Key achievements of the EMA's SME regulation

EMA Roundtable meeting - 15th anniversary of the SME Office

Presented by Leonor Enes on 27 November 2020
Scientific Officer | SME Office | Regulatory Science and Innovation Task Force (TRS)

Contents

SME regulation and EMA SME Office

EU SME regulation and EMA SME Office

SME regulation(EC) No 2049/2005 of 15 December 2005

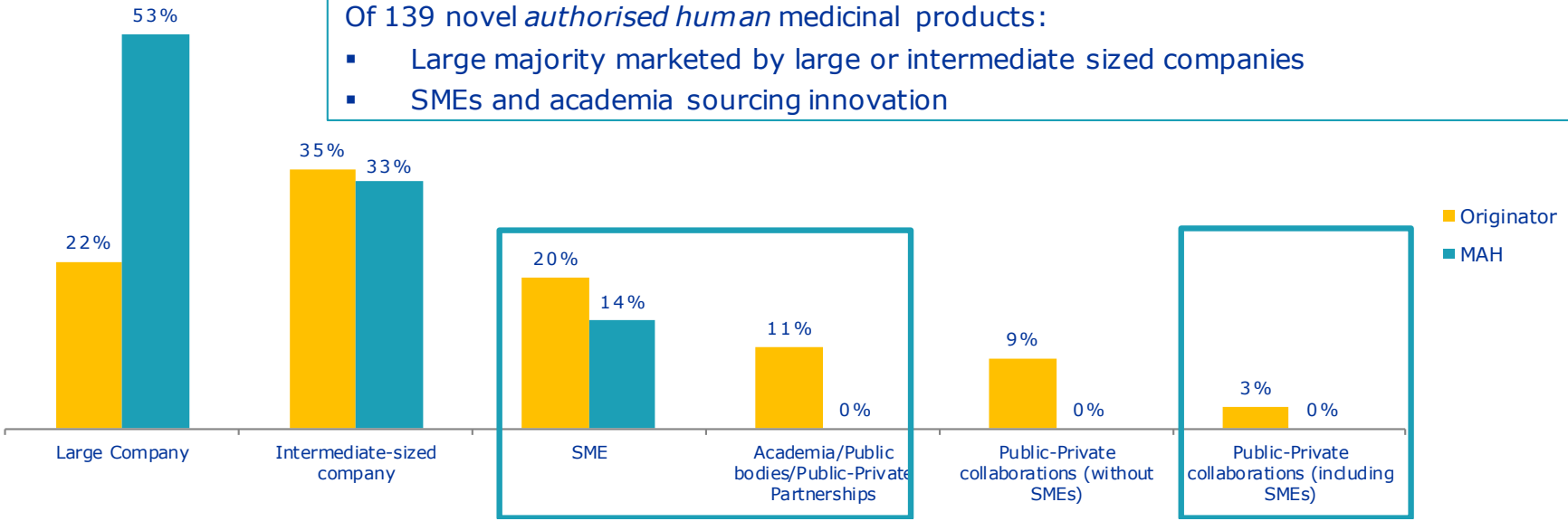
Aims to promote innovation and development of new medicines by SMEs

SME Office launch - 2005

Sourcing of Centralised Procedure novel medicines in the EU (2013-2015)

Of 139 novel *authorised human* medicinal products:

- Large majority marketed by large or intermediate sized companies
- SMEs and academia sourcing innovation



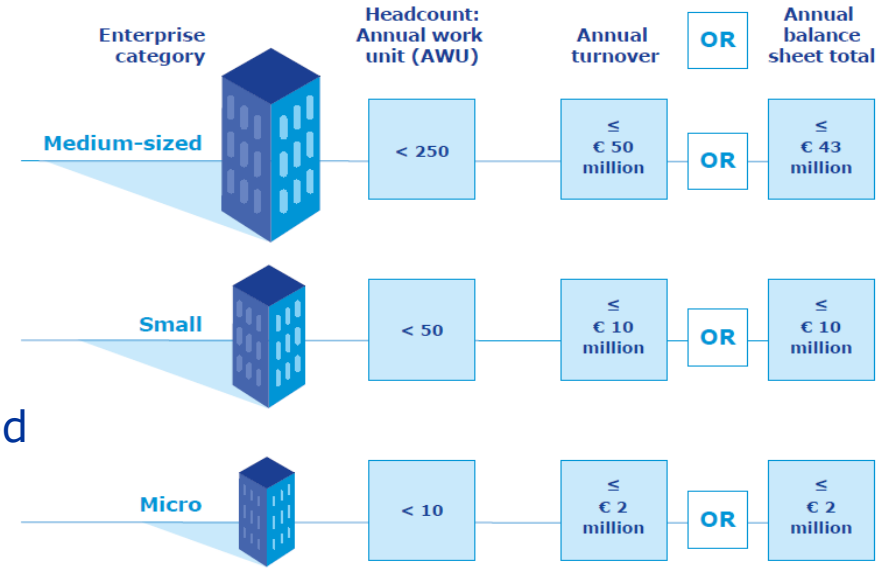
Assistance to SMEs

- Assignment and renewal of SME status
- Regulatory Assistance
- SME Briefing Meetings
- Fee Incentives*
- Translation Assistance for the product information
- Training and Awareness via info days, SME Newsletters and mailings targeted at SMEs
- Partnering and Networking

