

第2章 TTC の概念の発展と評価機関における規制への適用

毒性学的懸念の閾値（TTC、Threshold of Toxicological Concern）とは、あらゆる化学物質についてそれ以下の暴露量では明らかな有害影響が現れないとするヒト暴露の閾値として設定される（ILSI 2005）。この TTC アプローチを適用するには、その物質の化学構造の情報とヒト暴露量に関する情報のみが必要とされる。ただし、暴露量は過小評価ではないとの確信がなければならない（EFSA 2012a）。

TTC の概念は、化学構造がわかっているが、毒性が明らかでない物質でその既知の暴露量によるリスクを予備的に評価できるツールとして開発された。食事中の化学物質の安全性評価に TTC の概念を適用する場合には、その化学物質の摂取量又は暴露量を適切な構造クラスの TTC 値と比較する。もしその摂取量又は暴露量が当該 TTC 値よりも低い場合は、安全性上の懸念の可能性はないことを示唆している。その摂取量又は暴露量が TTC 値を超える場合には、化学物質固有の毒性データも含め追加情報がリスク評価を遂行するのに必要であることを示唆している。つまり、TTC アプローチはリスク評価者やリスク管理者がさらなる評価、もしくは安全性データの追加の必要性に関する化学物質の優先順位を決定するツールとなる。

(ILSI 2005)

1. 評価機関の報告書等

TTC の概念について、海外の評価機関において検討されてきた経緯及び規制への適用状況を調査するに当たり、評価機関から公開されている関連する報告書等を表 2-1-1 のとおり収集した。収集した報告書等のうち、表 2-1-1 の網掛けで示したものを本調査の対象とした。

表 2-1-1 評価機関の報告書等

地域等	機関名	文献のタイトル	発行年
国際機関	WHO	WHO Project to Review the Threshold of Toxicological Concern Approach, Call for data	2013
		TTC Applications: approaches and challenges	2011
		Background Paper on Dietary Exposure Assessment Prepared for the WHO Expert Meeting on Toxicological and Health Aspects of Melamine and Cyanuric Acid	2009
		Principles for the assessment of risk to human health from exposure to chemicals.	1999
	IPCS	Environmental Health Criteria 240, Principles and Methods for the Risk Assessment of Chemicals in Food, Chapter 9 PRINCIPLES RELATED TO SPECIFIC GROUPS OF SUBSTANCES	2009
		Principles and Methods for the Risk Assessment of Chemicals in Food SUMMARY	2009
国際機関	JECFA	Evaluation of certain food additives and contaminants. WHO Technical Report Series 960. Seventy-third report of the Joint FAO/WHO Expert Committee on Food Additives.	2010

地域等	機関名	文献のタイトル	発行年
		Evaluation of Certain Food Additives and Contaminants. WHO Technical Report Series 952. Sixty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives	2009
		Evaluation of certain food additives and contaminants. WHO Technical Report Series No. 940. Sixty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives.	2007
		Evaluation of certain food additives and contaminants. WHO Technical Report Series No. 947. Sixty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives	2007
		Evaluation of Certain Food Additives. WHO Technical Report Series 934. Sixty-fifth report of the Joint FAO / WHO Expert Committee on Food Additives	2006
		Evaluation of Certain Food Additives: WHO Technical Report Series 934 Sixty fifth report of the Joint FAO/WHO Expert Committee on Food Additives 2006b.	2006
		Evaluation of certain food additives. WHO Technical Report Series No. 928. Sixty-third report of the Joint FAO/WHO Expert Committee on Food Additives.	2005
		Evaluation of certain food additives and contaminants. WHO Technical Report Series No. 901. Fifty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives.	2001
		Evaluation of certain food additives. WHO Technical Report Series No. 884	1999
		Evaluation of certain food additives and contaminants. WHO Technical Report Series, No. 868. Forty-sixth Report of the Joint FAO/WHO Expert Committee on Food Additives.	1997
		Evaluation of certain food additives and contaminants. WHO Technical Report Series 859. Forty-fourth Report of the Joint FAO/WHO Expert Committee on Food Additives.	1995
	OECD	Guidance on grouping of chemicals, second edition, Series on Testing & Assessment No. 194	2014
		OECD Guideline For The Testing Of Chemicals 417, Toxicokinetics	2010
		Workshop report on OECD Countries Activities Regarding testing, Assessment and Management of Endocrine Disrupters. Series on Testing and Assessment.	2010
		Report on the Regulatory Uses and Applications in OECD Member Countries of (Quantitative) Structure-Activity Relationship [(Q)SAR] Models in the Assessment of New and Existing Chemicals. OECD Environment Health and Safety Publications Series on Testing and Assessment No. 58	2006
		Report of the Validation of the Updated Test Guideline 407: Repeat Dose 28-day Oral Toxicity Study in Laboratory Rats.	2006
米国	FDA	Threshold of Regulation (TOR) Exemptions	2014
		Packaging & Food Contact Substances (FCS)	2014
		Regulatory Report: Assessing the Safety of Food Contact Substances	2014

