Cost of Current Industry-Based Device Evaluation

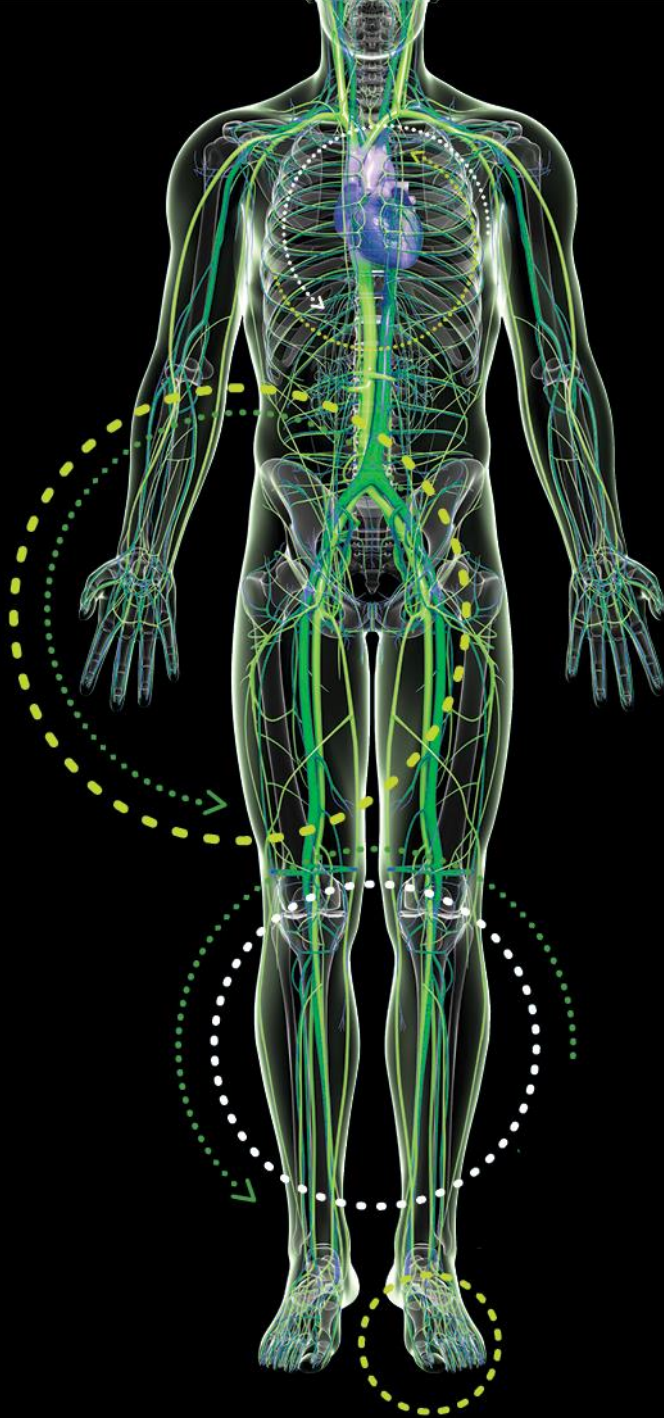Brad J. Martinsen, Ph.D.
Director of Scientific Affairs, Clinical
Cardiovascular Systems, Inc. (St. Paul, MN)

Medical Device Epidemiology Network

MDEpiNet

Registry Assessment of Peripheral Interventional Devices (RAPID)
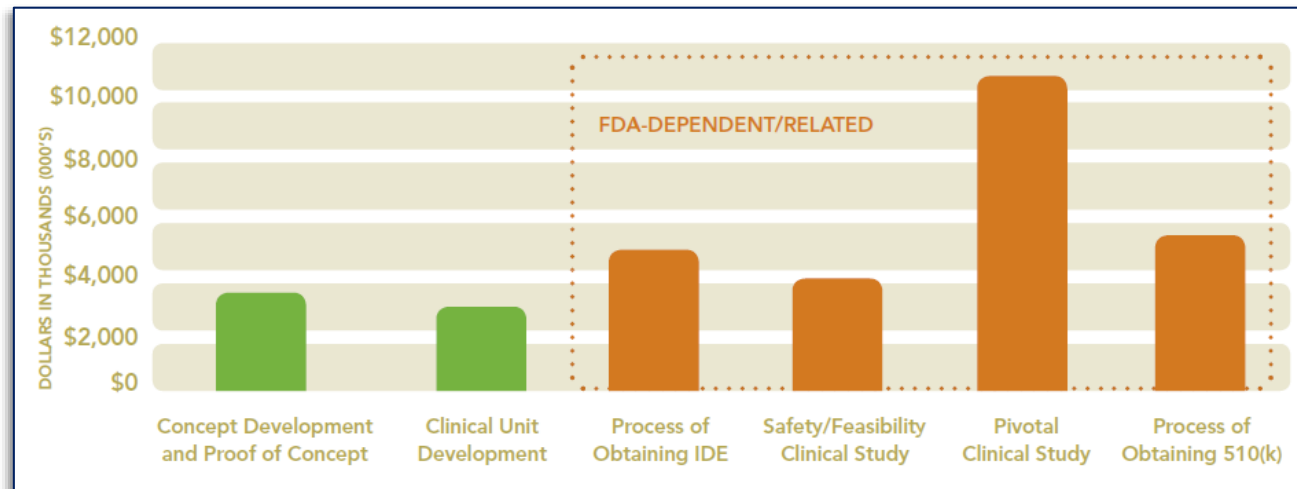Phase II/III Working Group Meeting

