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Sources of innovation: an assessment of intellectual property

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An analysis of US Food and Drug Administration (FDA)-approved new molecular entities (NMEs) reveals dynamism in terms of new innovation. An assessment of the first patent for each drug shows that the pharmaceutical industry, particularly large, established companies in North America, tend to dominate the field. Over the past 10–15 years, European and Asian organizations have begun to close the gap. A dynamic inventive environment in drug discovery is suggested by the fact that NMEs for biologics or awarded to biotechnology companies often have inventors from the pharmaceutical and academic sectors. Whereas inventors continue to found biotechnology companies at a steady rate, recent trends suggest these inventors more often come from the private sector.

Introduction

Q2 Invention has always been at the core of drug discovery. To assess sources of innovation in the creation of new medicines, we accumulated information about all NMEs approved by the FDA through to the end of 2013 [1]. As one source of innovation, we identified the first-identifiable patent for each NME. This was performed primarily by analyzing databases from the US Patent and Trade Office (USPTO), the World Intellectual Property Organization (WIPO; for patents after 1970), SciFinder (American Chemical Society), and Google Patents (Google). Specifically, our approach sought to identify the earliest US patent approved for each NME based on its generic name. If this information was insufficient, secondary searches were performed based on the chemical structure and Chemical Abstracts Service (CAS) Registry numbers. Information was captured about the name, dates, and locations of the inventors and the assignees. Importantly, the work herein focuses solely on the earliest application date to avoid variability in review times, which impact final decisions as to patent issuance. Although some patents include inventors from different organizations, the location and assigned of the primary inventor was utilized for ease of analysis. For multinational companies or those where consolidation might have altered ownership (e.g. between the time of submission and issuance), the location of the primary inventor was likewise utilized to minimize potential confusion and the assignee was the original assignee (not a later acquirer). In cases where the submission date occurred after FDA approval, these were presumed to reflect improvements (rather than the first patent) and were not included in this analysis. This approach enabled us to determine the first-identifiable patents for 1374 of 1453 NMEs approved by the FDA (95%). Importantly, the work herein focused on the earliest patent and did not consider additional intellectual property and/or trade secrets that might be crucial for making, marketing, or gaining approval for a new medicine. Although every attempt was made to identify the earliest patent, we cannot exclude that some patents for related molecules might have been filed before those associated with the specific identifier (generic name, chemical formula, and/or CAS number).

The location of the first inventor was broadly divided into North America, Europe, Asia, and the Rest of World (ROW). The largest concentration of lead patent inventors was in North America, followed by Europe and Asia (Fig. 1a). When viewed over time, the geographic distribution of inventors of the first patents of FDA-approved NMEs has evolved. From the 1930s through to the 1960s, approximately 80% of inventors and assignees were located in North America, with European contributors capturing most of the remaining patents. Starting with

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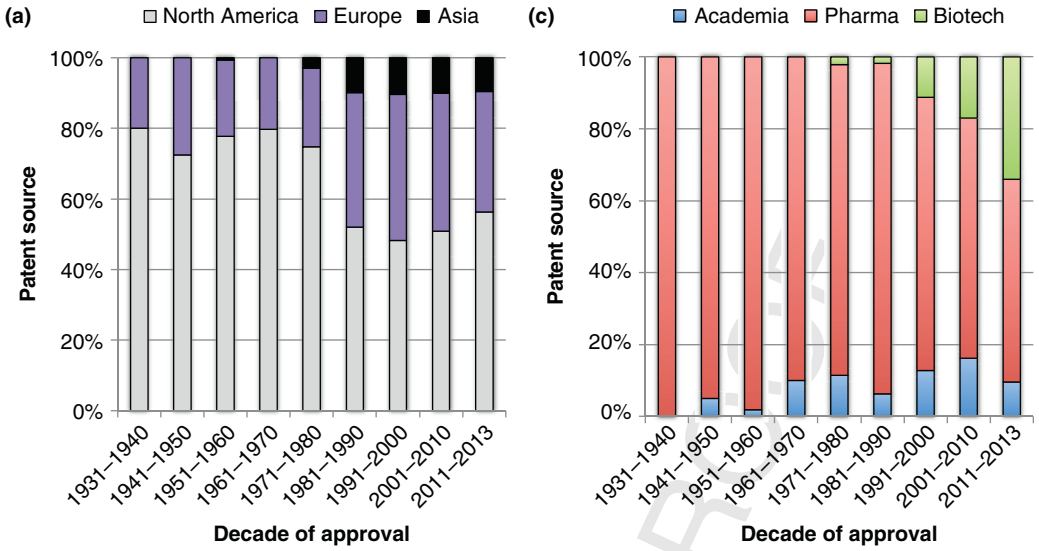