地域等	機関名	文献のタイトル	発行年
米国 (続き)	FDA (続き)	CFR - Code of Federal Regulations Title 21 Food and Drugs Chapter I--Food And Drug Administration, Department Of Health And Human Services, Subchapter B--Food For Human Consumption (Continued), PART 170 -- FOOD ADDITIVES Subpart B--Food Additive Safety Sec.170.39 Threshold of regulation for substances used in food-contact articles.	2014
		Guidance for Industry Genotoxic and Carcinogenic Impurities in Drug Substances and Products: Recommended Approaches	2008
		Guidance for Industry: Preparation of Premarket Submissions for Food Contact Substances: Chemistry Recommendations	2007
		Guidance for Industry: Use of Recycled Plastics in Food Packaging: Chemistry Considerations	2006
		Guidance for Industry: Submitting Requests under 21 CFR 170.39 Threshold of Regulation for Substances Used in Food-Contact Articles	2005
		Regulatory Report: FDA's Food Contact Substance Notification Program	2005
		Federal Register 1995.Food Additives; threshold of regulation for substances used in food-contact articles. Final rule.	1995
		Food additives: Threshold of Regulation for Substances Used in Food-Contact Articles. Federal Register 58	1993
	US EPA	Guidelines for Carcinogen Risk Assessment and Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens.	2005
	NRC	Toxicity testing in the 21st century: a vision and a strategy. National Research Council.	2007
Guidelines for Estimating Toxicologically Insignificant levels of Chemicals in Food.Food Protection Committee, Food and Nutrition Board, National Research Council.		1969	
欧州	EC	4th report on the implementation of the “Community Strategy for Endocrine Disrupters” a range of substances suspected of interfering with the hormone systems of humans and wildlife (COM (1999) 706).	2011
		Corrigendum to Regulation (EC) No.1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the registration, evaluation, authorization and restriction of chemicals (REACH), establishing a European Chemicals Agency, amending Directive199/45/EC and repealing Council regulation (EEC) No.793/93 and Commission Regulation (EC) No.1488/94 as well as Council Directive 76//769/EEC and Commission Directives 91/155/EEC, 93/105/EC and 2000/21/EC.	2007
		Guidance document on dermal absorption.	2004
		Commission Decision of 23 January 2002 amending Commission Decision 1999/217/EC as regards the register of flavouring substances used in or on foodstuffs.	2002
		European Workshop on the Impact of Endocrine Disrupters on Human Health and the Environment.	1997

地域等	機関名	文献のタイトル	発行年
欧州 (続き)	EC (続き)	Report on methodologies for the monitoring of food additive intake across the European Union (Final report submitted by the Task Co-ordinator 16 January 1998). Reports of a working Group on Scientific Co-operation on questions relating to food.	1998
	EC ETOC	Overview of TTC Values (February 2010)	2010
		Assessment factors in human health risk assessment. In: Technical reports European Chemical Industry Ecology and Toxicology Centre.	1995
	ECB	Risk Assessment Vinyl Acetate, CAS#: 108-05-4, EINECS#: 203-545-4.	2008
	EFSA	Threshold of Toxicological Concern Approach: Conclusions and Recommendations of the EFSA/WHO Expert Workshop DRAFT for public consultation.	2015
		EFSA/WHO Expert meeting to review the science underlying the Threshold of Toxicological Concern (TTC) Concept	2014
		SCIENTIFIC REPORT OF EFSA Modern methodologies and tools for human hazard assessment of chemicals	2014
		Scientific Opinion on the safety assessment of the process “Phoenix - ESPS”, used to recycle post-consumer PET into food contact materials	2014
		Modern methodologies and tools for human hazard assessment of chemicals, EFSA Journal 12(4):3638	2014
		Scientific Opinion on Exploring options for providing advice about possible human health risks based on the concept of Threshold of Toxicological Concern (TTC)	2012
		Outcome of the public consultation on the draft EFSA opinion on Exploring options for providing preliminary advice about possible human health risks based on the concept of Threshold of Toxicological Concern (TTC)	2012
		FAQ on the Threshold of Toxicological Concern: EFSA Homepage. 2012b: http://www.efsa.europa.eu/en/faqs/faqttc.htm :	2012
		SPECIAL ISSUE Food contact materials, flavouring substances and smoke flavourings	2012
		GUIDANCE of EFSA Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment	2011
		Draft Scientific Opinion on Exploring options for providing preliminary advice about possible human health risks based on the concept of Threshold of Toxicological Concern (TTC).	2011
		Scientific Opinion on the criteria to be used for safety evaluation of a mechanical recycling process to produce recycled PET intended to be used for manufacture of materials and articles in contact with food	2011
		Scientific opinion on the risks for animal and public health related to the presence of Alternaria toxins in feed and food. European Food Safety Authority.	2011

