ASSESSING ENTREPRENEURSHIP AND INNOVATION IN MEDICAL DEVICES

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ABSTRACT

Entrepreneurship and innovation are closely related. Entrepreneurship is viewed in economics as one of the basic factors that facilitates economic growth. Without entrepreneurship the problem of how to continuously rearrange the factors of production to realize a more efficient output, both in the process of producing – productive efficiency, as well as with the output itself – allocative efficiency, remains unanswered. “The OECD … says innovation can be defined as ‘new products, business processes and organic changes that create wealth or social welfare.’ … ‘fresh thinking that creates value’.” (The Economist 2007)

This paper examines a question fundamental for research into entrepreneurship and innovation: how to assess them? It looks at the high-risk medical device market in the United States of America and introduces a previously under-researched dataset to assess its entrepreneurial and innovatory activities. The paper discusses the use of US Food and Drug Administration product approval data for the purpose of assessing entrepreneurship and innovation in the high-risk medical device market and provides early findings utilising these data.
INTRODUCTION

It is generally agreed that entrepreneurship and innovation are important ingredients to economic growth (Schumpeter 1943, Schmookler 1962, Scherer 1965a, Scherer 1992). Entrepreneurship by definition includes some component of newness, which is either a new business or a new product or both, but also some entrepreneurial contribution by an entrepreneur in combining resources in a new way, for a new purpose or meeting a new market (Formaini 2001). Less agreement is found when considering questions such as whether small or large businesses are the proportionately bigger source of innovation (Schmookler 1959, Rothwell 1988, Acs et al. 2007); whether R&D inputs are more or less efficiently converted into innovation output in small or large businesses (ibid.); how much influence market structures and technological opportunity have on entrepreneurship and innovation (Mansfield 1962, Kamien et al. 1982, Jovanovic 1982, Loasby 2000, Malerba 2005, Stel et al. 2007); and how to accurately measure entrepreneurship and innovation (Sanders 1962, Scherer 1965b, Comanor et al. 1969, Graham et al. 2007).

The analysis is complicated further by attempts to assess entrepreneurship and innovation across different geographic markets, different market structures, and in different time periods. The definition of input and output indicators that are being used to assess these concepts provides a further source of complication. One possible approach to disentangle the complex relationship between market setting, inputs and outputs in relation to entrepreneurship and innovation is to reduce the focus of the analysis to one industry, and to segments in that one industry, and use measures specifically defined for this purpose.

The focus of this paper is on high-risk medical devices (MDs) in the US market, using a previously under-researched US Food and Drug Administration (FDA) dataset of high-risk device pre-market approvals (PMAs) from 1992 to 2007. MDs are mainly regulated for the risk they pose to patients and others involved in MD use. They accordingly require official approval before they are allowed to be marketed. MD regulation has as its main aim to ensure the safety and effectiveness of MDs. Typically, and especially for high-risk devices, MD regulatory regimes require the manufacturer to provide significant amounts of information, so that the approval body can determine whether the device is safe and effective. The approval process erects a structural barrier for MD manufacturers that must be overcome before they can enter the final product market, both in terms of entrepreneurial first-time market entry as well as innovatory steps throughout the lifecycle of a product. In this paper entrepreneurship and innovation will be evaluated at this point of market entry for a new entity, a new device or a new feature for an already existing device.

The paper is organised as follows: The next section summarises previously utilised measures of entrepreneurship and innovation and discusses the shortcomings of these measures in high-risk MD markets. It further discusses the process of how firms enter the MD market and the typical market introduction of innovations. In the next section the FDA approval data are introduced and it is
discussed how they can be used to measure entrepreneurship and innovation. Hypotheses are provided to be tested with the dataset in the next section. To help demonstrate the potential of the dataset, the paper will present some initial findings in the last section which also discusses potential further uses for the FDA dataset and possible future directions of research.

ENTREPRENEURSHIP AND INNOVATION IN MEDICAL DEVICES

Entrepreneurship
The literature on entrepreneurs as single persons, the entrepreneur’s characteristics, the process of entrepreneurship, firm formation on a national or regional level, corporate entrepreneurship which is sometimes called ‘intrapreneurship’, linkages between entrepreneurship and economic growth, and on the link between the structural environment and entrepreneurship is rich (Wennekers et al. 1999 and 2004, Reynolds 1999, Formaini 2001, Wong et al. 2005, Ireland et al. 2006, Scott 2006). However, studies looking at entrepreneurship and innovation in MDs, let alone high-risk MDs, are few and concentrate on entrepreneurs’ personal characteristics (Chatterji 2007) or the innovation process utilised in MDs (Rochford et al. 1997, Ulwick 2002).