*Orphan regulation, ATMP and Pharmacovigilance fee regulations

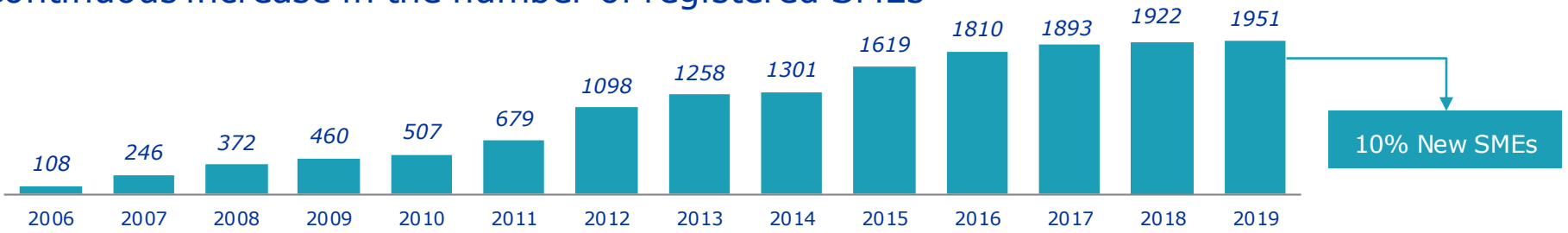
SME Definition
Commission recommendation 2003/361/EC

SME thresholds



SMEs registered with EMA

Continuous increase in the number of registered SMEs



2019

Type

human 78%
veterinary 4%
human/veterinary 4%
service providers 14%

Size

micro 40%
small 34%
medium 26%

Ownership structure

autonomous 48%
linked 44%
linked/partner 5%
partner 3%

Almost half of enterprises are micro and autonomous

Increase in the percentage of academic spin offs from 9% (2016) to 12% (2019)

Profile of SMEs registered with EMA: 2019

SME in 2019

Increase in the number of companies developing orphan and paediatric medicines versus 2016

2019

Vaccines ***4%***
Therapeutics ***66%***
Diagnostics/Imaging ***6%***
Combined medicines and devices ***6%***

➡ **53%** Chemical entities
12% Biologicals
10% Advanced therapies
➡ **27%** Orphan medicines
➡ **12%** Paediatric medicines
25% Generic medicines

Changes in geographical distribution due to BREXIT

2016

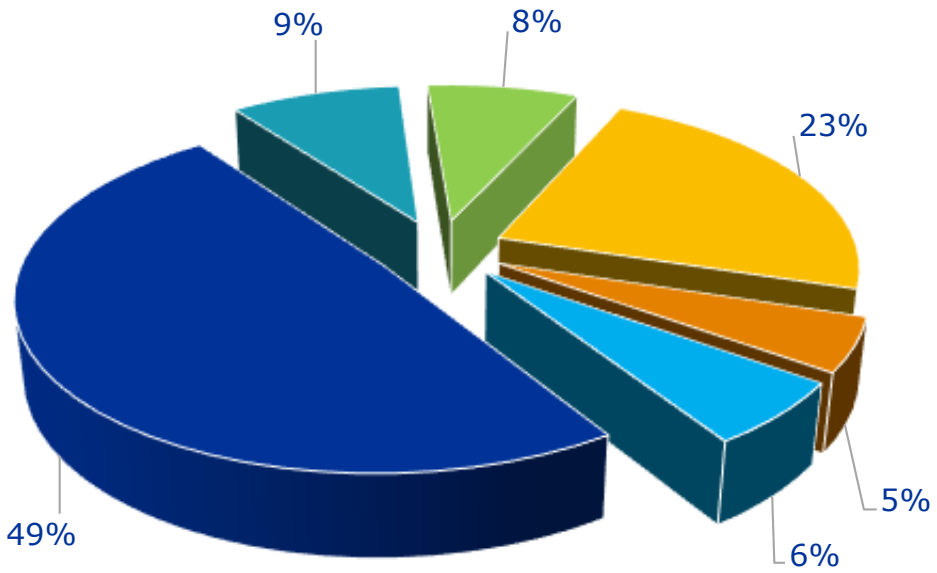
Germany 13%
France 9%
Italy 6%
Spain 5%
UK 17%
Non-EU/EEA 7%

