EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Development and Evaluation

Outcome of the EMA survey on ATMP certification for SMEs - Commission Regulations (EC) No. 1349/2007 and No. 668/2009

1. Background, objectives and scope of the survey

The Regulation (EC) No 1394/2007 on advanced therapy medicinal products (ATMPs), introduced through implementing Regulation (EC) No 668/2009, an incentive for Small and Medium-sized Enterprises (SMEs) developing an ATMP to 'certify, independently of any marketing authorisation application, quality and, where available, non-clinical data developed for an ATMP, which are submitted to the European Medicines Agency (EMA)'.

The objective of the survey, which was launched and finalised in 2012, was to obtain feedback directly from SMEs developing ATMPs and their stakeholders on the following:

- Why the certification procedure is not more widely utilised by applicants since so far only two applicants have applied for the certification.

- Suggestions on how to improve the procedure to make it a more attractive incentive.

Certification is reserved for SMEs and therefore the survey only targeted SMEs developing ATMPs and stakeholders representing SMEs.

The consultation took place over a period of 2 months through a web-based survey. The mailing list was drawn from the SME database and contained 126 SMEs developing ATMPs generated. Twenty two (22) entries delivered a failure delivery receipt and 104 records were successfully delivered. The survey was also sent to SME stakeholders. Registered SMEs which attended the 2011 European Society of Gene and Cell Therapy (ESGCT) congress were also invited to complete the survey.

2. Profile of respondents

Forty three (43) responses were received representing a response rate of 41%. All records were considered in this report irrespective of whether some questions were skipped.

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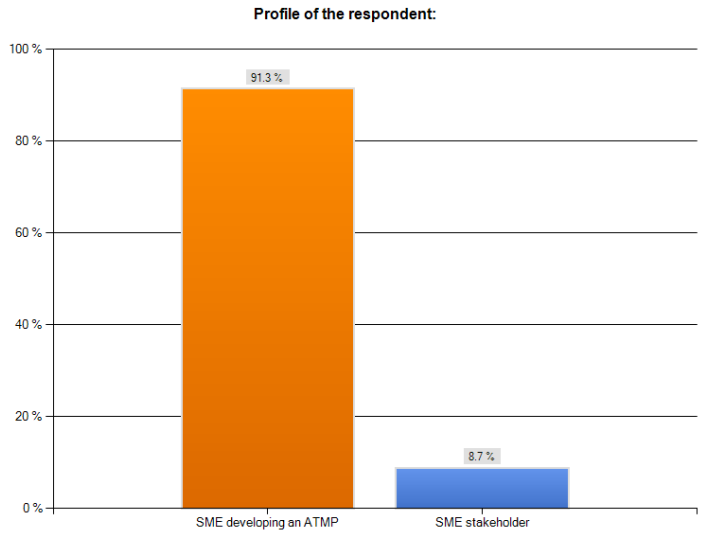
The questionnaire was anonymised with the option for respondents to provide details about the name of the company and the contact details. The respondents providing this information were 17 (16%).

The profile of the respondents was as follows:

- 91% were SMEs developing an ATMP
- 8.7% were SME stakeholders (such as pharmaceutical trade associations)

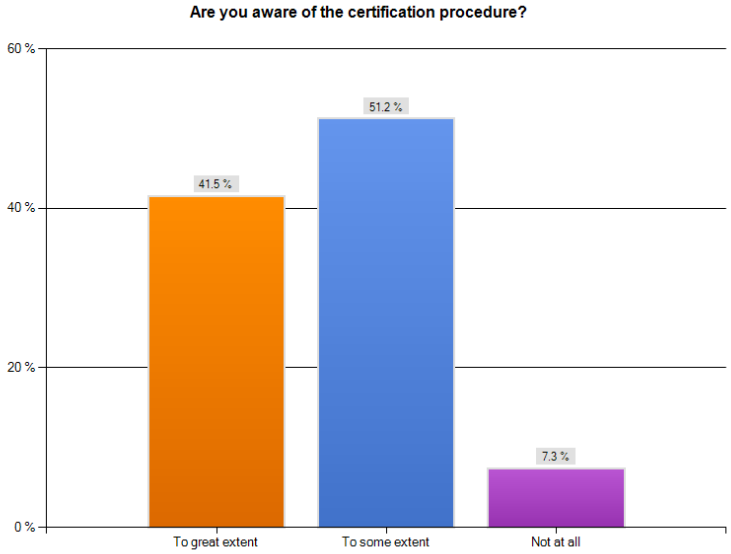


3. Findings from the survey

Awareness of the certification procedure

The first question sought feedback on the general level of awareness of the certification procedure for ATMPs. The respondents providing feedback to this question were 41 (39%).

The majority of the respondents (93%) indicated they are aware of this procedure with 51% rating it 'to some extent' and 42% 'to a great extent'. Only 7% of the respondents declared they are 'Not at all' aware of this procedure.