The questions addressed by this paper have not been assessed before: How ‘entrepreneurial’, in terms of new firm formation or firm entrance, is the high-risk MD sector? Can FDA approval data be utilised to evaluate entrepreneurial activities in the high-risk MD sector? What do they tell us?

Innovation
There exists a plethora of approaches and methods to assess innovation (Sanders 1962, Scherer 1965b, Comanor et al. 1969, Graham et al. 2007). Input indicators, such as capital investment figures, venture capital employed in start-up firms (also used in entrepreneurship studies), R&D expenditures and employment, output measures like forward and backward citation-weighted patent counts, trademark counts, trade show registers, and combinations of input and output indicators such as R&D productivity, have been used to explain innovatory patterns across nations, industries and time.

There are certain advantages and disadvantages when using any of these measures. The measures come at different times during the innovation process, measure different things and are therefore not easily substitutable. They are not necessarily correlated and do often not explain the same thing. Of course, some measurements are used because no alternative measurement can be found. It is debatable whether the most commonly used measures such as patent counts, citation-weighted patent counts, trademarks, etc. are appropriate proxy measures for innovatory activities (Sanders 1962, Scherer 1965a 1965b, Comanor et al. 1969, Cohen et al. 2000, Mendoca et al. 2004, Lanjouw et al. 2004, Graham et al. 2007). In the pharmaceutical industry, which is an industry under a similarly stringent regulatory
regime as the high-risk MD industry, patent counts do not appear to be reliable measures for firm innovative activity (Graham et al. 2007). Which measures should be used in high-risk MDs?

Depending on the subject of analysis, all measures of innovation have different degrees of relevance. Specifically, a focus on high-risk MDs makes it nearly impossible to relate these measures to the actual products and innovations being introduced to the final market. Capital investment figures and venture capital employed in start-up firms provide a measurement of investment in entrepreneurial firms, however, they do not include firms which have secured their funding through other channels (e.g. private or public funding). R&D expenditures and R&D employee counts are input indicators which come to pass relatively early in the innovation process of a high-risk MD. The patent count measure also has some deficiencies as it is difficult to relate patents to actual products in the high-risk MD sector. The patent quality, e.g. patents differing in the number and nature of claims they make, and the patent family size (the number of national laws a patent is aimed at), can lead to further difficulties in measuring innovation (Lanjouw et al. 2004). There are some indications that patents can be viewed as an input to the innovation process rather than an output measure (Comanor et al. 1969, Graham et al. 2007). Innovators not uncommonly stake claims over their technological field of interest (often referred to as ‘patent blocking’). The costs of enforcing a patent and the know-how needed to patent might lead to small innovators choosing a confidentiality or secrecy strategy as an alternative to patenting (Cohen et al. 2000, Lanjouw et al. 2004). Trademarks are equally problematic as the patent count measure. Not every product will be trademarked, while some might be trademarked multiple times. Trade show registers, where new products can be presented to interested parties, can be incomplete as not every firm will be present at trade shows. In fact trade shows in medical technology predominately focus on supplies and services to the MD industry, not on the products manufactured in the MD industry. The sales process in high-risk MDs is centred around a close, often personal relationship between sales representatives, medical specialists and purchasing managers at the level of health service providers (e.g. hospitals, health insurance companies, etc.).

On the output side, sales are probably the most commonly used measure to assess aspects of innovation. Innovation should generate sales, and ultimately profits. Crucial to this is the quality of sales data. If sales data are not available for every product individually, it might be difficult to relate sales output to one specific product, given that a lot of MD firms diversify and provide products in different medical specialties and product areas or even outside MDs. R&D productivity is often derived from a combination of input and output measures, basically defined as output per input. Often output will be some kind of patent measure or a sales measure, input either a monetary input or input in terms of employee headcounts. Sometimes time lags are introduced to allow for the effects of inputs that come to pass only after a certain period of time.

