11 December 2018
EMA/818520/2018
Veterinary Medicines Division

Monthly report on application procedures, guidelines and related documents for veterinary medicines

November 2018

This report, which is updated every month, provides current information related to the volume and evaluation of pre- and post-authorisation applications for medicinal products for veterinary use received by the European Medicines Agency (EMA) for the current and previous three years on:

- scientific advice requests;
- applications for initial evaluations, extensions, variations and renewals concerning marketing authorisations (MAs);
- applications for initial evaluations, extensions, modifications and extrapolations for maximum residue limits (MRLs);
- arbitration and referral procedures;
- requests for classification and re-classifications of products as Minor Use Minor Species (MUMS)/limited market.

In addition, the report includes a summary table of the opinions issued by the Committee for Medicinal Products for Veterinary Use (CVMP) in the current year, as well as a list of adopted guidelines and other public guidance documents.

The purpose is only to provide ongoing factual information. Commentaries and analysis are provided in the Agency's annual reports.

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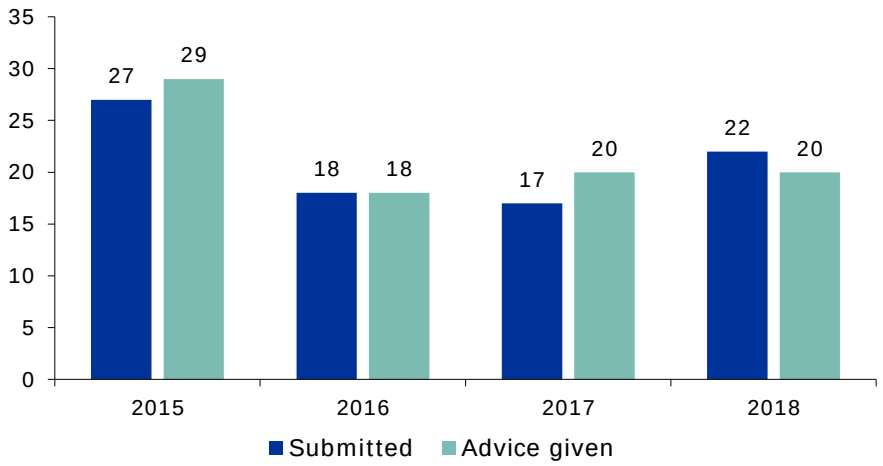
Statistics on pre- and post-authorisation applications for medicinal products for veterinary use

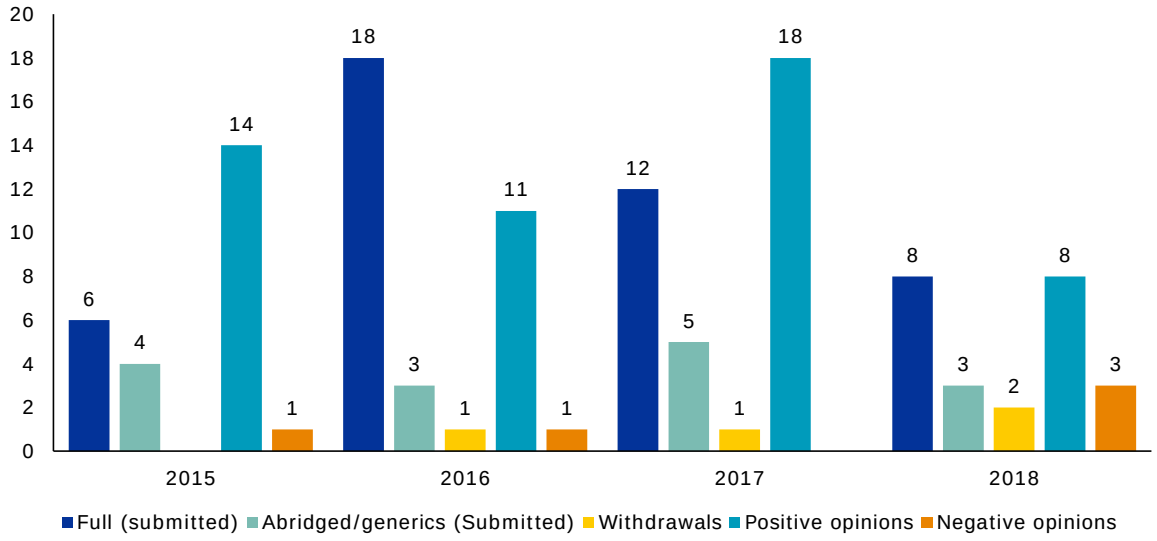
Scientific advice requests				
	2015	2016	2017	2018
Submitted and validated	27	18	17	**22**
Advice given	29	18	20	**20**

