30 May 2017
EMA/790421/2016
Stakeholders and Communication

SME Office annual report 2016

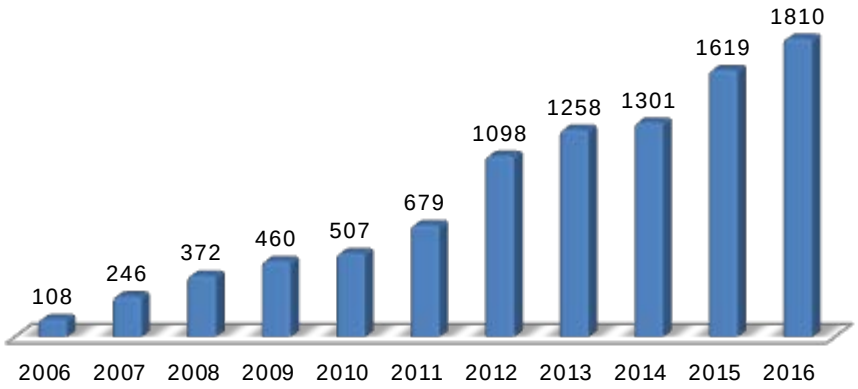
The annual report is prepared by the EMA SME Office and provides an overview of the SME related activities at the European Medicines Agency in 2016.

1. Profile of registered SMEs

The data presented below is based on the information provided in the SME declaration forms submitted to EMA. The data relate to companies with a valid SME status at year end 2016. SMEs qualified by EMA are included in the online SME register, which is a public source of information on European Union (EU)/European Economic Area (EEA)-based SMEs involved in the manufacturing, development or marketing of both human and veterinary medicines.

A total of 1810 SMEs were registered at year end 2016. This represents an increase of 12% compared to 2015 and an increase of more than 10 fold compared to 2006, the first year of implementation of the Commission Regulation (EC) No 2049/2005 – the 'SME regulation'.

Number of registered SMEs (2006-2016)



While the number of SMEs registered at the EMA continued to increase, the profile of the SMEs in 2016 remained similar in terms of size, ownership, demographic distribution and area of activity.

Size: most SMEs (41%) were micro- (<10 staff; turnover or balance sheet < € 2 mil), 34% small- (<50 staff; turnover or balance sheet < € 10 mil), and 25% medium-sized companies (<250 staff; turnover < € 50 mil or balance sheet < € 43 mil).

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Ownership: the majority of companies were privately owned either by natural persons (~ 50%) or private corporations (~ 20%). Funding by venture capital and other private investments (e.g. investment firms and institutional investors) accounted each for 7% and business angels for 5%. Interestingly, among companies incorporated over the last three years funding by venture capital investment was 13%. 9% of the registered companies are academic spin-offs.

Geographic distribution: remained unchanged in 2016 compared to previous years. The highest proportion of SMEs were based in the United Kingdom (17%), followed by Germany (13%), France (9%), Italy (6%) and Spain (5%). The percentage of companies established outside the EU/EEA and accessing EMA incentives through EU/EEA service providers qualified as SMEs by EMA was 7%.

Areas of activity: the large majority of companies were biopharmaceutical companies developing medicinal products for human use (78%), 4% veterinary companies, 5% companies developing products for both human and veterinary use, and 13% service providers to the pharmaceutical industry. 19% of the companies are developing or marketing biologicals and advanced therapies. About 20% of SMEs perform their activities in the medical devices field or have combined devices and medicines pipelines.

2. Support to SMEs

Regulatory assistance and SME briefing meetings

In 2016, the SME Office addressed 174 requests for assistance from SMEs on regulatory and administrative aspects of the pharmaceutical legislation, the highest figure achieved since the introduction of the 'SME regulation'. Assistance was provided through the dedicated SME Office helpline, by email, teleconference or face-to-face meetings[1].

In addition the SME Office continued to provide support to enterprises through SME briefing meetings (13). This platform provides assistance to enterprises which are unfamiliar with the EU regulatory approval system and facilitates early interaction with the Agency. It provides an opportunity for SMEs to informally discuss their planned regulatory strategy and development programme. Topics discussed include pharmaceutical, non-clinical, clinical development; paediatric investigational plans, orphan designations, good manufacturing or clinical practices and scientific advice. It also helps companies to navigate the range of support mechanisms on offer from EMA. The meetings are supported by a multidisciplinary team of EMA staff working in the development, evaluation and monitoring of medicines.

Innovation Task Force (ITF)

The ITF is a multidisciplinary group that works in co-operation with EMA working parties and provides a platform for early dialogue with applicants developing emerging innovative therapies and technologies. 20 out of 41 ITF meetings held in 2016 were set up for SMEs applicants.