2019

Germany 13%
France 9%
Italy, Spain, Ireland, Netherlands 5% each
⬇ UK 12%
Non-EU/EEA 9%

Profile of SMEs registered with EMA: 2019

Distribution of shareholders profile



Regulatory assistance

Administrative, regulatory and procedural queries from SMEs

SME@ema.europa.eu

SME Helpline:

+31 (0)88 781 8787

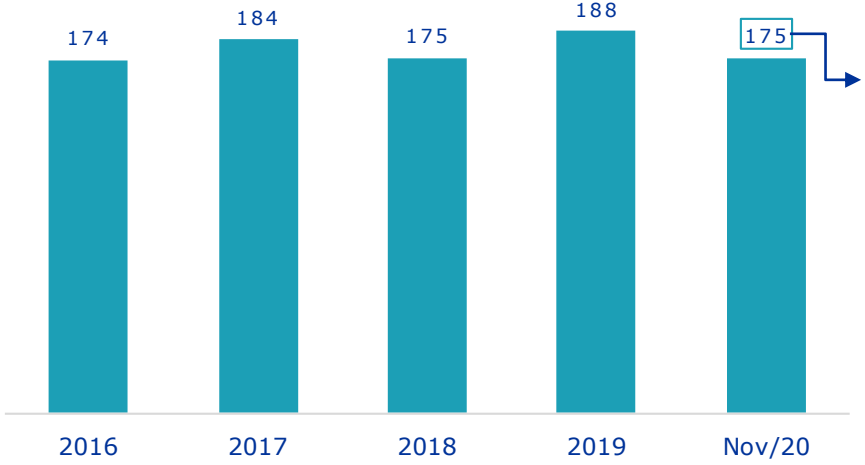
Response by email or phone

Interaction with other EMA offices

Meetings

Most common topics addressed

- SME definition and incentives
- Early development advice: Scientific advice /PRIME/ITF
- Regulatory topics (e.g. eligibility to CP, legal basis, data protection)
- Criteria for orphan designation, market exclusivity
- Paediatric requirements
- BREXIT



~200 at year end

Continued high levels of regulatory assistance

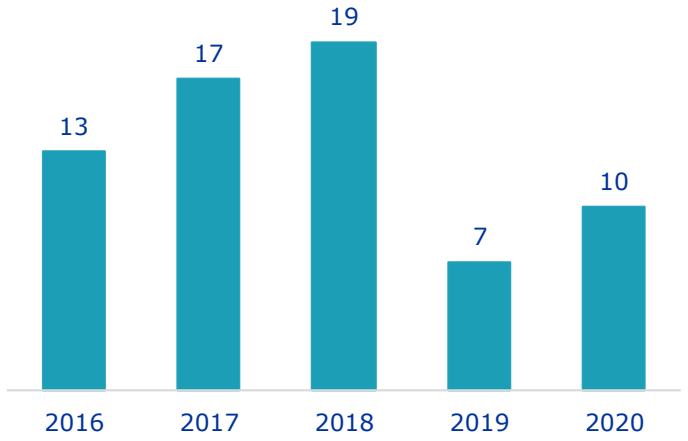
SME briefing meetings

- Platform for early dialogue with SMEs.
- Discuss the regulatory strategy of a medicinal product development & navigate the range of procedures and incentives available.
- Multidisciplinary EMA group.
- Joint screening SME/ITF meeting requests within Regulatory Science and Innovation Task Force (TRS)

→ Therapeutic indications: mainly oncology, rare diseases, anti-infectives and CNS
Majority at early stage of development

Year	Average N. of meetings
2006-2010	5
2011-2015	9
2016-2020	13

N. of SME Briefing meetings



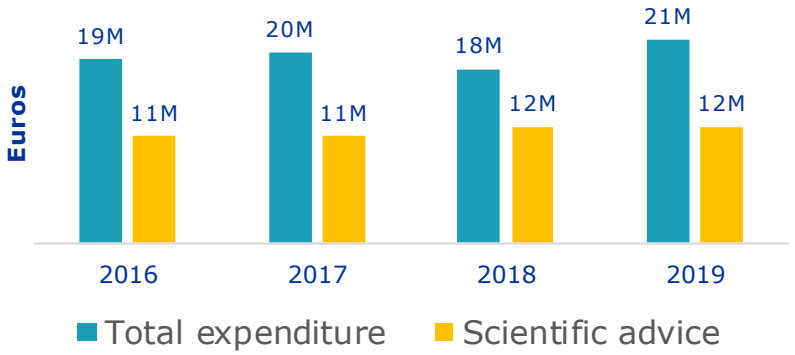
Fee incentives

- Scientific advice (SA)
  - *90% fee reduction; 100% for orphan products**
- Application for MAA
  - *Fee deferral to 45 days after EC decision*
  - *Fee waiver for SME orphan MAA**
  - *Conditional fee exemption where EMA SA followed and dossier not successful*
- Inspection (pre- and post-authorisation) - *e.g. 90% fee reduction (and deferral on pre-authorisation inspections)*
- Translation assistance - *Assistance with translations of the product information (PI) documents submitted in an initial marketing authorisation application*
- Post-authorisation procedures and PharmacoVigilance**
  - *40% fee reduction for small/medium enterprises (exemption for micro enterprises)*
- Maximum Residue Limit (MRL) - *90% fee reduction for establishment, extension or modification of MRLs*