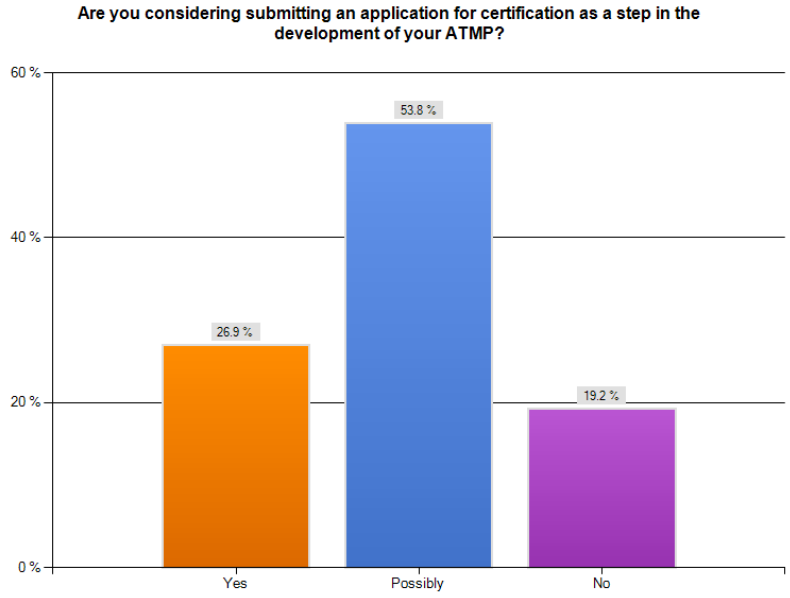


Intent to apply for certification

The respondents providing this information were 26 (25%).

Twenty seven percent (27%) of the respondents replied that they would consider seeking certification as a step in the development of their ATMP. Fifty four percent (54%) indicated they might consider applying and 19% answering categorically no.

Cost was rarely mentioned as an issue that might deter SMEs, except for micro-sized SMEs for which one respondent indicated the certification procedure may be still prohibitive, despite the 90% fee reduction.



Value of the certification

Twenty two (22) respondents provided feedback on this open question (21%).

The responses should be considered carefully as there is limited experience of companies with certification. There also seems to be a misunderstanding on its scope with two respondents considering the certification to be an opinion on the scientific recommendation on classification of an ATMP or an orphan drug designation.

Fourteen (14) respondents (64%) provided a positive feedback with the perceived advantages being the following:

- To act as an important incentive to develop ATMPs
- To offer an early strategic dialogue between the SMEs and regulators
- To facilitate the preparation of a marketing authorisation application with a view to simplify the future filing
- To clarify regulatory requirements and provide feedback on the quality and completeness of the CMC and non-clinical data package
- To facilitate the evaluation of an application for clinical trial

- To increase the value for companies when funding is sought or at time of in/out licensing
- To reduce risk, time and development costs of ATMPs
- To speed up the approval and access to market of ATMPs, in particular if the certificate ensures that the certified data would not be subject to a full review at time of marketing authorisation.

Six (6) respondents (27%) considered the certification to be of limited value with the perceived disadvantages being the following:

- Lack of direct link between certification and marketing authorisation procedure.
- Certification is independent of the marketing authorisation review process, it does not count as a partial marketing authorisation approval, and its potential impact on the marketing authorisation is unclear.
- Lost relevance of the certification over time in particular in funding and licensing negotiations.
- Length of the process.
- Resources needed to prepare a certification application.
- No added value compared to scientific advice procedure, which provides sufficient guidance on the development of the product in view of a future MAA submission and is perceived by investors to be just as appropriate.
- Certification restricted to SMEs developing ATMPs with other 'small' structures (e.g. research groups and academia) excluded from the incentives.

Feedback on the procedural aspects

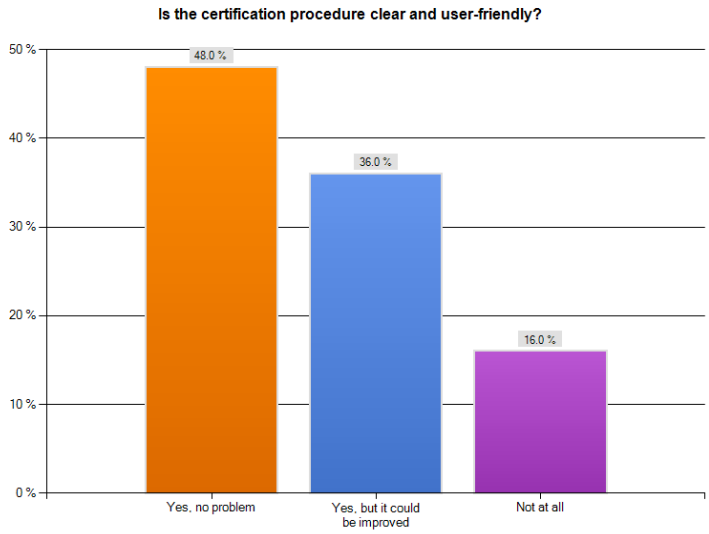
The questionnaire went on to request feedback on the procedure outlined in the guideline EMA/CAT/418458/2008/corr.

The respondents providing feedback to this question were 25 (24%).

The comments are based on how the procedure is perceived in the guideline as there is limited practical experience of companies with certification.