5.25.17

Cost and Time of Device Clearance/Approval

How Much Does a 510(k) Device Cost?

- The average cost to bring a low-to-moderate 510(k) product from concept to market is **$31 million**.

- More than 77% of that, **$24 million**, is spent on FDA-dependent or related activities.[1-2]

1. Makower et. al. FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies. November 2010
2. http://www.mddionline.com/blog/devicetalk/how-much-does-510k-device-cost-about-24-million

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Cost and Time of Device Clearance/Approval

How Much Does a PMA Device Cost?

- High-risk PMA costs averaged **$94 million**, with **$75 million** spent on FDA-linked stages.

- Average of **4.5 yrs** from first contact with FDA to device approval.[1-2]
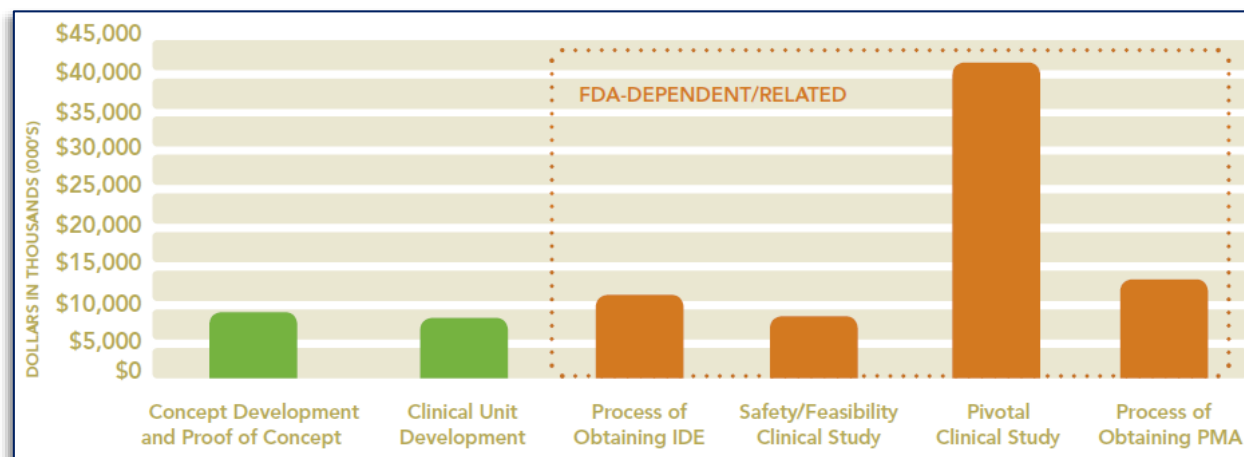
1. Makower et. al. FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies.   November 2010
2. http://www.mddionline.com/blog/devicetalk/how-much-does-510k-device-cost-about-24-million

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Medical Device Trial Cost

Estimated Cost of a Medical Device Trial?

- Estimated cost of medical device clinical trials to support approval by the FDA, ranges from **$1 million to $10 million** or more.

Medical Device Trial Cost

- The **cost of clinical trials** for manufacturers of pharmaceuticals, biologics, and medical devices, as well as for public health investigators, **continues to escalate.**

- In pharmaceuticals (where this trend has been best documented), the costs have increased **7.4 percent annually** over inflation for the last 20 years

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Impact of Location on Trial Cost (OUS vs US)

Impact of Study Location on Cost?

- A clinical study conducted **outside the U.S.** can result in **savings of 30% to 50% or more**, compared to the cost of corresponding research in the U.S.

- Thus, the use of foreign clinical data can produce meaningful savings.