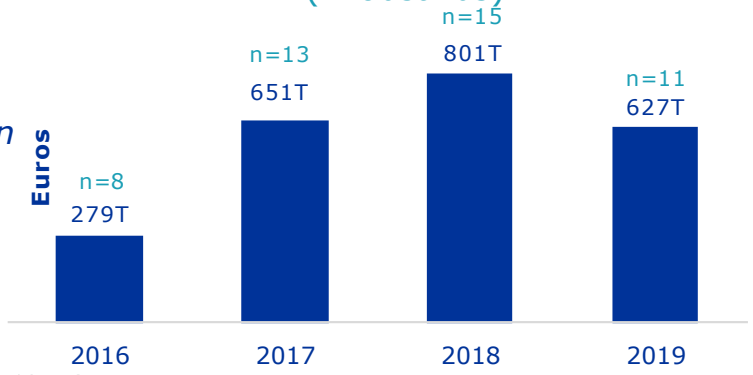
*Orphan regulation

** Pharmacovigilance regulation

SME Fee incentives (Millions)



Translation assistance costs (Thousands)



Training & awareness

Info days

Regulatory training courses tailored for SMEs.

Newsletters

Circulated quarterly; published on EMA Website.

Announcements

Information sent by email to SMEs and stakeholders.

SME User Guide

Partnering & networking

SME Register

- *to increase information available on SMEs.*
- *to facilitate and promote interaction, partnering and networking between SMEs.*

Participation to conferences and events

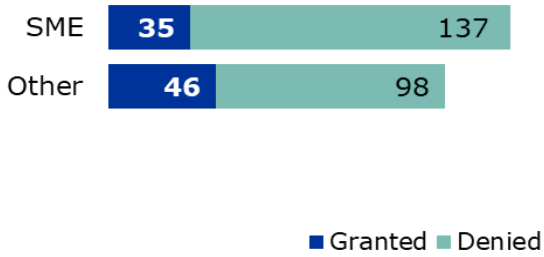
Human medicines

Support to development

PRIME (PRIority Medicines): figures as of November 2020

figures as of November 2020

- SMEs represent more than half of the requests for eligibility
- **Almost 50% of products in PRIME are from SME developers (35)**
- Lowers success rate of applications for PRIME for SMEs 20% (vs 32% for medium large companies)
- Few early entry requests (2 granted)
- **63% orphan medicines (22)**
- **43% ATMPs (15)**
- Therapeutic areas more represented: oncology/haematology, neurology, infectious diseases



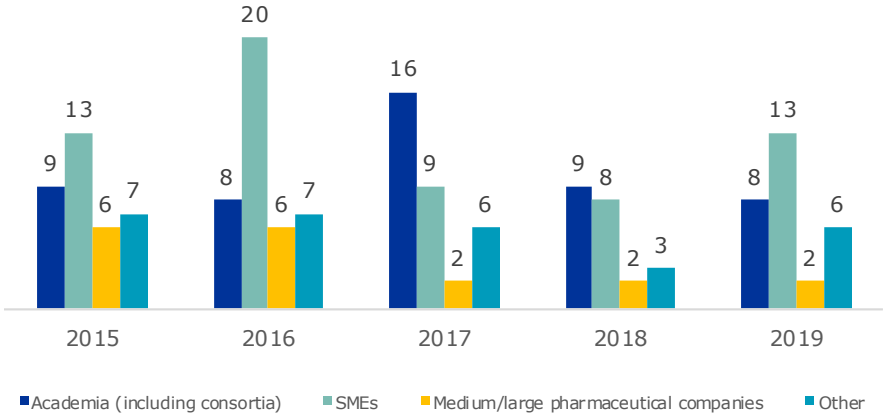
INCENTIVES

- Early entry point for SMEs: on the basis of compelling non-clinical and tolerability data from initial clinical trials
- SME briefing meetings: opportunity to discuss and receive guidance on PRIME