Regardless of whether research utilises single indicators on the input side or the output side, or whether indicators are combined in the analysis, what needs to be ensured is that the indicators are specific to the subject of analysis – here, high-risk MDs.
The high-risk MD innovation process

An innovation process model for MDs is depicted in Figure 1, and is based on the ‘coupling’ model of innovation (Rothwell 1994). This model sees a combination of demand pull and technology push. As MDs are intended to deliver better quality of life for patients and sometimes even life prolonging and life saving features, there will be demand ‘pulling’ the development of innovative MDs. MD manufacturers pushing technological feasibility, driving idea generation and the R&D process, generate a ‘push’. They push new technologies and innovations into the market. Additional to the standard model there is the process element of regulatory affairs (RA). RA refers to the activities related to preparation and submission of files to authorities for approval before market entry and the maintenance of files during the lifecycle of a MD.

![Figure 1: Innovation in high-risk MDs](image)

The typical innovation process in high-risk MDs includes a considerable time period dedicated to proto-typing, design specification, actual development of the device, development of its production processes, a phase of clinical testing, and delivery to the market through the ‘gate-keeping’ approval process – the pre-market approval (PMA) (as per a typical stage-gate process, Cooper 1990). A firm seeking approval for a new device, a change to an existing device, its manufacturing process or its intended use will have to provide clinical and technical evidence that the safety and effectiveness standards of the device are sufficient. The approval is the final gate before any development in high-risk MDs can enter the market. The approval process by itself also takes substantial periods of time. Accordingly, this is one of the immediate questions to be addressed. How long does it take to introduce new devices or changes to existing devices to reach the market through the approval process? How much time does the approving body require to review the submitted files? This question may also throw some light on the incentives and barriers to innovate in MDs.

The development process is often not linear (Gelijns and Rosenberg 1994). MD manufacturers, especially in the high-risk sector, rely on medical expertise from surgeons and medical specialists in the development and refinement of MDs. Also of importance are customer inputs from the patient population (Ulwick 2002). Ideas need to be tested, technical possibilities assessed, design inputs from
various sources need to be combined and addressed into a later product, and the product needs to undergo substantial amounts of in-vitro testing. As one of the components for a later submission for approval to a regulatory body, a clinical testing phase has to be carried out – also under regulatory supervision (e.g. ethics committees at hospital and/or national levels, or approval of clinical studies at the FDA). These design inputs represent feedback loops into the development process from later innovation process stages. Whenever design features or processes used to produce the device are being changed, a supplementary submission to the FDA is required. As such, the development process is forced into sequential order for every innovatory step throughout the product lifecycle at the point of market entry. Only after successful approval will devices be allowed onto the market.

**Market structures in high-risk MDs**

The intensity of innovation activities will be different across market segments of MDs. It is therefore essential for this research to consider whether medical technologies form a uniform market and what actually constitutes a market (Loasby 2000). Are all MDs, or all high-risk MDs sufficiently homogeneous in either demand or supply conditions, i.e. close substitutes in demand or supply, to be classified as belonging in the one market? Does one have to consider the use of the actual product and thereby limit the definition of the market more narrowly to the end user’s perspective (in case of MDs the patient’s perspective)? It will be a too broad definition of high-risk MD markets to focus on medical specialty only. However, within medical specialties, not every product type segment will form a distinct market by itself. Another consideration is on the supply side. Can resources and capabilities of a firm be transferred to other segments easily? As will be seen in the results section, high-risk MD markets are quite fragmented.

**THE FDA DATASET**

**The data**

Since the enactment of the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act, United States Code of Federal Regulation, Title 21 (FDA 2008a) on May 28, 1976, newly developed high-risk MDs have to undergo a review before they are approved to be marketed (the PMA). The basic process of device approval has been unchanged since then.

US FDA MD data comprise product approvals in three MD risk classes. In the lower risk classes, Class I MDs are usually exempt from regulatory review and Class II MDs require a relatively simple pre-market notification (a PMN, which is also termed ‘510k’ after the form being used in this process) to the FDA. This PMN is usually completed within 90 days and establishes ‘substantial equivalence’ to an already existing device. It can therefore be argued that these devices provide rather small, incremental innovatory advances, sometimes only in the sense that they constitute a new offering of an already existing technological application. Class III MDs, high risk products, are approved using the
The pre-market approval (PMA) process. The amendments define a Class III device as one that supports or sustains human life or is of substantial importance in preventing impairment of human health or presents a potential, unreasonable risk of illness or injury (FDA 2008b). When the FDA receives a ‘510k’ application and the initial assessment shows that it is not substantially equivalent to a pre-existing device, and the device is seen to pose significant risks, the application will be upgraded to a PMA. After an original PMA has been approved, MD manufacturers are obligated to apply for approval of changes to the device, its manufacturing processes, and its indications for use in a so-called PMA supplement.