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Impact of Location on Trial Cost (OUS vs US)

- At present, it is estimated that more than **half** of all clinical trials are conducted **outside the U.S.**

- Between 2004 and 2009, the amount of U.S.-based clinical trials listed on ClinicalTrials.gov **decreased from 78.7% to 45%**.

- U.S.-based clinical trials for **medical technology** products, specifically, **dropped from 86.9% to 44.8%** during the same period.

1. Hogan 2015. How Will Conducting A Medical Device Clinical Trial Outside The U.S. Impact Your FDA Approval? From https://www.meddeviceonline.com/doc/how-will-conducting-a-medical-device-clinical-trial-outside-the-u-s-impact-your-fda-approval-0001
2. Ubl 2010. Testimony before the Senate Commerce Subcommittee on Competitiveness, Innovation, and Export Promotion June 22, 2010

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Trial/Study Costs—Peripheral Experience

- Peripheral endovascular core-lab adjudicated registry study (1200 subjects):
  ~$7-10 million

- BTK RCT (50 subjects):
  ~$650,000

- ATK RCT (50 subjects):
  ~$550,000

- Single ARM ATK with IVUS Imaging (26 subjects):
  ~$300,000

Study Design, Costs, and Resulting Study Limitations

❖ Traditional time-to-event endpoints in peripheral studies can be difficult to power due to the high number of subjects needed for sufficient sensitivity to detect statistical significance.[1]

❖ Such high number of subjects is cost prohibitive, resulting small and underpowered studies.

Table II. Sample size calculations for the traditional time-to-event analysis of the amputation free survival end point

Traditional time-to-event: major amputation or death*	Total sample size for scenario 1 (large effect)*	Total sample size for scenario 2 (medium effect)†	Total sample size for scenario 3 (small effect)‡
80% Power	702	1106	4502
90% Power	940	1482	6026

* Assuming a 39% 1-year rate of death or major amputation for the control group, and an event rate of 29% for the new therapy.
† Assuming a 39% 1-year rate of death or major amputation for the control group, and an event rate of 31% for the new therapy.
‡ Assuming a 39% 1-year rate of death or major amputation for the control group, and an event rate of 35% for the new therapy. Assumes a 1:1 randomization ratio, a two-sided type I error rate of 0.05, and that all subjects are followed for no more than one year. Calculations were performed in nQuery Advisor 6.0. For the time to death end point under scenarios 1 and 2, the required sample sizes are 2186 and 2926 for 80% and 90% power, respectively. For the time to death end point under scenario 3, the required sample sizes are 6242 and 8356 for 80% and 90% power, respectively.

1. Subherwal, et. al. Use of alternative methodologies for evaluation of composite end points in trials of therapies for critical limb ischemia. AHJ, Sept 2012.

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Study Design, Costs, and Resulting Study Limitations

❖ Thus, consistent terminology and endpoint definitions, as well as more efficient data collection methods for peripheral medical devices are needed.

❖ Global Rank Method and RAPID could solve this issue.

Ranking	End point
1	Death
2	Major amputation
3	Minor amputation
4	Incomplete healing
5	Complete healing with pain
6	Complete pain resolution

1

Table IV. Power calculations using global rank method

Global rank power calculations*	Total sample size (scenario 1: large effect)	Total sample size (scenario 2: medium effect)	Total sample size (scenario 3: small effect)
80% Power	466	651	3182
90% Power	622	870	4258

*Based on event rates listed in Table II. The sample sizes are estimated using the formulas of Tang.[34]

1. Subherwal, et. al. Use of alternative methodologies for evaluation of composite end points in trials of therapies for critical limb ischemia. AHJ, Sept 2012.

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Costs and Resulting Limitations
Peripheral Experience

❖ The balance of study design, timelines, and costs are major considerations for the following studies—many of which are cost prohibitive to complete:

- OAS optimization—evaluation in sub-populations

- OAS utilization in conjunction with emerging technologies, such as DCB, BVS, DES

- OAS expanded indication

- Atherectomy device comparisons

Potential Benefits of RAPID—Conclusions

❖ Would enhance the quality and efficiency of device evaluation at all stages (feasibility, pivotal, and post-market), allowing for rapid iteration of devices at a lower cost.

❖ Enable a cost efficient method for gaining expanded indication of devices.

❖ Standardize definitions/endpoints to enhance poolability of data.

❖ Cost efficient method to compare a new device to standard of care.

❖ Establish best practices for the use of a device in sub-populations or different sub-specialties.

❖ Lower cost for long term follow-up which can be cost prohibitive for most studies.