地域等	機関名	文献のタイトル	発行年
欧州	EFSA	Guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain. European Food Safety Authority.	2011
		Scientific Opinion on the safety and efficacy of Koffogran (nicarbazin) as a feed additive for chickens for fattening”, March 2010. European Food Safety Authority.	2010
		Guidance on the data required for the risk assessment of flavourings to be used in or on foods. European Food Safety Authority.	2010
		Public consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR) on the Draft Guidance on Dermal Absorption and the Draft Scientific Opinion on the Science behind the Revision of the Guidance Document on Dermal Absorption. European Food Safety Authority.	2010
		Management of left-censored data in dietary exposure assessment of chemical substances. European Food Safety Authority.	2010
		Scientific report of the Endocrine Active Substances Task Force. European Food Safety Authority.	2010
		The potential risks arising from nanoscience and nanotechnologies on food and feed safety. Scientific opinion of the Scientific Committee.	2009
		Food Contact Materials. Note for Guidance. Updated on 30/07/08.	2008
		Guidance Document for the use of the Concise European Food Consumption Database in Exposure Assessment.	2008
		Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on Guidelines on submission of a dossier for safety evaluation by the EFSA of a recycling process to produce recycled plastics intended to be used for manufacture of materials and articles in contact with food	2008
		Opinion of the Scientific Committee on a request from EFSA on the introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA. European Food Safety Authority.	2007
		Guidance of the Scientific Committee on a request from EFSA related to Uncertainties in Dietary Exposure Assessment. European Food Safety Authority.	2006
		Opinion of the Scientific Committee on a request from EFSA related to A Harmonised Approach for risk assessment of substances which are both Genotoxic and Carcinogenic.	2005
	ECHA	Guidance on information requirements and chemical safety assessment. Chapter R.5: Adaptation of information requirements. May 2008.	2008
JRC	The Use of Computational Methods in the Toxicological Assessment of Chemicals in Food: Current Status and Future Prospects	2011	
	Analysis of the Cramer classification scheme for oral systemic toxicity - implications for its implementation in Toxtree. : JRC Scientific and Technical Report (Lapenna S and Worth A)	2011	

地域等	機関名	文献のタイトル	発行年
欧州 (続き)	JRC (続き)	Applicability of generally recognised diffusion models for the estimation of specific migration in support of EU Directive 2002/72/EC	2010
		Applicability of QSAR analysis to the evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment. External Scientific Report.	2010
		The Applicability of Software Tools for Genotoxicity and Carcinogenicity Prediction: Case Studies relevant to the Assessment of Pesticides.	2010
		Proceedings of the 1st International Forum Towards Evidence-Based Toxicology, Como, Italy 15-18 October 2007.	2009
	COSMOS	Thresholds of Toxicological Concern for Cosmetics	2014
	SCCP	OPINION ON Use of the Threshold of Toxicological Concern (TTC) Approach for Human Safety Assessment of Chemical Substances with focus on Cosmetics and Consumer Products	2012
		Draft Opinion on Use of the Threshold of Toxicological Concern (TTC) Approach for the Safety Assessment of Chemical Substances.	2008
		Opinion on review of the SCCNFP opinion on hair dye strategy in the light of additional information.	2006
	SCF	Opinion of the Scientific Committee on Food on the tolerable upper intake level of preformed vitamin A (retinol and retinyl esters).	2002
		Guidelines of the Scientific Committee on Food for the presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation (updated on 13 December 2001)	2001
		Opinion on a programme for the evaluation of flavouring substances (expressed on 2 December 1999).	1999
		Opinion on the scientific basis of the concept of threshold of regulation in relation to food contact materials (expressed on 8 March 1996).	1998
	SCP	Opinion of the Scientific Committee on Plants regarding the Draft guidance document on relevant metabolites	2000
	EMEA	Draft Guideline on the Assessment of Genotoxic Constituents in Herbal Substances/Preparations.	2007
		Guideline on the Limits of Genotoxic Impurities	2006
		Guidelines on the limits of genotoxic impurities.	2004
	ILSI	Threshold of Toxicological Concern Task Force	2014
		THRESHOLD OF TOXICOLOGICAL CONCERN (TTC) Threshold of toxicological concern: a tool for assessing substances of unknown toxicity present at low levels in the diet.	2005
		Threshold of toxicological concern for chemical substances present in the diet.	2000

地域等	機関名	文献のタイトル	発行年
デンマーク	Danish EPA (Nielsen and Larsen)	The Threshold of Toxicological Concern (TTC) concept: Development and regulatory applications	2011
オーストラリア	AU (Government of Western Australia Department of Health) DOH-WA	Development and Application of the Threshold of Toxicological Concern to Screening Evaluation of Air Toxics	2010
	AU	Australian Guidelines for Water Recycling: Augmentation of Drinking Water Supplies 2008. Environment Protection and Heritage Council, National Health and Medical Research Council, Natural Resource Management Ministerial Council	2008