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Human Medicines Research and Development Support Division

Report to the European Commission

on companies and products that have benefited from any of the rewards and incentives in the Paediatric Regulation[1] and on the companies that have failed to comply with any of the obligations in this regulation

Year 2018

Prepared by: Paediatric Medicines Office
Product Development Scientific Support Department
European Medicines Agency

[1] REGULATION (EC) No 1901/2006 of the EUROPEAN PARLIAMENT AND OF THE COUNCIL on medicinal products for paediatric use (Regulation (EC) No 1901/2006 Regulation (EC) No 1902/2006)

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Acronyms, abbreviations

ASD	Autism spectrum disorder
CHMP	Committee for Medicinal Products for Human Use
CML	Chronic myelogenous leukaemia
EC	European Commission
EMA, the Agency	European Medicines Agency
HAE	Hereditary angioedema
INN	International non-proprietary name
MA	Marketing authorisation
MAH	Marketing authorisation holder(s)
MS	Member States
NCA	National Competent Authorities
NPO	National patent offices
PA	Protocol assistance
Paediatric Regulation	REGULATION (EC) No 1901/2006 of the EUROPEAN PARLIAMENT AND OF THE COUNCIL on medicinal products for paediatric use
PDCO	Paediatric Committee
PIP	Paediatric investigation plan
PUMA	Paediatric use marketing authorisation
SA	CHMP scientific advice
SAWP	Scientific Advice Working Party
SPC	Supplementary protection certificate
VKC	Vernal keratoconjunctivitis

1. Introduction

1.1. Scope of the report

REGULATION (EC) No 1901/2006 of the European Parliament and of the Council on medicinal products for paediatric use (Paediatric Regulation) entered into force on 26 January 2007.

Article 50(1) states:

"*On the basis of a report from the Agency, and at least on an annual basis, the Commission shall make public a list of the companies and of the products that have benefited from any of the rewards and incentives in this Regulation and the companies that have failed to comply with any of the obligations in this Regulation. The Member States shall provide this information to the Agency.*"

This report covers year 2018 and lists the companies benefiting from and infringing the regulation.

1.2. Data collection and methodology

In December 2018 the Agency contacted the national patent offices (NPO) of each Member State (MS) with regards to the medicinal products that had obtained a six-month extension of the supplementary protection certificate (SPC) in 2018.

The Agency received contributions from the following Member State NPOs: Austria, Belgium, Bulgaria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

In February 2019, companies identified as potentially infringing the Paediatric Regulation in 2018 with regard to non-completion of a paediatric investigation plan (PIP) by the agreed date and non-submission of an annual report on deferred measures by the due date, were given an opportunity to provide comments on the finding before publication of the identified infringement. All information received by 28 February 2019 was considered for finalisation of this report.

2. Companies and products that have benefited from the rewards and incentives in the regulation

2.1. Scientific advice or protocol assistance from the EMA

In accordance with Article 26 of the Paediatric Regulation, the Agency provides free scientific advice (SA) or protocol assistance (PA) on any question related to paediatric development of a medicinal product. The advice is prepared by the Scientific Advice Working Party (SAWP) and is adopted by the Committee for Medicinal Products for Human Use (CHMP). For the requests on paediatric development, members of the paediatric committee (PDCO) routinely contribute as experts to the provision of scientific advice through the SA procedures (Table 1).

The number of SA/PA procedures including paediatric questions (paediatric only advice and advice concerning adult and paediatric medicines development) has been increasing steadily since the implementation of the Paediatric Regulation, whereas the number of paediatric only advice procedures registered a substantial decrease when compared to 2017. In 2018, 25% of the requests for SA or PA were of paediatric relevance. PDCO members are involved in procedures relating to paediatric development and, in 2018, PDCO members were also involved in procedures that did not directly include paediatric questions but where paediatric development could be affected.