Scientific advice requests submitted and advice given



Initial evaluation of marketing authorisation applications				
	2015	2016	2017	2018
Full (submitted)	6	18	12	**8**
Abridged/generics (submitted)	4	3	5	**3**
Withdrawals	0	1	1	**2**
Positive opinions	14	11	18	**8**
Negative opinions	1	1	0	**3**

MMA submissions and outcomes

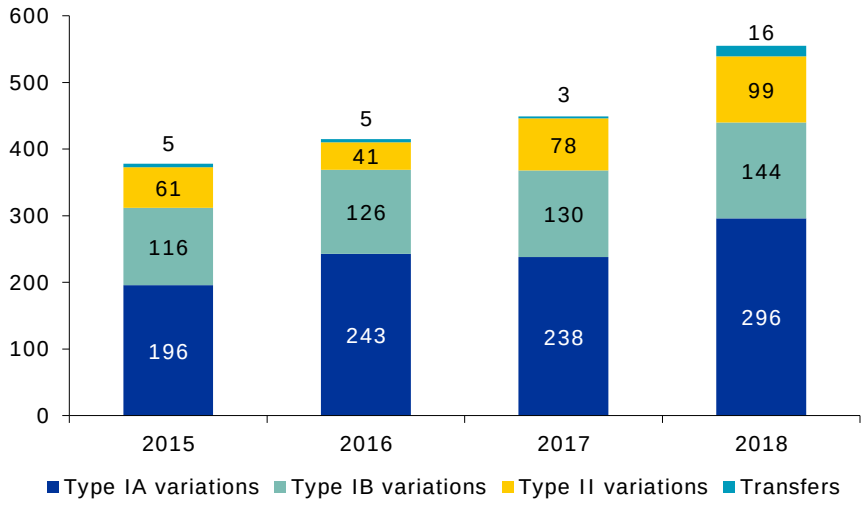


Marketing authorisations				
	2015	2016	2017	2018
Granted	17	7	18	**9**
Withdrawals	3	1	0	**6**
Refusal	1	0	0	**0**
Not renewed	0	1	0	**1**

Extensions — applications				
	2015	2016	2017	2018
Submitted	3	3	5	**1**
Withdrawals	0	0	0	**0**
Positive opinions	6	5	2	**4**
Negative opinions	1	0	0	**0**

Variations — applications submitted				
	2015	2016	2017	2018
Type-IA variations	196	243	238	**296**
Type-IB variations	116	126	130	**144**
Type-II variations	61	41	78	**99**
Transfers	5	5	3	**16**

Post-authorisation: submissions of variations and transfers



Renewals — applications				
	2015	2016	2017	2018
Submitted	24	13	9	**22**
Positive opinions	19	14	10	**12**
Negative opinions	0	0	0	**0**

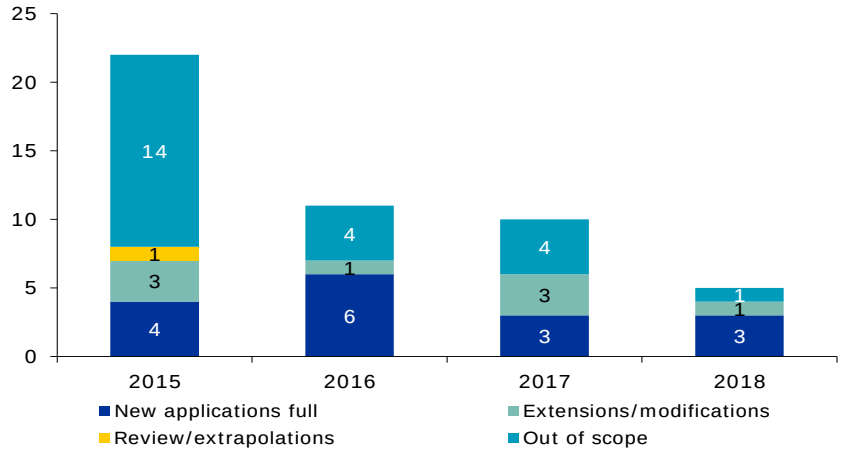
Establishment of MRLs for new substances[1] — applications				
	2015	2016	2017	2018
Submitted	4	6	3	**3**
Withdrawals	1	0	2	**2**
Positive opinions[2,3]	3 (1)	2	4	**1**
Negative opinions	0	0	0	**0**

