BIOBUSINESS BRIEFS

REGULATORY WATCH

Outcomes of EMA marketing authorization applications: does partnering have an influence?

Combining strengths in drug discovery and development by partnering and outsourcing has been shown to increase the likelihood of success in bringing new products to the clinic (*Clin. Pharmacol. Ther.* **87**, 272–277; 2010). In this context, a recent analysis by Lincker *et al.* from the European Medicines Agency (EMA) investigated the origin of new active substances (NASs) that were approved to enter the European market between 2010 and 2012 (*Nature Rev. Drug Discov.* **13**, 92–93; 2014). They showed that a substantial proportion (~45%) of the 94 NASs approved in this time originated from small companies, academic institutions and public–private partnerships, and that most had been transferred to larger companies during development. However, this analysis did not assess whether the origin of a NAS is also associated with approval success or failure. Therefore, in this study we investigated whether self-originated NASs differed from acquired NASs with regard to the outcome of marketing applications at the EMA.

We included all NASs for which the EMA Committee for Medicinal Products for Human Use (CHMP) issued an opinion on the marketing authorization application (MAA) from 2009 to 2013 and categorized each NAS as either acquired or self-originated. The outcome was either 'approved' (positive opinion by the CHMP) or 'failed' (negative opinion or withdrawn by the applicant before a CHMP opinion). Furthermore, we stratified acquisitions according to the size of the applicant. For a more extensive description of the methodology and other investigated factors, see Supplementary information S1 (box), S2 (figure), S3 (table).

The CHMP issued an opinion on 172 NASs in the period 2009–2013 under the centralized MAA procedure. Of these 172, 133 (77%) were granted a positive opinion. Overall, 54 (41%) of these approved products originated from small companies, non-governmental organizations or academic institutions (FIG. 1a), again highlighting the importance of these sources of new products for the European market. Also in line with previous research, NASs from small applicants had a higher failure rate (40%) than did those from medium- or large-sized applicants (17%) (FIG. 1b).

Overall, 69 (40%) of the investigated NASs were acquired. We found no difference in the percentage of MAA failures between acquired and self-originated NASs (23% and 22%, respectively; Supplementary information S2 (figure)). When stratifying acquisition by the size of the applicant, NASs that were self-originated by small applicants had a lower percentage of MAA failures (37%) than did NASs acquired by small applicants (47%). In the medium- and large-sized applicant groups, we found no difference between the percentages of failed MAAs for acquired NASs and for self-originated NASs (both 17%; FIG. 1b).

Considering the 69 product acquisitions in more detail, most acquisitions (26) were whole product acquisitions (that is, where the acquirer took over responsibility for all further development and marketing), followed by whole company acquisitions (22) and partial license agreements (21) (for example, allowing the acquirer to market the product in a specific geographic region). Notably, when comparing failure percentages among the different types of acquisition, the failure rate of whole product acquisitions (38%) was twice the failure rate of products with partial license agreements (19%) and four times the failure rate (9%) of whole company acquisitions (Supplementary information S1 (box), S2 (figure)). One possible explanation for the lower failure rates in the second two groups is because the development team in those situations remains the same or at least the new developers continue to have access to their expertise.

The finding that small companies still have higher failure percentages for MAAs — both for acquired and self-originated NASs — than do larger companies implies that the regulatory dialogue between small companies and regulators needs improvement. Furthermore, our findings indicate that small companies may not be optimally skilled for in-licensing, as the NASs acquired by small applicants had a particularly high percentage (47%) of failed MAAs. Overall, as also indicated by previous analyses, collaborating with larger companies may be a more effective strategy for smaller companies to bring new products successfully to the European market.

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SUPPLEMENTARY INFORMATION
See online article: S1 (box) | S2 (figure) | S3 (table)
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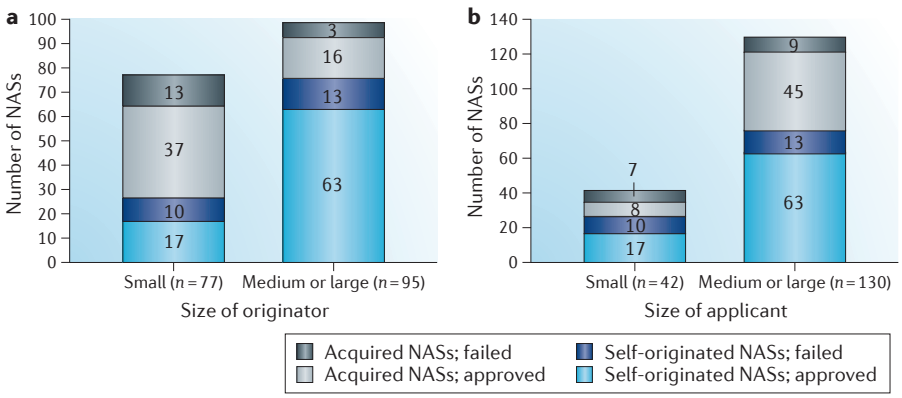

Figure 1 | **Numbers of new active substances (NASs) approved or failed between 2009 and 2013.** **a** | NASs stratified according to the size of the originator. **b** | NASs stratified according to the size of the marketing authorization applicant.