Table 1 - Scientific advice and protocol assistance, incl. follow-ups (by the EMA, SAWP and CHMP, p/a 2009-2018)

	2009	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Total no. of advice (SA and PA)	388	400	433	420	473	551	510	582	630*	634*
No. of SA/PA/qualification of biomarker procedures that included questions on paediatric development (Paediatric only advice)	74	80	57	91	96	97	109	142	127	70*
No. of SA/PA on paediatric-only and combined adult and paediatric medicines development that involved PDCO members as experts	68	80	55	91	93	88	97	138	138	161*

Source: EMA databases. *Includes also parallel consultation with regulators and health technology assessment bodies.

2.2. Rewards

2.2.1. Extensions of the supplementary protection certificate

Extensions of the supplementary protection certificate (SPC) are granted by National Patent Offices (NPO) therefore the data provided in this report relies on the information provided by these offices. This report provides data only for SPC extensions that have been granted, unlike in years prior to 2015 when pending SPC extensions were also reported. Furthermore, products may be mentioned in annual reports of several years because SPC expiration (and therefore extension) may not be simultaneous in all EU countries, and hence a product may obtain SPC extension in different years in the various countries.

In 2018, 24 active substances benefited from the six-month extension (see Table 2).

Table 2 - List of companies / products receiving six-month extension in 2018

Company / SPC holder	**Invented name(s)**	**INN**	**SPC extension granted in 2018**
Astellas Pharma	Vesicare and associated names	Solifenacin	Belgium Finland Hungary Luxembourg Portugal United Kingdom
Biogen	Tysabri	Natalizumab	Austria Belgium Finland France Greece Luxembourg Portugal Spain Netherlands
E. R. Squibb & Sons	Yervoy	Ipilimumab	Austria Bulgaria Denmark Estonia Finland Germany Ireland Italy Portugal Slovenia Spain Sweden Netherlands United Kingdom
Genentech	Avastin	Bevacizumab	Belgium Finland Greece Luxembourg Portugal Spain United Kingdom
Genzyme Corporation	Cholestagel	Colesevelam	Austria Belgium
Gilead Sciences	Truvada	Emtricitabine / tenofovir disoproxil	Denmark Belgium Italy

Company / SPC holder	Invented name(s)	INN	SPC extension granted in 2018
Gilead Sciences	Viread	Tenofovir disoproxil	Finland
Gilead Sciences and Janssen-Cilag International (Cyprus)	Tybost	Cobicistat	Bulgaria Cyprus Estonia Greece Italy Latvia Luxembourg Malta Portugal Slovenia Spain Netherlands
GlaxoSmithKline	Nucala	Mepolizumab	Bulgaria Denmark Italy Latvia Lithuania Malta Portugal Slovenia Spain Netherlands
Janssen Biotech	Simponi	Golimumab	Austria Finland Greece Luxembourg Poland Spain
Laboratoire Theramex	Zoely	Nomegestrol and estradiol	Greece Poland Slovakia Spain Czech Republic
Medimmune (Austria and Finland); University of Rochester (Belgium); The Government of the United States of America (Germany and Luxembourg)	Gardasil/Silgard	Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed)	Austria Belgium Finland Germany Luxembourg
Merck Sharp & Dohme	Ivemend	Fosaprepitant	Italy

Company / SPC holder	Invented name(s)	INN	SPC extension granted in 2018
Merck Sharp & Dohme	Emend	Aprepitant	Bulgaria Germany Hungary Luxembourg Slovakia United Kingdom
Novartis	Certican/Afinitor	Everolimus	France Hungary Slovakia
Novartis	Reyataz	Atazanavir	Austria Belgium Finland France Greece Luxembourg
Novartis	Ilaris	Canakinumab	Austria Finland France Greece Luxembourg Spain
Novartis	Exjade	Deferasirox	Bulgaria Cyprus Denmark Ireland Italy Latvia Lithuania Luxembourg Poland Portugal Slovenia Sweden Netherlands
Novo Nordisk	Tresiba	Insulin degludec	Greece Ireland Luxembourg Spain
Novo Nordisk	Levemir	Insulin detemir	Hungary United Kingdom
Roche Registration (UK) and Chugai Seiyaku Kabushiki Kaisha (Italy)	RoActemra	Tocilizumab	Italy United Kingdom