Extensions / modifications of MRLs[4] — applications				
	2015	2016	2017	2018
Submitted	3	1	3	**1**
Withdrawals	0	1	0	**0**
Positive opinions[2]	2	3	2	**2**
Negative opinions	0	0	0	**0**

Review of opinions / extrapolations of MRLs[5] – requests from Commission or Member States				
	2015	2016	2017	2018
Submitted	1	0	0	**0**
Opinion[2]	3	0	0	**1**

Substances considered as not falling within the scope of Regulation (EC) No 470/2009 — requests				
	2015	2016	2017	2018
Submitted	14	4	4	**1**
Agreed	18	3	2	**1**
Not agreed	2	0	0	**0**
Scientific advice recommended	1	1	1	**1**

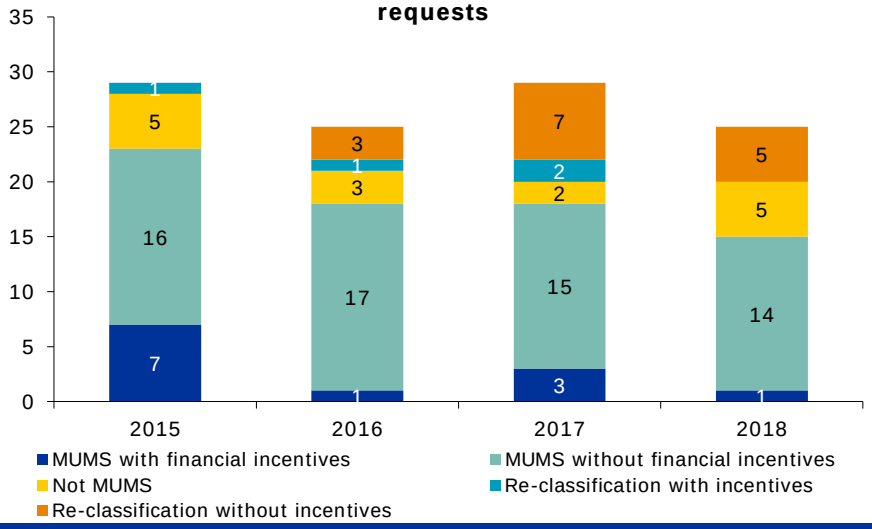
MRL-related submissions



[1] Establishment of MRLs for new substances under article 3 of Regulation (EC) No 470/2009.
[2] Including opinions recommending the extension of the expiry date for provisional MRLs or definitive MRLs for substances previously with provisional MRLs.
[3] Re-examinations of opinions are indicated in brackets.
[4] Extension or modification of MRLs under article 3 of Regulation (EC) No 470/2009.
[5] Review of opinions under article 11 of Regulation (EC) No 470/2009 or requests under article 27 of Regulation (EC) No 470/2009.

