (B1 + B2 + G1 + G2), nor for the fumonisins B2, or the sum of fumonisins (B1 + B2). Therefore, a $BMDL_{10}$ of 0.00017 mg AFB1/kg bw day (EFSA, 2007), and a NOAEL of 0.2 mg FB1/kg bw day (EFSA, 2005a,b) were used as conservative estimated surrogate values (Table 2).

2.1.2. Exposure estimate (E)

E is an estimate of an average individual's exposure to a chemical hazard. It was derived on the basis of data for its concentration in food and intake of foods as indicated in Eqs. (1)–(4). The variable c_i corresponds to the concentration of a given chemical hazard measured in a given food for the sample i ($i = 1, 2, 3 \ldots n$; with n