Company / SPC holder	Invented name(s)	INN	SPC extension granted in 2018
Sanofi Pasteur	Menveo	Meningococcal Group A, C, W-135 and Y Conjugate Vaccine	Germany
Sanofi Pasteur	Vaxelis	Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and Haemophilus type b conjugate vaccine (adsorbed)	Greece Ireland Portugal Spain United Kingdom
Shire-NPS Pharmaceuticals	Mimpara	Cinacalcet	Austria Belgium France Greece Hungary Spain Czech Republic Netherlands United Kingdom

Source: NPO survey

2.2.2. Orphan market exclusivity extension

In 2018, one orphan medicinal product has benefited from a two-year extension of their respective market exclusivity:

- Verkazia by Santen Oy for the treatment of severe vernal keratoconjunctivitis (VKC) in children from 4 years of age and adolescents.

2.3. Paediatric use marketing authorisation

Two new paediatric use marketing authorisations (PUMA) were granted in 2018:

- Kigabeq (vigabatrin) by ORPHELIA Pharma SAS received a positive CHMP opinion in July 2018 for the treatment in monotherapy of infantile spasms (West's syndrome) in infants and children from 1 month to less than 7 years of age, and the treatment in combination with other antiepileptic medicinal products for patients with resistant partial epilepsy (focal onset seizures) with or without secondary generalisation, that is where all other appropriate medicinal product combinations have proved inadequate or have not been tolerated, in infants and children from 1 month to less than 7 years of age. The EC decision was adopted in September 2018;
- Slenyto (melatonin) by RAD Neurim Pharmaceuticals EEC Ltd. received a positive CHMP opinion in July 2018 for the treatment of insomnia in children and adolescents aged 2-18 with Autism Spectrum Disorder (ASD) and/or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient. The EC decision was adopted in September 2018.

2.4. Placing on the market

The Agency continues to maintain the "Register of deadlines to put a medicinal product on the market" (Article 33 of the Paediatric Regulation), established in 2012. It lists the two-year deadlines by which marketing authorisation holders (MAH) have to place their medicinal products on the market following completion of an agreed PIP and obtaining a paediatric indication. The register includes information on the fulfilment of this requirement. This information is either provided voluntarily by MAHs or following requests by the Agency after a deadline expiration.

Link to the register:

https://www.ema.europa.eu/en/human-regulatory/post-authorisation/paediatric-medicines/deadlines-placing-paediatric-medicines-market

3. Failure to comply with the obligations set out in the Paediatric Regulation

3.1. Submission of PIP and waiver applications to the PDCO

Article 16 of the Paediatric Regulation requires pharmaceutical companies to submit applications for a PIP and a waiver no later than upon completion of the human pharmacokinetic (PK) studies in adults specified in Section 5.2.3 of Part I of Annex I to Directive 2001/83/EC, except when duly justified.

Late submissions are being reported since 2010 (Table 3) for applications with a delay greater than six months. From 2014 only those considered by the PDCO as not justified are being reported.

Table 3 – Number of procedures with a time lag six months or longer between completion of adult PK studies and submission of PIP or waiver application

Procedure type	2010	2011	2012	2013	2014	2015	2016	2017	2018
PIPs (% of total granted)	65 (74%)	44 (59%)	34 (39%)	18 (20%)	12 (13%)	7 (10%)	20 (23%)	24 (28%)	9 (16%)
Full waivers (% of total granted)	26 (59%)	13 (42%)	11 (23%)	6 (11%)	4 (8%)	4 (8%)	14 (27%)	14 (16%)	9 (20%)

Source: EMA Paediatric database

In 2018, a total of 58 PIPs received a positive opinion and 46 full product-specific waivers were granted by the PDCO.

The list of unjustified late submissions of PIPs is presented in Annex I.