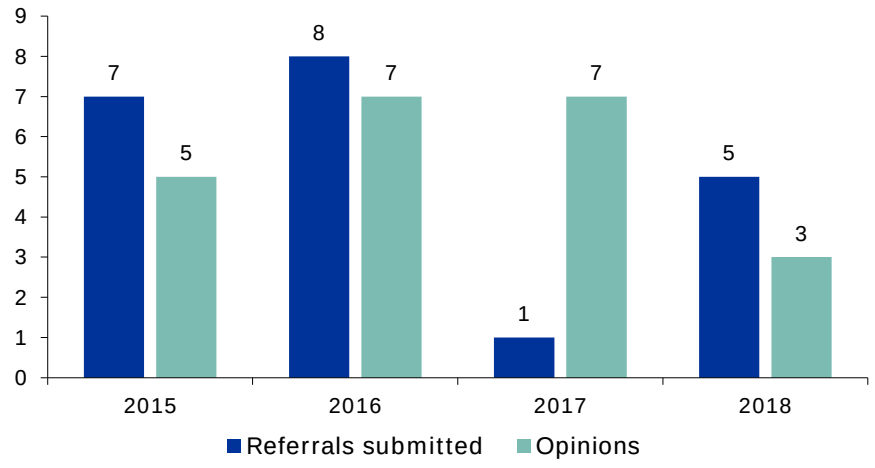
MUMS/limited market (re)classification requests — outcome				
	2015	2016	2017	2018
MUMS/limited market with financial incentives	7	1	3	**1**
MUMS/limited market without financial incentives	17	17	15	**14**
MUMS/limited market reclassification with financial incentives[6]	1	1	2	**0**
MUMS/limited market reclassification without financial incentives[6]	0	3	7	**5**
Not MUMS/limited market	5	3	2	**5**

Outcome of MUMS/limited market (re-)classification requests



Arbitrations and referrals				
	2015	2016	2017	2018
Arbitrations and referrals submitted	7	8	1	**5**
Opinions[7]	5	7	7(1)	**3(1)**

Arbitrations and referrals submissions and opinions



[6] For re-classification the first year available is 2014.
[7] Re-examinations of opinions are in brackets.

CVMP opinions in 2018 on medicinal products for veterinary use

Positive opinions

Product • Invented name • INN/Common name	Marketing authorisation holder	Target species	Regulatory information • Procedure number • Opinion date
• Clevor • ropinirole	• Orion Corporation	• Dogs	• EMEA/V/C/004417/0000 • 15/02/2018
• Bravecto Plus • fluralaner/moxidectin	• Intervet International B.V.	• Cats	• EMEA/V/C/004440/0000 • 15/03/2018
• Dany's BienenWohl • oxalic acid dihydrate	• Dany's BienenWohl GmbH	• Honey bees	• EMEA/V/C/004667/0000 • 19/04/2018
• Ubac • *Streptococcus uberis* vaccine (inactivated)	• Laboratorios Hipra, S.A.	• Cattle	• EMEA/V/C/004595/0000 • 22/05/2018
• Arti-Cell Forte • chondrogenic induced equine allogeneic peripheral blood-derived mesenchymal stem cells	• Global Stem cell Technology NV	• Horses	• EMEA/V/C/004727/0000 • 21/06/2018
• Cortacare • hydrocortisone aceponate	• Ecuphar NV	• Dogs	• EMEA/V/C/004689/0000 • 21/06/2018
• Isemid • TORASEMIDE	• CEVA Santé Animale	• Dogs	• EMEA/V/C/004345/0000 • 08/11/2018
• Syvazul BTV • Bluetongue virus vaccine (inactivated) (multistrain: 1-2 strains out of a set of 3)	• LABORATORIOS SYVA, S.A.U	• Sheep, Cattle	• EMEA/V/C/004611/0000 • 08/11/2018

Negative opinions

Product • Invented name • INN/Common name	Applicant	Target species	Regulatory information • Procedure number • Opinion date
• Horse Allo • Allogeneic equine adipose-derived mesenchymal stem cells	• Centauri Biotech SL	• Horses	• EMEA/V/C/004328/0000 • 21/06/2018

Product • Invented name • INN/Common name	Applicant	Target species	Regulatory information • Procedure number • Opinion date
• HorStem • Equine umbilical cord mesenchymal stem cells	• EquiCord-Ymas S.L.	• Horses	• EMEA/V/C/004265/0000 • 11/10/2018
• Longrange • eprinomectin	• Merial	• Cattle	• EMEA/V/C/004291/0000 • 11/10/2018

CVMP opinions in 2018 on establishment of MRLs

Positive opinions

Product • Substance	Target species	Regulatory information • Procedure number • Opinion date
• Paromomycin	• Poultry eggs	• EMEA/V/MRL/003517/EXTN/0003 • 15/02/2018
• Isoflurane	• Porcine	• EMEA/V/MRL/003647/EXTN/0002 • 15/03/2018
• Diflubenzuron	• Salmonidae	• EMEA/V/MRL/003135/MODF/0003 • 15/03/2018
• Ovotransferrin	• Chicken and poultry	• EMEA/V/MRL/004856/FULL/0001 • 19/07/2018