Twelve (12) respondents (48%) stated that the procedure is clear and user-friendly, nine (36%) indicated that the procedure could be improved and four (16%) answered that the procedure is not clear and user-friendly.

Specific comments were mainly related to the formality, complexity and length of the certification procedure.



Feedback on data requirements for certification

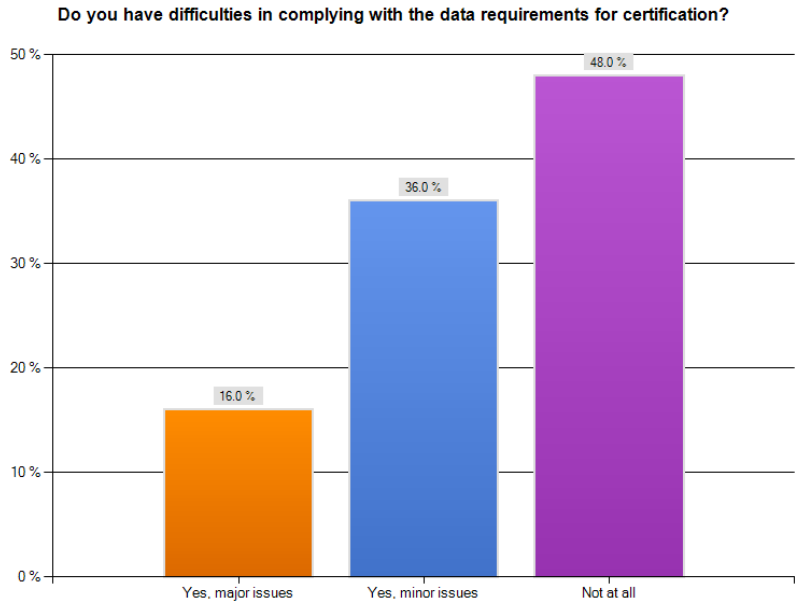
The survey asked whether any difficulties have been encountered in complying with the data requirements for certification, as described in guideline EMA/CAT/486831/2008/corr.

The respondents providing feedback to this question were 25 (24%).

The comments are based on how the procedure is perceived in the guideline as there is limited practical experience of companies with certification.

Twelve (12) respondents (48%) indicated that they would not have difficulties in submitting the data for certification, nine (36%) identified minor issues and four (16%) major issues in complying with the guidance requirements.

Specific comments were mainly related to: the extent of the data required by the guidance which might act as a deterrent rather than an incentive to seek certification; the use of limited regulatory resources in SMEs which are generally directed to compliance with mandatory development requirements (e.g. clinical trials) rather than optional regulatory incentives such as certification.



4. Conclusions

Considering the limited experience of companies with certification, the comments that were received related to the procedural aspects and the scientific requirements described in the guidance documents.

The main feedback received from the respondents are summarised as follows:

- The certification procedure is perceived to be a valuable incentive from SMEs developing ATMPs with a majority of companies indicating that they might consider applying at a certain point during the development of the product.
- The main perceived advantages are to clarify regulatory requirements, facilitate the preparation and simplify the filing and evaluation of a marketing authorisation application. Increasing the value of companies when funding is sought or at time of in/out licensing was also considered as an advantage with some companies questioning however the decreasing relevance of the certificate over time.
- The main disadvantage is the absence of a link between certification and marketing authorisation as it is unclear how the certificates would be considered during the assessment of marketing authorisation application.
- The procedural aspects of certification were considered to be clear and user-friendly. However, few comments qualified the procedure as too formal, complex and lengthy.
- A majority of companies indicated that they would not have difficulties in complying with the data requirements for certification, as long as the certificate would be used in the review of a future marketing authorisation dossier.
- The overlap with formal scientific advice was raised with a discussion on the relevance of a certificate where a Scientific Advice would be already considered sufficient to obtain feedback on the development of the product. The understanding of the scope of the certification procedure emerged as a potential issue, as it was perceived by a few respondents to be an opinion on the scientific recommendation on classification of an ATMP or relating to the orphan designation. It could be assumed that the scope of certification and how it could be used vis-à-vis other regulatory procedures might be one of the reasons for companies not considering applying.
- Cost was rarely mentioned as an issue that might deter SMEs, except for micro-sized SMEs.
- Finally, it was suggested to possibly extend the scope of the certification procedure, which is currently restricted only to SMEs developing ATMPs to research groups and academia. Of note, the certification procedure is only applicable to SMEs according to Article 18 of Regulation (EC) No 1394/2007.

The European Medicines Agency is taking into consideration all the feedback received through this survey. Although the Agency has made available guidance on the ATMP certification procedure (see references below), this survey reveals the need to further clarify the scope of certification. In particular, the Agency will further clarify the place of certification within the range of services provided by the EMA to support SMEs in developing ATMPs. The Agency will also bring the results from this survey to the attention of the European Commission.

5. References

Procedural advice on the certification of quality and nonclinical data for small and medium sized enterprises developing advanced therapy medicinal products.

Guideline on the minimum quality and non-clinical data for certification of advanced therapy medicinal products