3.2. Completion of PIPs

The EMA decisions on PDCO opinions contain the expected date of PIP completion.

For the analysis of timely completion, the PIPs with an expected completion date until 30 June 2018 were reviewed. This cut-off date was chosen to account for the fact that applicants must submit the completed study reports within six months of completion (Art. 46) and studies (and PIPs) completed after June 2018 may not have yet been subjected to a final compliance check.

In total, 272 PIPs were scheduled to finish by 30 June 2018; of those, 178 (65%) were completed; of the remaining 94 that have not been completed, 63 did not provide a valid justification (e.g. a modification to amend the date of completion is pending/ongoing or development has been discontinued etc.). The detailed list is provided in Annex II.

3.3. Annual reports on deferrals

According to Article 34.4 of the Paediatric Regulation, MAHs should submit an annual report to the Agency providing an update on progress of deferred paediatric studies in accordance with the EMA decision agreeing the PIP and granting a deferral. In 2018 the EMA received 62 annual reports on deferred measures. Three MAHs did not submit their annual report on deferred measures due in 2018.

The list of companies that did not submit one or more annual reports is included in Table 4. The complete list of annual reports that were not received is to be found in Annex III.

Table 4 - List of companies not submitting annual reports on deferred measures in due time

Company	2011	2012	2013	2014	2015	2016	2017	2018
Aastrom Biosciences DK Aps					1			
Actelion Registration Ltd						1	1	
Aegerion Pharmaceuticals						1	1	
AMAG Pharmaceuticals, Inc.					1		1	1
Amgen Europe B.V.			1					
APEIRON Biologics AG								1
Clinigen Healthcare Ltd						1		
Clinuvel (UK) Limited					1			
Eisai Ltd.	1					1		
Forest Laboratories Limited				1	1			
Genzyme Europe B.V.	1							
GlaxoSmithKline	1							
Ipsen Pharma								1
Janssen-Cilag International N.V.	1				1			
Kowa Pharmaceutical Europe Company Ltd	1	1	4					
Merck Sharp & Dohme (Europe) Inc.	2	1	2					
Novartis (Europharm Limited, Vaccines and diagnostics)		2	1					
Novo Nordisk A/S	1	1	2					
N.V. Organon						1		
Nycomed Danmark ApS						1		
Omrix Biopharmaceuticals SA			1		1			
Pfizer Limited	2							
Pharmaxis Pharmaceuticals Limited					1			
Roche Registration Limited	1	1	1		1			
Seqirus S.r.l.						1		
Sigma-Tau SpA		1	1		1			
Takeda Global Research and Dev. Centre (Europe) Ltd		1			1			
Teva Pharma GmbH						1		
Theravance, Inc.		1	1					
Total companies p/a:	**11**	**9**	**14**	**1**	**11**	**8**	**3**	**3**

Source: EMA database (PedRA)

Annex I. List of non-justified late submissions of applications for PIPs or waivers

This list includes only applications for which a decision on a PIP or a waiver was adopted by the European Medicines Agency in 2018; applications that were withdrawn or whose discussion is ongoing are not listed.

The number of months of delay is calculated from the date of the completion of PK studies in adults as declared by the applicant in the application for a PIP or a product-specific waiver request.

The below table shows the agreed PIPs or waivers submitted in 2018 with a significant delay for which none or no acceptable (by the PDCO) justification was provided. The timing of submission should not be later than the end of healthy subject or patient PK, which can coincide with the initial tolerability studies, or the initiation of the adult phase II studies (proof-of-concept studies). In cases where a phase II study in adults is already completed by the time of the PIP submission, the submission is in principle considered delayed unless justified. Further information on the timing of a PIP application can be found on the EMA website.