PMA supplements are reviewed at the FDA’s Centre for Devices and Radiological Health (CDRH) under different review tracks based on the significance of the change. Manufacturers typically apply for a review track which is then either affirmed by the FDA or changed into another review type. These different review tracks can take from just a few days, to up to several months to complete. The FDA-assigned review tracks and the resulting actual review times are indicators of how important the FDA thinks a change might be and of the actual significance the change has.

Once an application has been approved it will be listed in the PMA database. Each PMA / PMA supplement is individually identified by a PMA and a supplement number. Each file contains data such as the applicant firm (the PMA owner), the medical specialty the product falls into, the product type inside a medical specialty it has been assigned to, submission and approval dates, review type, plus generic and trade names of the device. Only approved applications will show up in the PMA database.

For the purpose of this paper the main question is: How can these data be used to assess entrepreneurship and innovation in high-risk MDs? What else do they tell?

**Measures of entrepreneurship**

The measures used in this study are entrepreneurial market entry (EME), defined as the first successful approval in high-risk MDs for an applicant firm; first order diversifying market entry (D1ME) in high-risk medical device segments, depicted by entry into a new medical specialty area by an existing applicant firm; and second order diversifying market entry (D2ME), when an existing applicant firm successfully gets approval for another product in the same medical specialty area but a different product type area. Even within EMEs one might assume a substantial proportion of diversification by firms originating from outside the high-risk MD sector. At this stage it has not been possible to identify firms which have been previously active in lower risk MD markets or other markets before entry into the high-risk MD sector. This analysis can only cover a few aspects of MD entrepreneurship. However, it contributes insights into the effects of structural barriers (e.g. the requirement for PMAs) to entry into the high-risk MD sector.
Measures of innovation

Measures for innovation include the supposedly big innovatory step each PMA application introduces to a medical specialty or product type market. PMA supplements accordingly involve the smaller, incremental changes to an already existing product. With these measurements it is possible to look at the product lifecycle and assess the level of innovatory activities from various comparative perspectives. For example, are medical specialty areas equally active in terms of product introduction and innovatory changes of products? Does increased activity by one firm within a product type market spark increased activity by competing firms?

HYPOTHESES

The discussion of different perspectives on entrepreneurship, innovation and the regulatory setting governing these activities and the resulting market structures in high-risk MDs, leads to several testable questions. The following simple hypotheses can be tested in a first attempt to gain insights into the potential the dataset provides for analysing entrepreneurial activities and market structures:

Hypothesis 1: Review times for foreign EMEs will be significantly longer than for US EMEs.

Hypothesis 2: Review times for EMEs will be significantly longer than for other market entries.

Hypothesis 3: The more original PMAs a firm has successfully submitted (approved original PMAs) the more PMA supplements there will be for these PMAs.

Hypothesis 4: Firms that diversify have significantly more PMA supplements approved (with faster review times) than firms that do not diversify.

Hypothesis 5: Diversification within medical specialty will be more prevalent than into other medical specialties. If firms diversify across medical specialties they will also diversify within medical specialties but across product sub-markets.

Hypothesis 6: The level of innovatory activity (PMA supplements) after a successful original PMA is significantly higher for US applicants compared to foreign applicants.

Hypothesis 7: Review times for foreign PMA supplements will be significantly longer than for US PMA supplements.
FINDINGS AND CONCLUSIONS

General findings
The dataset contains approximately 5600 observations of original PMA and PMA supplement applications submitted and approved over the years 1992 to 2007. Descriptive statistics show that only a few countries outside the US are active in high-risk MDs for the US market. These countries include Australia, Canada, Japan and a few European countries. The biggest foreign contributor to original PMA and PMA supplement applications is Germany.