Arbitrations and referrals in 2018

Ongoing procedures

Type of procedure	Date • Clock start • CVMP opinion	Product • Product name • INN
• Referral under Article 34 of Directive 2001/82/EC (re-examination)	• 13/07/2016 • 05/10/2017 • 15/02/2018	• Girolan and its associated name Apralan • Apramycin sulfate
• Referral under Article 13 of Regulation (EC) No. 1234/2008	• 06/09/2017 • 15/02/2018	• Seresto and its associated name Foresto • Imidacloprid and flumethrin
• Referral under Article 35 of Directive 2001/82/EC	• 14/02/2018	• Veterinary medicinal products containing 50 mg closantel per ml presented as solutions for injection for subcutaneous use in sheep • Closantel
• Procedure under Article 30(3) of Regulation (EC) No. 726/2004	• 14/03/2018 • 19/07/2018	• Veterinary medicinal products for food producing species containing diethanolamine as an excipient • Diethanolamine (excipient)
• Procedure under Article 30(3) of Regulation (EC) No. 726/2004	• 18/04/2018 • 08/11/2018	• Veterinary medicinal products containing gentamicin for parenteral administration to horses • Gentamicin
• Referral under Article 35 of Directive 2001/82/EC	• 10/10/2018	• Veterinary medicinal products containing paromomycin to be administered parenterally to pigs • Paromomycin
• Referral under Article 35 of Directive 2001/82/EC	• 10/10/2018	• Veterinary medicinal products containing tylosin presented as solution for injection to be administered to sheep • Tylosin

Guidelines and working documents in 2018

CVMP quality

Reference number	Document title	Status
EMA/CVMP/QWP/798401/2015	Guideline on Manufacture of the veterinary finished dosage form	Adopted for consultation February 2018 (End of consultation 31 August 2019)
EMA/CHMP/CVMP/QWP/496873/2018	Guideline on the quality of water for pharmaceutical use	Adopted for consultation July 2018 (End of consultation 15 May 2019)
EMA/CVMP/QWP/153641/2018	Reflection paper on risk management requirements for elemental impurities in veterinary medicinal products	Adopted for consultation November 2018 (End of consultation 31 August 2019)
EMEA/CVMP/134/02 Rev 4	Guideline on Active Substance Master File Procedure	Adopted November 2018

CVMP safety

Reference number	Document title	Status
EMA/CVMP/SWP/779037/2017	Concept paper for the revision of the guideline on safety and residue data requirements for pharmaceutical veterinary medicinal products intended for minor use or minor species (MUMS)/limited market	Adopted for consultation January 2018 (End of consultation 28 February 2018)
EMA/CVMP/SWP/721059/2014	Guideline on user safety of topically administered veterinary medicinal products	Adopted April 2018
EMA/CHMP/CVMP/SWP/246844/2018	Questions and answers on implementation of risk-based prevention of cross-contamination in production and 'Guideline on setting health-based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities'	Adopted April 2018
EMA/CVMP/ERA/103555/2015	Guideline on assessing the environmental and human health risks of veterinary medicinal products in groundwater	Adopted April 2018

Reference number	Document title	Status
EMA/CVMP/SWP/735325/2012	Guideline on determination of withdrawal periods for edible tissues	Adopted September 2018

CVMP efficacy

Reference number	Document title	Status
EMA/CVMP/383441/2005-Rev.1	Guideline on the summary of product characteristics (SPC) for veterinary medicinal products containing antimicrobial substances	Adopted for consultation April 2018 (End of consultation 30 September 2018)
EMA/CVMP/EWP/278031/2015	Guideline on data requirements for veterinary medicinal products for the prevention of transmission of vector- borne diseases in dogs and cats	Adopted for consultation July 2018 (End of consultation 31 August 2019)
EMA/CVMP/EWP/310225/2014	Reflection paper on resistance in ectoparasites	Adopted for consultation September 2018 (End of consultation 31 August 2019)