Company	Substance	Application type
Agios Pharmaceuticals, Inc.	Ivosidenib	PIP
Aziende Chimiche Riunite Angelini Francesco - A.C.R.A.F. - S.p.A.	Gabapentin / trazodone hydrochloride	Waiver
Cascadian Therapeutics Luxembourg S.A.R.L.	Tucatinib	Waiver
Eli Lilly and Company Limited	Lasmiditan	PIP
Farmalíder, S.A.	Ibuprofen / paracetamol	Waiver
Farmalíder, S.A.	Ibuprofen	Waiver
GE Healthcare, Inc.	Flurpiridaz F18	Waiver
Kowa Research Europe Ltd	Pemafibrate	Waiver
Kuhnil Pharm. CO.,Ltd.	Rosuvastatin calcium / Omega-3-acid ethyl esters 90	Waiver
Merck KGaA	Tepotinib	Waiver
Pfizer Limited	Tanezumab	PIP
Pfizer Limited	Janus Kinase-1 inhibitor (PF-04965842)	PIP
PledPharma AB	Calcium, N,N'-1,2-ethanediylbis[N-[[3-(hydroxy-2-methyl-5-[(phosphonooxy)methyl]-4-pyridinyl]methyl]glycine] manganese complexes	Waiver
Regeneron Ireland U.C.	Evinacumab	PIP

Company	Substance	Application type
SFL Regulatory Affairs Consulting Ltd.	Obiltoxaximab	PIP
Shionogi Limited	Cefiderocol	PIP
UCB Biopharma SPRL	Bimekizumab	PIP
Zealand Pharma A/S	Dasiglucagon	PIP

Source: EMA database PedRA

Annex II. List of PIPs not completed by the agreed date until 30 June 2018

It should be noted that this list does not specify if the development of the medicinal product has been discontinued or not, as the EMA may not have been informed by the sponsor accordingly. For the purpose of this analysis, a PIP is considered completed if there has been a positive final compliance check by the EMA/PDCO.

Procedure number	Substance(s)	Invented Name(s)	Company
EMEA-000029-PIP01-07	Docetaxel	Taxotere	Aventis Pharma Sa
EMEA-000350-PIP01-08	Mercaptopurine Monohydrate	N/A	Nova Laboratories Limited
EMEA-000658-PIP01-09	Estradiol / Nomegestrol	N/A	Nv Organon (Part Of Schering Plough)
EMEA-000532-PIP01-09	Sodium bituminosulphonate / clindamycin phosphate	Ichthoseptal N	Ichthyol -Gesellschaft Cordes, Hermanni & Co. (Gmbh & Co.) Kg
EMEA-000436-PIP01-08	Mannitol	Bronchitol	Pharmaxis Pharmaceuticals Limited
EMEA-000130-PIP01-07	Paracetamol, Eur. Ph.	N/A	Baxter World Trade Sa/Nv
EMEA-000221-PIP01-08	Glucose (monohydrate)	N/A	Cblaya & Mhuguet S.L.
EMEA-000134-PIP01-07	Purified antigen fractions of inactivated split virion Influenza A/Indonesia/5/05 (H5N1)	Arepanrix	GlaxoSmithKline
EMEA-000651-PIP01-09-M02	Cholic acid	N/A	Fgk Representative Service Gmbh
EMEA-000487-PIP01-08	Bromocriptine mesilate	Cycloset	Veroscience Eu Ltd
EMEA-000288-PIP01-08-M02	Moxifloxacin hydrochloride	Avalox, Avelox, Havelox, Izilox, Octegra, Proflox, Actimax and Actira.	Bayer Schering Pharma