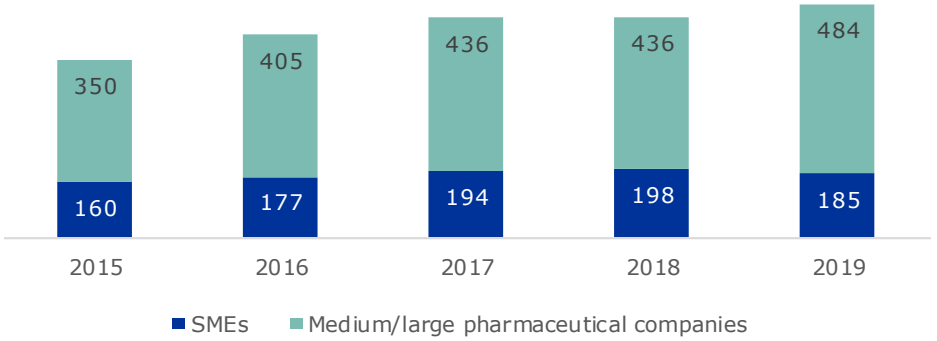
Scientific Advice (SA)/Protocol Assistance (PA)* and Innovation Task Force (ITF) - human medicines

In 2019 around 30% of SA/PA requests and 45% of ITF meetings were from SMEs

ITF briefing meetings by affiliation



Scientific advice requests by affiliation of requester



2019 Figures	Total	SME (%)
Scientific advice	549	144 (26%)
Protocol assistance	125	41 (33%)
Parallel consultations with HTA	20	3 (15%)
Qualification of novel methodologies	16	11 (69%)

➡ 13 ATMP certifications finalised (end 2019)

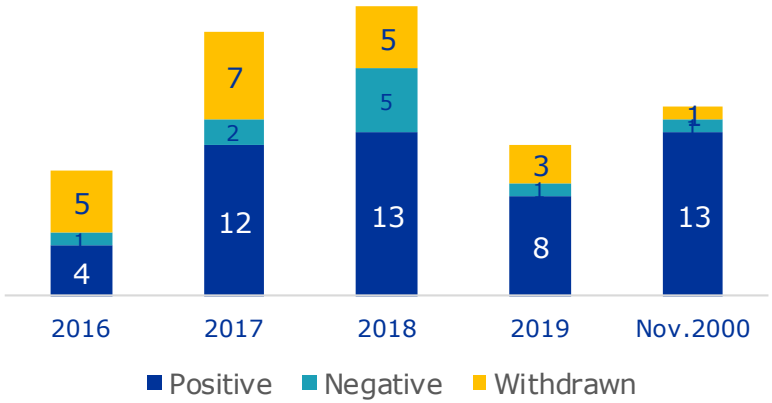
* Protocol assistance for designated orphan medicinal products.

Human medicines

Marketing authorisations

Marketing authorisations – human medicines

SME - MAA outcome per year (2016 – Nov.2020)



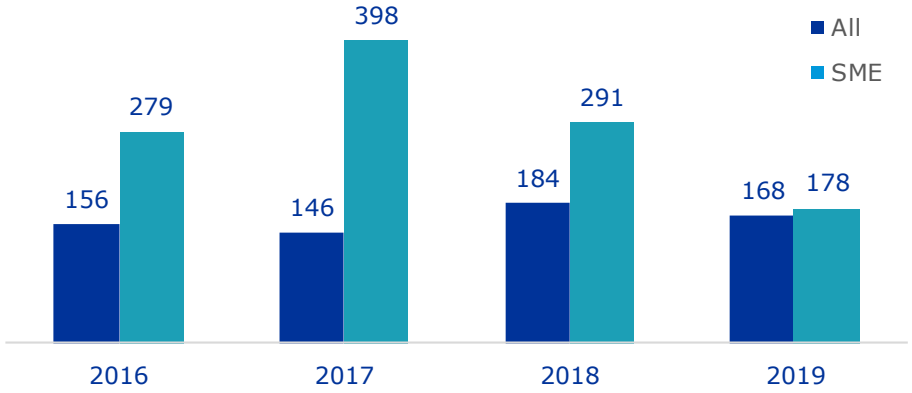
- Increase in success rate

	2016	2017	2018	2019	Nov. 2020
Success rate	40%	57%	57%	67%	87%

Updated 06.07.2021

2016-2019

- Reduction in average number of days of company clock-stop (positive opinions)