CVMP pharmacovigilance

Reference number	Document title	Status
EMA/CVMP/PhVWP/171122/2016	Revised recommendation for the basic surveillance of EudraVigilance Veterinary (EVVet) data for centrally authorised products (CAPs)	Adopted May 2018
EMA/CVMP/PhVWP/10418/2009-Rev10	Combined VeDDRA list of clinical terms for reporting suspected adverse reactions in animals and humans to veterinary medicinal products	Adopted June 2018
EMA/CVMP/PhVWP/288284/2007-Rev.11	Guidance notes on the use of VeDDRA terminology for reporting suspected adverse reactions in animals and humans	Adopted June 2018
EMA/CVMP/PhVWP/145186/2013	Q&A on adverse event reporting	Adopted June 2018
EMA/CVMP/PhVWP/126661/2009	Q&A on preparation, management and assessment of periodic safety update reports (PSURs)	Adopted June 2018

CVMP antimicrobials

Reference number	Document title	Status
EMA/CVMP/383441/2005-Rev.1	Guideline on the summary of product characteristics (SPC) for veterinary medicinal products containing antimicrobial substances	Adopted for consultation April 2018 (End of consultation 30 September 2018)
EMA/CVMP/AWP/721118/2014	Reflection paper on use of aminoglycosides in animals in the European Union: development of resistance and impact on human and animal health	Adopted June 2018
EMA/CVMP/AWP/706442/2013	Guideline on the assessment of the risk to public health from antimicrobial resistance due to the use of an antimicrobial veterinary medicinal product in food-producing animals	Adopted for consultation July 2018 (End of consultation 31 October 2018)
EMA/CVMP/849775/2017	Reflection paper on dose optimisation of established veterinary antibiotics in the context of SPC harmonisation	Adopted for consultation July 2018 (End of consultation 31 January 2019)
EMA/CVMP/AWP/842786/2015	Reflection paper on the use of aminopenicillins and their 5 beta-lactamase inhibitor combinations in animals in the 6 European Union: development of resistance and impact 7 on human and animal health	Adopted for consultation September 2018 (End of consultation 21 December 2019)
EMA/CVMP/AWP/237294/2017	Reflection paper on off-label use of antimicrobials in veterinary medicine in the European Union	Adopted November 2018

CVMP immunologicals

Reference number	Document title	Status
EMA/CVMP/IWP/315887/2017	Guideline on the use of adjuvanted veterinary vaccines	Adopted for consultation June 2018 (End of consultation 15 January 2019)

CVMP environmental risk assessment

Reference number	Document title	Status
EMEA/CVMP/ERA/172074/2008 Rev. 6	Questions and Answers on the implementation of the CVMP guideline on environmental impact assessment for veterinary medicinal products in support of the VICH GL6 (Phase I) and GL38 (Phase II)	Adopted January 2018
EMA/CVMP/ERA/103555/2015	Guideline on assessing the environmental and human health risks of veterinary medicinal products in groundwater	Adopted April 2018
EMA/CVMP/ERA/632109/2014	Reflection paper on antimicrobial resistance in the environment: considerations for current and future risk assessment of veterinary medicinal products	Adopted for consultation November 2018 (End of consultation 31 August 2019)

CVMP novel therapies

No guidelines or working documents have yet been agreed in 2018.

Replacement, Reduction, Refinement of animal testing (3Rs)

Reference number	Document title	Status
EMA/CHMP/CVMP/3Rs/677407/2015	Review and update of EMA guidelines to implement best practice with regard to 3Rs (replacement, reduction and refinement) in regulatory testing of medicinal products – report on actions taken	Adopted June 2018
EMA/CHMP/CVMP/3Rs/164002/2016	Reflection paper providing an overview of the current regulatory testing requirements for veterinary medicinal products and opportunities for implementation of the 3Rs	Adopted June 2018

General

Reference number	Document title	Status
EMA/CVMP/VICH/517152/2013	VICH GL57: Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing species: marker residue depletion studies to establish product withdrawal periods in aquatic species	Adopted for consultation January 2018 (end of consultation 15 June 2018)

Reference number	Document title	Status
EMA/CVMP/VICH/335918/2016	VICH GL58 Stability Testing of New Veterinary Drug Substances and Medicinal Products in Climatic Zones III and IV	Adopted for consultation July 2018 (end of consultation 31 December 2018)
EMA/CVMP/VICH/176637/2014	VICH GL56 on Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing species: study design recommendations for residue studies in honey for establishing MRLs and withdrawal periods	Adopted July 2018