Scientific advice

For human medicines, 177 scientific advice and protocol assistance[2] requests were submitted by SMEs, which represents an increase of 11% compared to 2015. Around 26% of all finalised scientific advice

[1] C. Ziogas; A regulator's insights for SMEs in the biologics and advanced therapies sectors (Regulatory Rapporteur – Vol 13, No 2, February 2016)
[2] Protocol assistance is scientific advice for designated orphan medicinal products.

and 46% of all protocol assistance were from SMEs. These figures highlight the significant contribution of SMEs to the development of medicines, in particular orphan medicines.

In addition, 6 out of 23 (26%) parallel scientific advice with health technology assessment (HTA) bodies were finalised for SMEs. This represents a major shift compared to 2014 when no such procedure was used by SMEs. Biomarker qualification showed a sustained interest in this development support tool, with 6 out of 14 requests (42%) from SMEs.

Most SMEs sought advice on clinical development, in particular confirmatory studies. Half of the scientific advice requests were for anti-neoplastic, immunomodulating and central nervous system medicines containing chemical entities.

The use of specific incentives for SMEs developing advanced therapies such as the certification procedure, which enables early review of quality and non-clinical data, remained at the same level (2 certification procedures).

The number of requests for scientific advice for veterinary medicines submitted by SMEs was 9 in 2016, which represents 50% of all requests.

PRIME scheme

The newly launched PRIME scheme received substantial SME interest. Out of the 67 eligibility requests reviewed in 2016, 35 were from SMEs, and 7 out of 15 products granted eligibility to PRIME were from SMEs.

3. Marketing authorisations

From December 2005 to December 2016, 107 marketing authorisation applications (MAAs) for *human* medicinal products have been submitted by SMEs. Of those, 59 have received positive outcomes and 48 have resulted in negative outcomes (11 negative opinions and 37 withdrawals). In 2016, four positive opinions and one negative opinion were issued by CHMP and five applications were withdrawn. The success rate was lower than seen over the last three years (65%).

From December 2005 to December 2016, 26 marketing authorisation applications (MAAs) for *veterinary* medicinal products have been submitted. Of those, 21 have received positive outcomes and five have resulted in negative outcome (one negative opinion and four withdrawals). In 2016, five positive opinions were issued by CVMP and one application was withdrawn.

It should also be noted that the results do not take into account products developed by SMEs which are subsequently filed by larger companies, which acquired the product or enterprise.

An analysis of major objections in SME applications for human medicines over 2011-2015 showed that approximately 88% of files had major clinical objections, 73% major quality objections and 19% non-clinical objections.

There was an important increase in the number of marketing authorisations applications submitted, for human medicines in 2016 (27 compared to 15 in 2015). The same trend was observed for veterinary medicines with nine applications submitted in 2016 compared to four in 2015.

4. Engagement with stakeholders

The SME Office enhanced its training and stakeholder engagement activities in 2016.

Two info days were organised in 2016. The first took place on 5 February 2016 and focused on statistical perspectives in regulatory clinical development programmes. The second took place on 3 October 2016 and focused on non-clinical medicines development. Videos and presentations were published on the EMA website. The topics were selected based on SMEs feedback and addressed the difficulties SMEs may experience during non-clinical and clinical development.

The SME Office website was updated to make it more user-friendly and easier to navigate. Areas of SME interest were added to the website. These include clinical data publication ('Policy 70') and the European Network of Paediatric Research activities (Enpr-EMA).

The SME user guide was subject to a major revision and updated to include new sections such as PRIME, conditional marketing authorisations, the clinical trial regulation and clinical data publication. The guide is a key document for SMEs as it consolidates and summarises the administrative and regulatory information on the EU legislative framework relating to medicines and the requirements for the development and authorisation of medicines for human or veterinary use into a single document.

The SME Office continued to publish quarterly SMEs newsletters, which aim to provide updates on regulatory and scientific guidance. The Office also increased targeted mailings in 2016 (26) with a view to provide efficient and timely information in a proactive manner to SMEs and their stakeholders.

5. Conclusions

SMEs continue to represent an important source of pharmaceutical innovation, in particular in orphan medicines or medicines that address an unmet medical need. In 2016 a significant number of SMEs benefitted from protocol assistance, the newly launched PRIME scheme and the support of the Agency's Innovation Task Force.

SMEs filing marketing authorisations applications for veterinary medicines experienced a higher success rate in 2016 than in previous years. This is not the case for human medicines where the quality and clinical documentation were the most challenging areas where objections are most frequently raised. Figures for human and veterinary medicines applications submitted to the EMA in 2016 were at an all-time high with figures doubling compared to 2015.

The EMA remains committed to fostering an environment which provides incentives to SMEs. These include in particular dedicated platforms for early dialogue such as SME Office briefing meetings or PRIME kick-off meetings, which aim to provide guidance on the overall development plan and regulatory strategy.

In 2017, the EMA will start implementing an action plan for small and medium-sized enterprises, which include a series of actions addressing challenges identified through SMEs and stakeholders consultations[3]. The actions will focus on increasing awareness of the EMA SME initiative, providing training and education, supporting innovative medicines' developments, and further engaging with SMEs, partners and stakeholders.

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[3] Report on the 10th anniversary of the SME initiative