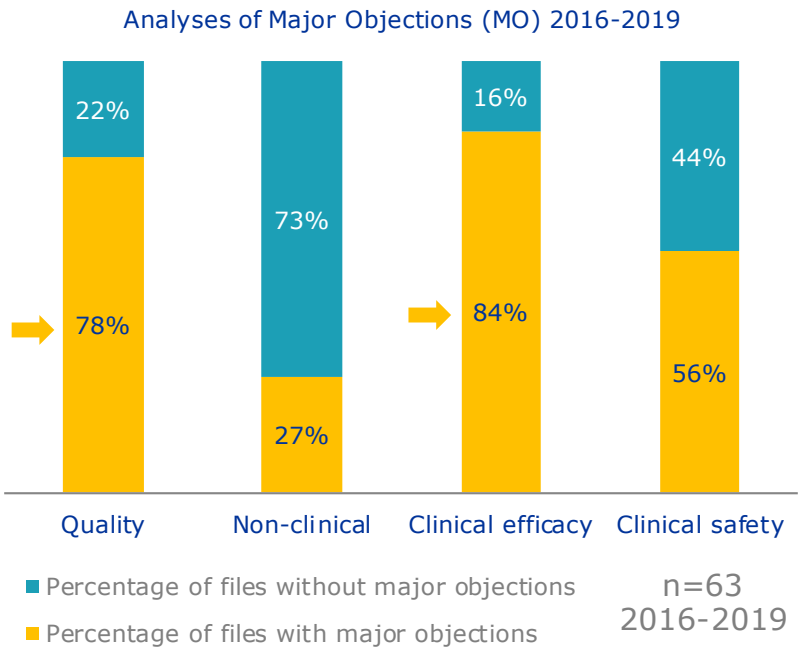


- Prior scientific advice: 62%
- Legal basis: 67% full application

Marketing authorisations – human medicines

Major Objections (MO) quality and clinical efficacy

SMEs



Orphan medicines


REVIEWS

Drug Discovery Today • Volume 23, Number 2 • February 2018

ELSEVIER

Reviews • POST SCREEN

Marketing authorisation of orphan medicines in Europe from 2000 to 2013

Matthias P. Hofer[1], Hanna Hedman[1,†], Maria Mavris[1], Franz Koenig[2], Thorsten Vetter[1], Martin Posch[2], Spiros Vamvakas[1], Jan Regnstrom[1] and Stiina Aarum[1]

[1] European Medicines Agency, 30 Churchill Place, Canary Wharf, London E14 5 EU, UK
[2] Center for Medical Statistics, Informatics, and Intelligent Systems, Section for Medical Statistics, Medical University Vienna, Spitalgasse 23, 1090 Vienna, Austria

ATMPs


Molecular Therapy
Methods & Clinical Development
Original Article

Mitigating Deficiencies in Evidence during Regulatory Assessments of Advanced Therapies: A Comparative Study with Other Biologicals

Magdi Elsallab,[1] Christopher A. Bravery,[2] Andreas Kurtz,[1] and Mohamed Abou-El-Enein[1,3]

[1]BIH Center for Regenerative Therapies (BCRT), Charité–Universitätsmedizin Berlin, 13353 Berlin, Germany; [2]Consulting on Advanced Biologicals (Advbiols) Ltd, London, UK; [3]Berlin Center for Advanced Therapies (BeCAT), Charité–Universitätsmedizin Berlin, Berlin, Germany

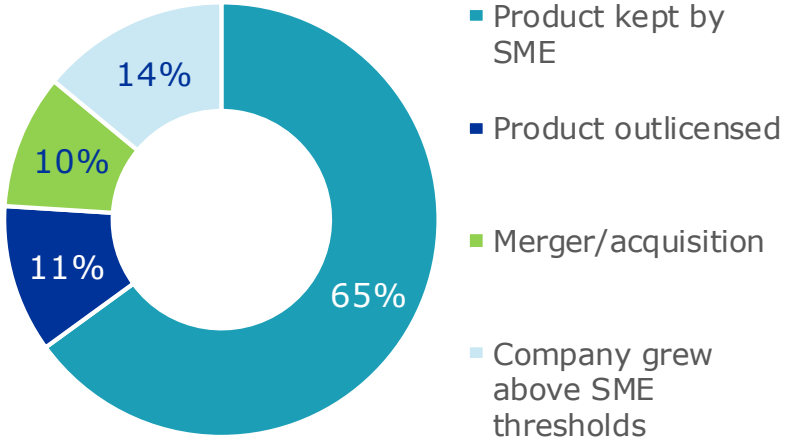
Advanced therapy medicinal products (ATMPs) comprising cell therapy, gene therapy, and tissue-engineered products, offer a multitude of novel therapeutic approaches to a wide

and manufacturing problems contributed to the other withdrawals.[4,5] It is expected that pharmaceutical development programs generate safety and efficacy evidence that is not only sufficient to support

Out-licensing/ merger and acquisitions

Out of 63 products with an SME applicant at the time of MAA and with a positive opinion over 2016-10/2020

- 65% (41) of products kept by SMEs which maintained SME status
- 14% (9) of products kept by SMEs which grew above thresholds



Product kept by SME	Company grew above SME thresholds	Merger/acquisition	Product out-licensed
41 (65%)	9 (14%)	6 (10%)	7 (11%)