Among the 456 original PMAs from 1992 to 2007 there are 207 EME cases where there had been no previous PMA by the same applicant since 1976 (the starting date of the PMA data collection at the FDA). It is, however, at this point unclear whether some of these first-time market entries into high-risk MDs are actually diversification by pre-existing companies from outside high-risk MDs (e.g. a medical device company which has been active in lower risk classes for some time and now enters the high-risk sector for the first time). The percentage of non-US PMAs each year fluctuates around a mean of roughly 21% with apparently no clear pattern. The yearly non-US contribution to PMA supplements is lower than the contribution to original PMAs (mean is approximately 12.5%). This indicates a lower level of innovatory activities which translate into change approvals for non-US MD firms.

There are about 300 companies which ‘own’ the PMA applications contained in the dataset. The distribution of PMA and PMA supplement applications as per firm ownership is quite skewed. There are only 35 companies which have successfully had more than two PMAs approved. The 18 companies which have submitted five or more original PMA applications are the originators of a third of all PMA applications and more than half of all PMA supplement applications. The four biggest contributors, namely Medtronic, Abbott, Boston Scientific and Guidant (now part of Boston Scientific) are responsible for 69 out of 456 PMAs (mostly in the cardiovascular products area) and a third of all PMA supplement applications (e.g. there are 880 PMA supplements for Medtronic alone).

There are 19 medical specialty areas (see Figure 2 for PMA numbers in medical specialties), with cardiovascular products providing the biggest contribution to original PMAs (31.8%). Within medical specialties the number of product type areas (sub-segments) points to quite different market structures. In cardiovascular products there are 41 product type areas with an average of over 3.5 original PMAs for each product type area over the time period 1992 to 2007, whereas medical specialties like anaesthesiology, pathology, physical medicine and clinical toxicology have only one or two product type areas with only one original PMA. In these latter medical specialties it seems that there would be little if any competition within high-risk MDs. However, there might be competition with products outside the definition of a high-risk MD, e.g. with pharmaceutical products.
While one might think that high-risk MD markets are not highly concentrated, these results point to relatively high market concentrations in product type markets. What needs to be considered in this context is the definition of what constitutes a market – e.g. determined by demand-side and supply-side substitution. What adds to the concentration is that often original PMAs will change ownership as firms merge or are being acquired by other firms. The dataset shows 164 ownership changes. There are 47 firms that have not submitted original PMAs but now own PMAs. The non-US contribution is smaller in all medical specialties but in ear, nose and throat devices.

**Hypotheses’ results**

The following provides some of the initial findings for the hypotheses put forward in this paper. This research is of exploratory nature. The discussion of the findings is therefore somewhat preliminary and speculative.

**Hypothesis 1**

A one-way ANOVA test indicates that there is a significant difference in review time for EME PMAs between US and non-US based applicants between 1992 and 2007, F(1,205)=5.47, p<.05. The actual means are as per the table below:

<table>
<thead>
<tr>
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<th>EME PMA cases</th>
<th>mean review time (days)</th>
<th>standard deviation (days)</th>
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<tbody>
<tr>
<td>non-US</td>
<td>51</td>
<td>553.27</td>
<td>333.74</td>
</tr>
<tr>
<td>US</td>
<td>156</td>
<td>437.53</td>
<td>297.47</td>
</tr>
<tr>
<td>total</td>
<td>207</td>
<td>466.04</td>
<td>310.02</td>
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On average it takes nearly four months longer for the FDA to review a first-time application by a foreign applicant. One way of explaining the difference in review time between non-US and US firms is that the FDA is cautious when there is an applicant it has not seen before and it is from a foreign country. This would then mean that there is either a positive expectation towards first-time US applicants or a negative bias against foreign first-time applicants, or both. Another reason may be that the process of providing all the information required to the FDA is quite complex and requires special expertise more easily available to US firms than foreign firms. For these reasons it could be true that foreign submissions are more difficult to assess.

Hypothesis 2
Tests within the non-US group show a significant difference in review time between initial market entries (EMEs) and diversifying market entries (D1MEs, D2MEs), the statistical values being F(1,93)=6.98, p<.05 (one-way ANOVA), as per the table below. The same test within the US group reveals no significant differences.