Procedure number	Substance(s)	Invented Name(s)	Company
EMEA-001354-PIP01-12	2,6-Bis-{(1-napthalenyl-3,6-disulfonic acid)-oxyacetamido}-2,6-bis-2,6-bis-2,6-bis-(2,6-diamino-hexanoylamino)-2,6-diamino-hexanoic acid (diphenylmethyl)-amide, polysodium salt	Vivagel	Starpharma Pty Ltd
EMEA-000337-PIP01-08	Grass pollen preparation	N/A	Allergopharma J. Ganzer KG
EMEA-001069-PIP01-10	Secretin	Safinea	Repligen Europe Limited
EMEA-000898-PIP01-10-M02	Meropenem	N/A	NeoMero Consortium
EMEA-001298-PIP01-12	Azithromycin	Azytinn	Only For Children Pharmaceuticals
EMEA-001134-PIP01-11	Chimeric Monoclonal Anti-Shiga Toxin (Stx) Antibodies Castx1 And Castx2	Shigamabs	Albany Regulatory Consulting Limited
EMEA-001145-PIP01-10	Azithromycin (monohydrate)	N/A	Ixodes AG
EMEA-001324-PIP01-12-M01	Glibenclamide	Glibentek	Ammtek
EMEA-000282-PIP01-08-M02	Clevidipine	Cleviprex	Chiesi Farmaceutici S.p.A
EMEA-000057-PIP01-07-M05	Zoledronic acid	Aclasta	Novartis Europharm
EMEA-001156-PIP01-11-M07	Rdesat-6 (Recombinant Dimer Of 6 Kd Early Secretory Antigenic Target)/ Rcfp-10 (Recombinant 10 Kd Culture Filtrate Protein)	N/A	Statens Serum Institut
EMEA-000044-PIP01-07	Tgplpth1-34	N/A	Kuros Biosurgery International Ag
EMEA-001120-PIP01-10	Budesonide	Budiair And Associated Names	Neurosis Consortium
EMEA-001513-PIP01-13	Estetrol & Levonorgestrel	N/A	Estetra S.A.

Procedure number	Substance(s)	Invented Name(s)	Company
EMEA-000786-PIP01-09-M02	Autologous CD34+ cells transduced with lentiviral vector containing the human Wiskott Aldrich Syndrom Protein gene	N/A	Genethon
EMEA-001599-PIP01-13	Ibuprofen (sodium dihydrate)	N/A	Proveca Limited
EMEA-000698-PIP02-10-M01	Methyl aminolevulinate hydrochloride	Visonac	Photocure AS
EMEA-001057-PIP01-10-M01	(S)-3'-(OH)-Desazadesferrithiocin-Polyether, Magnesium Salt (FBS0701)	N/A	Shire Pharmaceutical Development Ltd
EMEA-001238-PIP01-12	Alpha Tocotrienol Quinone	Vincerinone	Edison Orphan Pharma Bv
EMEA-001352-PIP01-12-M01	Metformin hydrochloride	N/A	Effrx Pharmaceuticals Sa
EMEA-000281-PIP01-08-M02	Humab IGF-1R - A Recombinant Human Monoclonal Antibody To The Insulin-Like Growth Factor-1 Receptor	N/A	Roche Registration Limited
EMEA-000488-PIP02-11	Rubidium-82	Cardiogen-82	Advanced Accelerator Applications
EMEA-001314-PIP01-12	Dinutuximab Beta / Chimeric Anti-Disialoganglioside (GD2) Monoclonal Antibody (Ch14.18/CHO)	N/A	Apeiron Biologics Ag
EMEA-000205-PIP01-08-M02	Ceftobiprole medocaril sodium	Zevtera	Basilea Pharmaceutica International
EMEA-000649-PIP01-09	Taspoglutide	N/A	Ipsen Pharma
EMEA-000973-PIP01-10-M03	Recombinant Human N-Acetylgalactosamine-6-Sulfatase	Vimizim (Elosulfase Alfa)	Biomarin Europe Limited
EMEA-000266-PIP01-08-M01	Nalfurafine hydrochloride	N/A	Toray International U.K. Limited