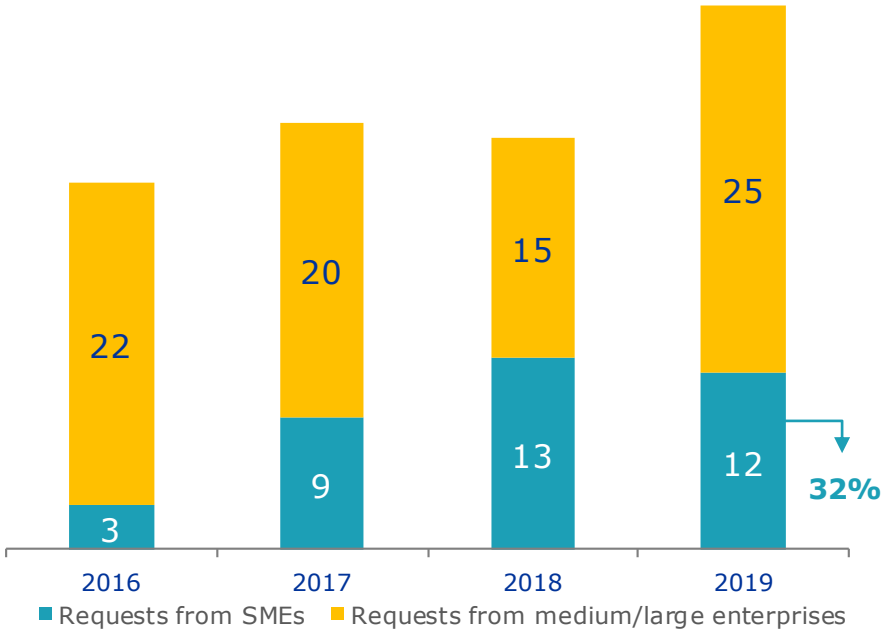
Veterinary medicines

Support to development & marketing authorisations

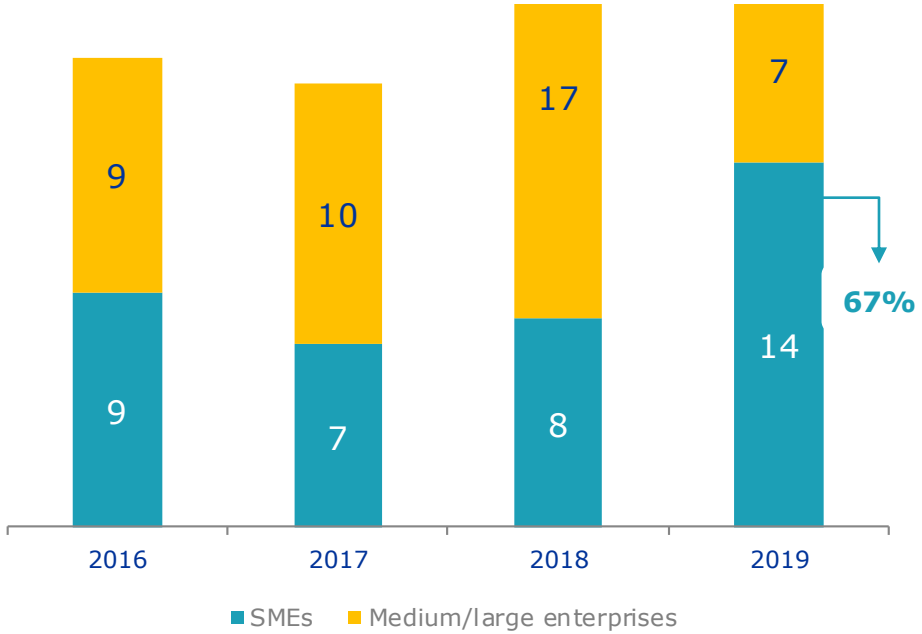
Support to development - veterinary medicines