<table>
<thead>
<tr>
<th>Non US PMA cases</th>
<th>mean review time (days)</th>
<th>standard deviation (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMEs</td>
<td>51</td>
<td>553.27</td>
</tr>
<tr>
<td>D1MEs, D2MEs</td>
<td>44</td>
<td>406.23</td>
</tr>
<tr>
<td>total</td>
<td>95</td>
<td>485.17</td>
</tr>
</tbody>
</table>

The review could take longer because first time foreign applications (EMEs) are more difficult to review due to language issues or due to more sophisticated technologies being used. However, it could also be argued that language issues are not likely to be the cause for differences in review time. Within the non-US group no difference should be expected between first-time submissions and later submissions to the FDA, if an equal influence of language issues is assumed. A learning curve effect could be involved in that the applicants learn over time with more submissions to the regulator how to improve their submissions. It could further take some time to build a good reputation with the FDA.

Hypothesis 3
A bivariate correlation test (Pearson’s r) shows a significant, strong and positive relationship between the number of original PMAs and subsequent PMA supplements per applicant firm – r(300)=0.818, p<.001. If the analysis excludes the biggest firms and only focuses on firms with less than seven original PMAs the relationship is still reasonably strong – r(292)=0.651, p<0.001.

Hypothesis 4
Hypothesis 4 was analysed utilising a one-way ANOVA (does the fact that a firm diversifies predict the number of PMA supplements per original PMA?) with the results being non-significant. However, there is a dynamic element that has not been considered as yet. These hypotheses will have to be explored further in a time-series model.
Hypothesis 5
There is more diversification within medical specialties (174 cases) than across medical specialties (46 cases). A bivariate correlation test (Pearson’s r) shows a significant, reasonably strong and positive relationship between diversification across and within medical specialties, r(20)=0.509, p<0.05. These results point to the fact that firms that diversify across medical specialties also diversify into the niches one medical specialty provides (and the other way around).

Hypotheses 6
Due to the skewed distribution of PMAs and PMA supplements per firm and the within groups nature of the data (more than one PMA / PMA supplement for some firms) a hierarchical regression with categorical predictors was required. The applicant firm identifier was used as a control variable, testing whether the origin of the applicant firm (US, non-US) predicts significant differences in the number of PMA supplements per original PMA. The regression results show that the applicant firm’s country of origin does not predict the number of PMA supplements for PMA supplements.

Hypothesis 7
Again using the hierarchical regression approach, controlling for the applicant firm, the origin of the applicant is no significant predictor for review times for PMA supplements. This opens the question which other factors influence review times?

Possible future directions of research
What does this research tell about entrepreneurship and innovation in high-risk MDs? FDA approval data can be used to identify first-time market entries into high-risk MDs. At this stage, though, it has not been possible to determine how much ‘intrapreneurship’ and diversification from sectors outside high-risk MDs contribute to first-time market entries in original PMAs. It will be important to enrich the dataset with other input and output variables, such as firm-, and possibly product-level variables, R&D expenditures, R&D employee counts, RA employee counts, sales figures, unit prices, et cetera. Combining different measures poses additional problems, some of which have been mentioned earlier in this paper.

One important insight is that FDA data could potentially be used to assess market structures in high-risk MDs. The dataset can be analysed per medical specialty (this is decided by the advisory committee used to assess the PMA application) and by product type codes inside one medical specialty. This second step lends itself to a case study approach. For example a case study could broadly look at cardiovascular devices, and within these, focus on coronary stents.

Further analysis should be aimed at providing answers to questions like: Do R&D expenditures, R&D or RA employee inputs predict innovation outcomes (measured by successful approvals)? How concentrated are high-risk MD markets in terms of innovatory activities? Can innovatory activities?
predict later market shares? If yes, what is an appropriate time lag for such a prediction? Can a Herfindahl-like index be used for innovatory activities and does this index show similar concentration ratios for innovatory activities and time-lagged market share? Does innovatory activity by one firm in a market spark activities by the competing firms? Another angle of analysis is to evaluate first movers and followers in market entry. While there might be a relatively large number of EMEs among original PMA applications, the number of ‘true’ first movers into a completely new market should be limited.

The analysis of FDA approval data in high-risk MDs is a promising path for further insights into market structures and dynamics. The US market will provide an important benchmark against which to compare other geographic markets. Entrepreneurial and innovatory activities, and also market structures, can be identified and will be used in further studies as variables to test different models of market structures and dynamics.


FDA 2008a, *Code of Federal Regulation*, Title 21, Volume 8, Part 814, *Premarket Approval of Medical Devices*


Schumpeter JA 1943, *Capitalism, Socialism, Democracy*, 1966 reprint, Unwin University Books


