Inhalation products in emerging markets: Is it really any easier?

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Summary

There are numerous articles and publications (1) (2; 3) (4) which point to “emerging markets” offering significant potential for companies of all shapes and sizes. This theme has regularly been carried through in to discussions related to inhalation products. On the face of it to an organization with an established product or service the attraction of a significant un-met need/ population when coupled with a less tortuous regulatory pathway can’t be ignored. Equally for a company established in those markets where margins may be challenging, the attraction of “margin multiples growth” is a significant justification for investing for export growth. However as is often the case the reality of the situation in transfer in either direction is not that clear cut. Commercially developing a strategy for expanding current markets (in either direction (from or to a developed market)) makes sense, but any strategy has to consider many factors, some of which are easy to quantify some are less tangible and therefore more challenging. Many companies with a manufacturing base in these emerging markets have developed their technical and quality systems to a point at which they believe they can compete globally, however the constantly changing regulatory expectations in some markets can sometimes produce un-wanted surprises. This presentation seeks by use of example and reference to give an overview of the types of considerations which need to be made and how these can impact on planning and strategy.

Introduction

In considering Inhalation products in emerging markets, it is critical to define the scope of any discussion. The various listings (International Monetary Fund, Dow Jones list, Emerging Markets Index etc.) typically list 20 to 30 countries based on primarily financial metrics. For the consideration of the opportunities and challenges facing inhalation products, it may be far more appropriate to consider markets where there are (or potentially will be) domestically manufactured inhalation products. By considering these markets it is possible to consider the following

- Entering this market
- Exporting from this market

Discussion

Few people would argue that “emerging Markets” represent an attractive commercial opportunity, if the number of articles and presentations are to be believed. Currently it is estimated that the G7 (Canada, USA, France, Germany, Italy, Japan, and the UK) group of countries/ economies account for some 46% of the global GDP, while only containing 10.5% of the global population. To many these countries would also represent probably the most developed in respect of inhalation drug delivery products. Often the argument for the opportunities in emerging markets is simplified to a population distribution model. If the G7 countries account for around 10% of the global population then the less developed market contains some 6.4 billion people. However the inter-related factors of income and incidence of respiratory disease can-not be ignored.

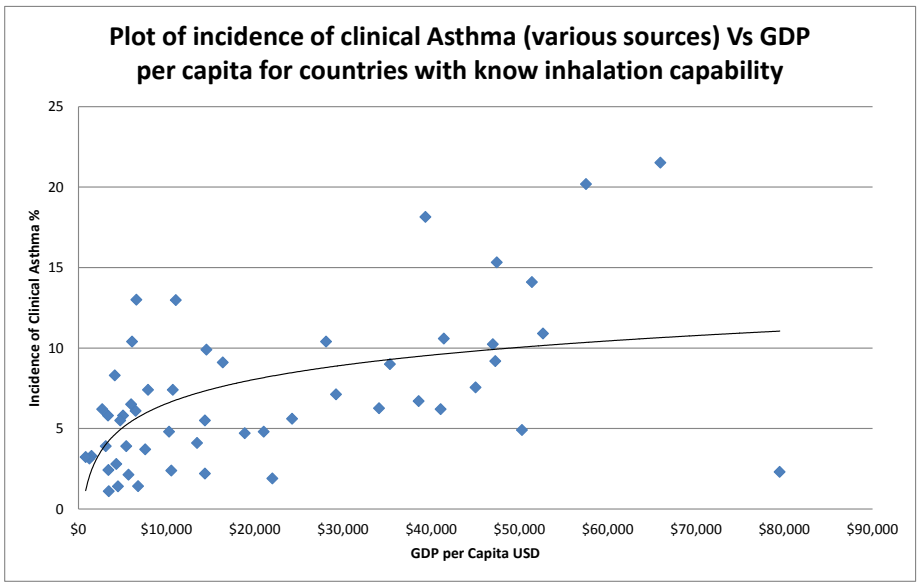

Figure 1 Plot of incidence of clinical Asthma Vs GDP per Capita for countries with inhalation product activity.

To provide a reliable platform for decision making, the consideration of inhalation products in emerging markets needs to consider many factors, not least of which is which markets should we consider as emerging. If the typical financial criteria, for the definition of an emerging market is used, a number of territories best described as pre-emergent from the perspective of inhalation products be included. While at the same time markets where there is an established or developing inhalation manufacturing and/ or development capability may be excluded. Equally some countries considered as "no longer emerging" Russia and China for example (both top ten economies based on GDP) have significantly under-developed inhalation markets when the potential patient population is considered. An alternate approach may be to try to consider countries that either currently have, or plan to have a domestic inhalation product capability (manufacture and or development). Further if the various aspects of a specific market are considered, it becomes clear that it is very difficult to develop definitive "cut-points" which would allow the classifications "developed", "emerging" and "pre-emergent" to be easily applied. By considering specific examples it is possible to develop a better understanding of the progression from a naïve to developed inhalation market and the resultant challenge in inter-market operation.

Countries with known or developing Inhalation product manufacture			
Algeria	Egypt	Japan	Singapore
Argentina	Finland	Jordan	South Africa
Australia	France	Malaysia	Spain
Bangladesh	Germany	Mexico	Sweden
Belarus	Greece	Netherlands	Switzerland
Bosnia and Herzegovin	Guatemala	Pakistan	Syria
Brazil	Hong Kong	Peru	Thailand
Canada	India	Philippines	Tunisia
China	Indonesia	Poland	Turkey
Colombia	Iran	Portugal	Ukraine
Cuba	Ireland	Puerto Rico	United Kingdom
Czech Republic	Israel	Russia	United States
Ecuador	Italy	Saudi Arabia	Uruguay
			Venezuela

Figure 2 Table of countries with established or potentially developing inhalation product activity. The shaded countries typically are not considered as emerging economies.