(b)

Country	Patents
USA	801 (58.3%)
Germany	118 (8.6%)
UK	95 (6.9%)
Japan	89 (6.5%)
Switzerland	69 (5.0%)

(d)

Organization	Patents
Merck	65 (4.7%)
Eli Lilly	41 (3.3%)
Pfizer	39 (2.8%)
Roche	38 (2.8%)
Upjohn	38 (2.8%)

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FIGURE 1

Geographic and organizational contributions to patents. **(a)** The source of first-identifiable patents for each US Food and Drug Administration (FDA)-approved new molecular entity (NME) is indicated on a decade-by-decade basis and distinguished by broad geographic region. **(b)** The five leading national sources of these patents are indicated, along with the number contributed by each. **(c)** Patent sources were distinguished by sector (academia, pharmaceutical, or biotechnology) as indicated. **(d)** The five leading organizational sources of these patents are indicated, along with the number contributed by each. A total of 1374 patents were analyzed.

NMEs approved during the 1970s, the proportion of patents awarded to European countries increased to approximately one-third and patents from Asia rose to almost 10%. In terms of individual nations (Fig. 1b), the USA contributed the largest number of first-identifiable patents (810 or 58.3%) followed by Germany (118 or 8.6%), the UK (95 or 6.9%), Japan (89 or 6.5%), and Switzerland (69 or 5.0%).

An analysis of assignees reveals a predominance of the pharmaceutical industry that persisted until recent years. Pharmaceutical companies were assigned the first patents for most NMEs (1118 or 81.4%) followed by academia (139 or 10.1%), and the biotechnology industry (8.5%). When assessing individual organizations, the most common assignees for the first-identifiable patents were Merck (4.7%), Eli Lilly (3.3%), Pfizer (2.8%), Roche (2.8%), and Upjohn (2.8%) (Fig. 1 d), which together account for one-sixth of all patents evaluated.

'Biotechnology' patents

The rise of biotechnology began during the early 1970s and redefined the discovery of new medicines [2,3]. As one means of assessing biotechnology patents, we first emphasized patents awarded for biologics-based products (generally polypeptide or antibody-based medicines). This necessarily limited the timeframe under investigation because the first biologic medicine was approved during the early 1980s. When analyzing geographic trends, comparable findings were obtained with biologics as seen with overall NME awards in that same time period. North American organizations were awarded approximately two-thirds of first-identifiable patents for biologics-based medicines, followed by European and Asian organizations (Fig. 2a).

Academic organizations captured a larger proportion of biologics-based medicines than was observed in the assessment of all NMEs (Fig. 2b). Academic institutions (including government laboratories) were the source of inventors for the first patent for approximately one-quarter of all biologics-based medicines. Biotechnology and pharmaceutical companies share approximately the same number of NME first patents. However, when viewed over time, biotechnology companies have increasingly displaced pharmaceutical companies.

As emphasized in previous studies [4], a second way to define 'biotechnology' is to emphasize companies that were founded during or after the 1970s. A startup-based definition is imperfect but enables one to distinguish more conventional pharmaceutical companies (often founded in or before the 19th century) from more recent startups. When viewed in this way, the first approvals for biotechnology companies were obtained during the early 1980s and continue today. In total, 191 patents for NMEs were captured by this definition of 'biotechnology.'

The results for the more broad definition of biotechnology largely reflected that seen with

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