Procedure number	Substance(s)	Invented Name(s)	Company
EMEA-000389-PIP01-08-M01	N-[4-(3-Amino-1H-Indazol-4 Yl) Phenyl]-N1- (2-Fluoro-5-Methylphenyl) Urea	N/A	Abbvie Ltd
EMEA-000711-PIP01-09	Morphine hydrochloride	N/A	Epmc Pharma Sprl
EMEA-001348-PIP01-12-M01	Cangrelor tetrasodium salt	N/A	Chiesi Farmaceutici S.p.A.
EMEA-001617-PIP01-14	Ethosuximide	N/A	Advicenne Pharma
EMEA-000665-PIP01-09	Taspoglutide	N/A	Ipsen Pharma
EMEA-001299-PIP01-12	Dry extract from Betulae cortex (Birch cork) (5 – 10:1); Quantification: 72 to 88% botulin; Extraction solvent: n-Heptane 95% m/m- 10mg	N/A	Birken AG
EMEA-001548-PIP01-13	Valaciclovir hydrochloride	Valaciclovir Pharmathen	Pharmathen S.A.
EMEA-000360-PIP01-08	Carisbamate	Comfyde	Janssen Cilag NV International
EMEA-000294-PIP02-12-M01	Idursulfase	N/A	Shire Human Genetic Therapies AB
EMEA-001460-PIP01-13-M02	Elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide	Genvoya	Gilead Sciences
EMEA-000067-PIP02-11-M02	Human heterologous liver cells	Heparesc	Cytonet GmbH & Co. KG
EMEA-000181-PIP01-08-M03	Cannabidiol/Delta-9-tetrahydrocannabinol	Sativex	GW Pharma Ltd
EMEA-000194-PIP03-10	Perflubutane	Imagify	Granzer Regulatory Consulting & Services
EMEA-000284-PIP01-08-M04	Modified Grass Pollen Extract	N/A	Allergy Therapeutics (UK) Limited
EMEA-000609-PIP01-09	Recombinant human glutamic acid decarboxylase (rhGAD65)	Diamyd	Diamyd Medical AB
EMEA-000736-PIP01-09	Culture expanded autologous chondrocytes	Hyalograft C autograft	Fidia Advanced Biopolymers S.r.l.

Procedure number	Substance(s)	Invented Name(s)	Company
EMEA-000976-PIP01-10	Grass pollen allergen extract from Cocksfoot (Dactylis glomerata L.)/ Sweet vernal grass (Anthoxanthum odoratum L.)/ Rye grass (Lolium perenne L.)/ Meadow grass (Poa pratensis L.)/ Timothy (Phleum pratense L.)	STALORAL 5 Grasses	STALLERGENES S.A.
EMEA-001203-PIP02-14-M02	Coagulation Factor VIIa (Recombinant)	N/A	LFB SA
EMEA-001516-PIP01-13	Enalapril (maleate)	Enalapril Pharmathen	Pharmathen S.A.
EMEA-001241-PIP02-13-M01	Enalapril (maleate)	N/A	Proveca Limited
EMEA-001311-PIP01-12-M01	Vancomycin	N/A	Fondazione PENTA Onlus
EMEA-001627-PIP01-14	Efinaconazole	N/A	PharmaSwiss Česká republika
EMEA-001514-PIP01-13	Octenidine (dihydrochloride)	N/A	Cassella-med GmbH & Co. KG
EMEA-001568-PIP03-14	Ceftriaxone (in the form of sodium salt)/ Sulbactam (in the form of sodium salt)	Elores	Venus Pharma GmbH
EMEA-001853-PIP01-15-M01	Human normal immunoglobulin for subcutaneous administration	N/A	Grifols Therapeutics Inc

Annex III. List of due annual reports on deferred measures that have not been submitted in 2018

Procedure number	Substance(s)	Invented name	Company (MAH)	Original MA Date	Annual report due date
EMEA-000373-PIP02-09	Ferumoxytol	Rienso	AMAG Pharmaceuticals, Inc.(Takeda Pharma A/S)	15/06/2012	15/06/2018
EMEA-001143-PIP01-11	Cabozantinib	Cometriq	Ipsen Pharma (Ipsen Pharma)	21/03/2014	21/03/2018
EMEA-001314-PIP01-12	Dinutuximab beta	Qarziba	APEIRON Biologics AG (EUSA Pharma (UK) Limited)	08/05/2017	08/05/2018