The above table is not exhaustive and based on the knowledge and experience of the author, therefore there may be other countries which should have been added to this list. As opposed to listing countries where inhalation products are sold, the table seeks to capture countries where inhalation products are either currently developed or manufactured or where interest/ activity exists in developing such products.

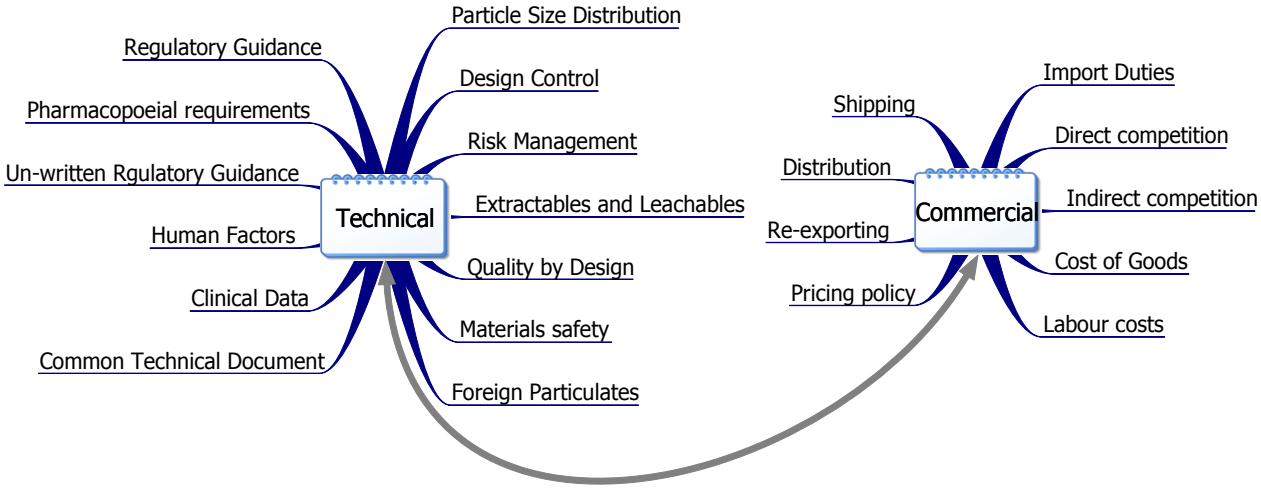

Figure 3 Mind map of some of the potential considerations in "alternate" market entry

Clearly as indicated in the mind map above there are numerous factors to be weighed and considered when looking at entry in to a new market. For example for an organization that has successfully registered an inhalation product in the USA, it is probable that they will have made significant investments in developing, justifying and validating some form of routine extractables control procedure. The costs of these routine controls are typically absorbed in the overall cost of goods (CoG). If the same product is considered for a market, where currently demonstration of extractables control is not a requirement, creating a "two-tier" approach to product quality may not be practical, in which case this additional burden on CoG will potentially impact on the competitiveness of the offering when compared to locally produced products. There are considerations in the reverse direction also, in many less regulated markets Inhalation product development has been viewed as "dynamic" resulting in very short durations to market, simply put design it, make-it, if it works sell-it, if there's an issue "tweak" it. With the publication in 2013 of the FDA Final Rule Current Good Manufacturing Practice Requirements for Combination Products **(5)**, the requirement to demonstrate appropriate design control in the development of the device element of an inhalation combination products became mandatory for the US. In such dynamic product development environments the evidence of "appropriate" levels of control on aspects such as material selection, risk mitigation, determination of design space and design verification, may be very difficult to produce. Other evolving initiatives such as FDAs "Human Factors and Medical Devices" **(6) (7)**and Quality by Design **(8) (9) (10) (11)** will also place requirements on inhalation products developed in a less evolved market, potentially after the products were developed and commercialised.

The examples above tend to indicate a binary difference between markets, however this is far from the case, by considering specific areas of inter-market differences across multiple territories, it may be observed that for many factors there is an "evolutionary scale" present, ranging from extremely low requirements to extremely demanding ones. Global opportunities certainly do exist, however the key to success is developing a clear understanding of the challenges and the implementing appropriate plans to close gaps which may have been identified.

In addition to the more tangible factors reflected in figure 3 above, often cultural, political and geographic factors can play a secondary role in amplifying the importance of a particular factor, beyond that which would have normally been anticipated. One example is the impact that health and safety policy (equipment guards) could potentially have on output efficiency, in less regulated countries where requirements may be lower, the combination of lower labour rates combined with greater output efficiency, may significantly reduce CoG. For a company manufacturing in a more regulated territory, to import in to this market with less stringent requirements, the local manufacturer has a potential commercial advantage. Often associated with a less demanding Health and Safety environment is a less well developed understanding of risk management, both in respect of the product and the end user. As with design control remedial implementation programmes are possible, but are both challenging and carry an element of project risk.

Commercially developing a strategy for expanding current markets (in either direction (from or to a developed market)) makes sense, but any strategy has to consider many factors, some of which are easy to quantify some are less tangible and therefore more challenging.

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