High number of SME applicants for both MUMs and Scientific Advice

Number of MUMs classification requests

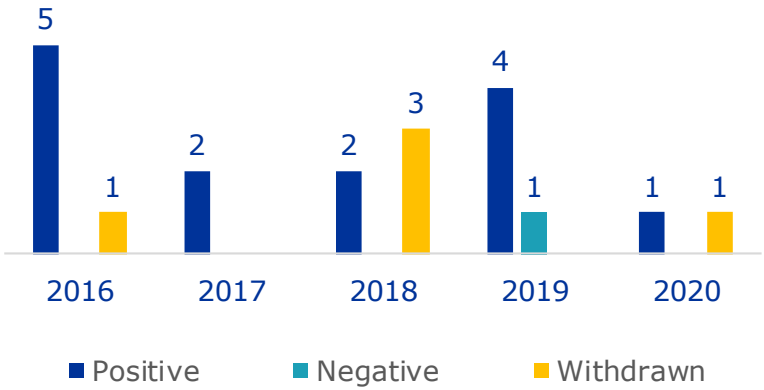


Veterinary scientific advice requests by affiliation of requester

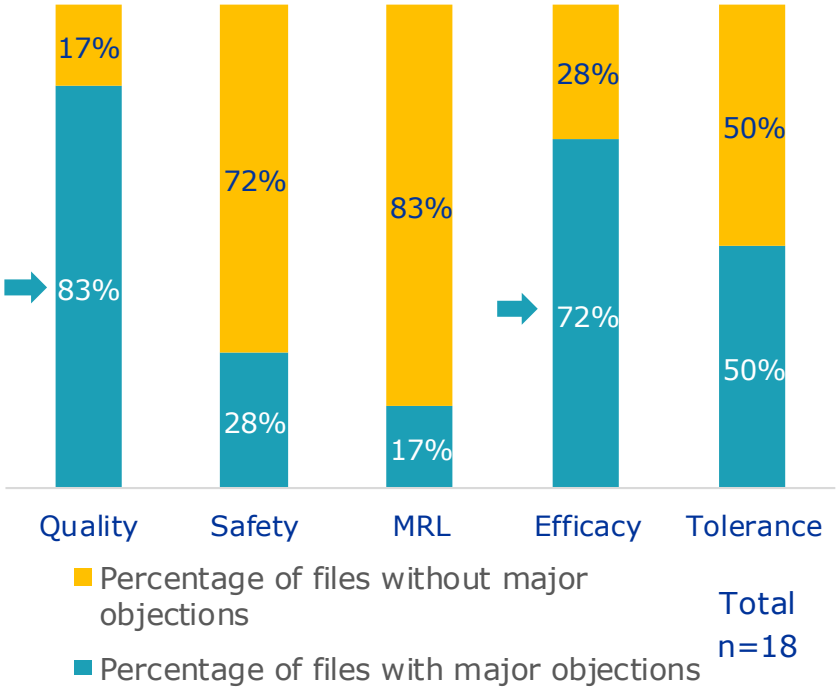


Marketing authorisations - veterinary medicines

SME - MAA outcome per year (2016-2020)



Analysis of Major Objections (2016-2019)



2016-2019

- Success rate for veterinary products: 76%
- Prior scientific advice 56%
- Legal basis: 67% full

EMA SME action plan 2017-2020

Themes (11 objectives including 16 actions):

- Raising awareness of the EMA SME initiative to stakeholders in the innovation lifecycle;
- Developing regulatory knowledge base of SMEs in the pharmaceutical sector;
- Fostering pharmaceutical innovation for human and veterinary medicines;
- Engaging with SMEs, partners and stakeholders;

The plan delivered on the objectives and actions identified

Actions to be further developed:

- Training and education: e.g. veterinary; medical devices, building on networking structures and tools (EU-NTC and EU-IN)
- Promoting early interactions on medicine development (e.g. PRIME pre-submission meetings for SMEs, drug device combination products)
- Engaging with innovation clusters, bio-incubators, investors, academia and non-profit research organisations
- Cooperation with EU institutions, bodies, EU Network (e.g. SME definition; SME supporting measures)
- Engaging with international regulators

Key achievements of the EMA's SME regulation

1	Continuous increase in SMEs registered with EMA
2	Increased use by SMEs of regulatory assistance and fee incentives
3	High number of requests for support to development (SA, PRIME, ITF and SME briefing meetings)
4	High percentage of SMEs (orphan medicines and ATMPs) in PRIME scheme
5	Training and awareness (info days, webinars, SME newsletter, SME user guide, target communications)
6	Throughout the last 15 years >130 products were approved by EMA with SME active status. Much more were developed by SMEs

Selection of products developed by SMEs

EUROPEAN MEDICINES AGENCY

Strimvelis (H)

Opinion March 2016

New gene therapy for the treatment of children with ultra-rare immune disorder

SME during development

SME

Spherox (H)

Opinion May 2017

New advanced therapy to repair cartilage defects in the knee

SME at marketing authorisation

Slenyto (H)

Opinion July 2018

New paediatric-use marketing authorisations

SME

Syvazul BTV (V)

Opinion November 2018

Bluetongue virus vaccine (multi-strain) for sheep and cattle

SME

Zynteglo (H)

Opinion March 2019

New gene therapy to treat rare inherited blood condition

SME during development

Idefirix (H)

Opinion June 2020

New treatment to enable kidney transplant in highly sensitised patients

SME

Varromed (V)

Opinion October 2016

Treatment of varroosis, one of the main diseases of honey bees

SME

Yescarta (H)

Opinion June 2018

One of the first CAR-T cell medicines recommended for approval in the European Union

SME at marketing authorisation application

Luxturna (H)

Opinion September 2018

New gene therapy for rare inherited disorder causing vision loss

SME at marketing authorisation application

HorStem and Arti-cell Forte (V)

Opinion February 2019

Stem cell products Lameness in horses

SME

Hepcludex (H)

Opinion May 2020

Treatment of chronic hepatitis delta virus infection

SME

Libmeldy (H)

Opinion October 2020

New gene therapy to treat rare genetic disorder metachromatic leukodystrophy

SME

Thank you for your attention

Any questions ?

Further information

Contact me at sme@ema.europa.eu

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