Blood Contacting Device Testing without the "Bloodhound"

2021 America's Got Regulatory Science Talent Student Competition

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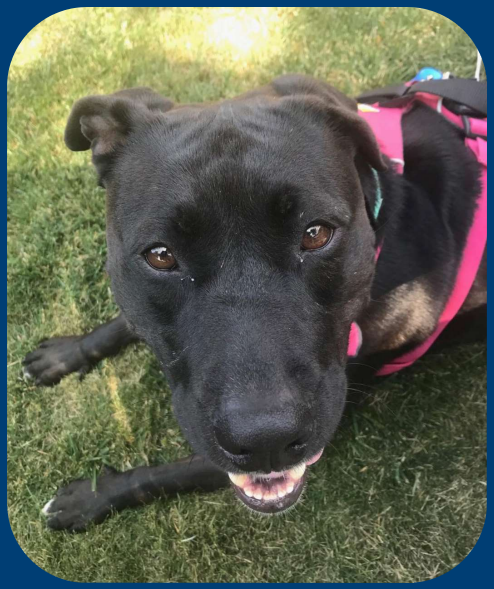


UNIVERSITY of ROCHESTER

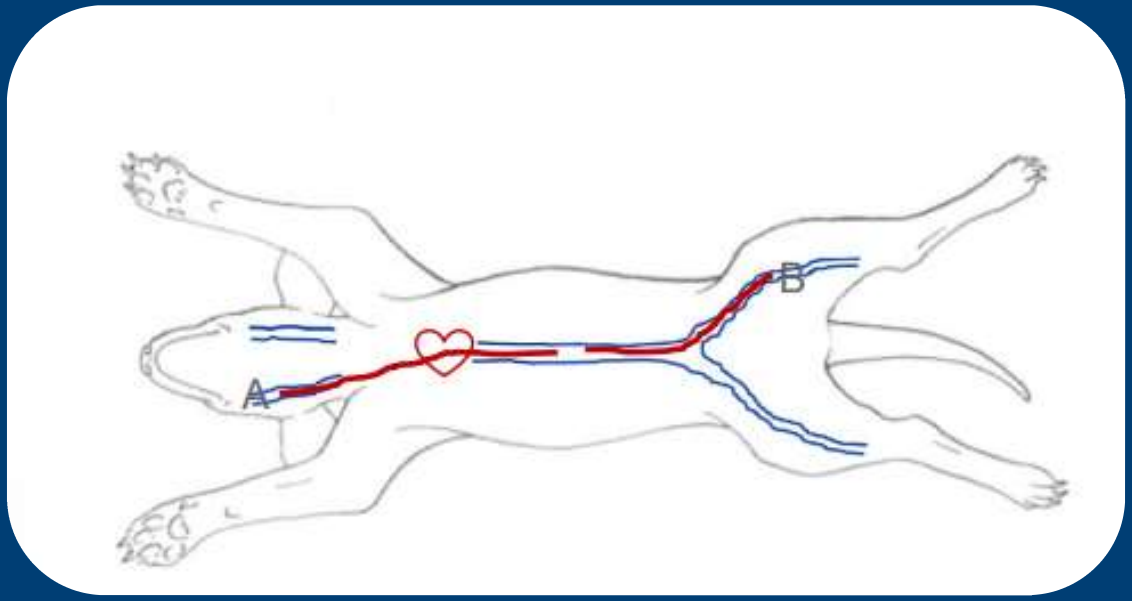
FDA Scientific Priority Area of Focus:
Section 1. Modernize Toxicology to Enhance Product Safety: Strategic Plan for Regulatory Science

1. **Develop better models of human adverse response:**
    1. Evaluate and promote the use of cell and tissue-based assays that more accurately represent human susceptibility to adverse reactions

60,000 Dogs per Year

Tan, Shen Wu, 2019. FDA Under Pressure to End Drug Research on Animals, Starting with Dogs. Available at: https://www.washingtontimes.com/news/2019/oct/29/fda-urged-end-dog-use-drug-testing/#:~:text=FDA%20under%20pressure%20to%20end%20drug%20research%20on,of%20the%20United%20States.%20%28Associated%20Press%2FFile%29%20more%20%3E. Accessed May 18, 2021.

Current Method of Thrombogenicity Testing



- First developed in 1976
- Non-anticoagulated venous implant model (NAVI) Test
- External communicating blood contacting devices, blood contacting implant devices
  - Cardiovascular stents

Fda.gov. 2021. *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" Guidance for Industry and Food and Drug Administration Staff*. [online] Available at: <https://www.fda.gov/media/85865/download> [Accessed 2 March 2021].

Problem with Current Thrombogenicity Method

- Limited test advancements made in past 45 years
- Poor metrics and statistical accuracy

> *"More clinically relevant and/or reliable methods of thromboresistance evaluation are needed."* (FDA, 2014)

John, M., 2021. *The FDA Perspective on Thrombogenicity Testing of Coronary Interventional Devices: Insights From the Large Animal Testing*. [online] Fda.gov. Available at: <https://www.fda.gov/media/88365/download> [Accessed 2 March 2021].

Alternative *In Vitro* Method

- *In vitro* blood flow assay
  - Pulsatile flow
  - Controlled wall shear stress
  - Human blood
  - Introduce and monitor heparin anticoagulant

Staff, M., 2021. *Animal tests: This new assay could reduce the need for them*. [online] Medical Design and Outsourcing. Available at: <https://www.medicaldesignandoutsourcing.com/new-assay-reduce-animal-tests/> [Accessed 2 March 2021].

Validation for *In Vitro M*ethod

- Tested alongside *in vivo* canine models
  - Same or better results on thrombogenicity evaluation

- Utilize FDA Guidance Document for validation plan
- Increase statistical analytics capability

Fda.gov. 2011. *Guidance for IndustryProcess Validation: General Principles and Practices* . [online] Available at: <https://www.fda.gov/media/71021/download> [Accessed 2 March 2021].

Fda.gov. 2021. *Methods, Method Verification and Validation*. [online] Available at: <https://www.fda.gov/media/73920/download> [Accessed 2 March 2021].

Benefits of *In Vitro* Model

- Greater Statistical Accuracy
- Eliminate Canine Death
- FDA Priority Area
- Cost Effective

References

Engels, G., Blok, S. and van Oeveren, W., 2016. In vitro blood flow model with physiological wall shear stress for hemocompatibility testing—An example of coronary stent testing. *Biointerphases*, 11(3), p.031004.

Fda.gov. 2011. *Guidance for IndustryProcess Validation: General Principles and Practices* . [online] Available at: <https://www.fda.gov/media/71021/download> [Accessed 2 March 2021].

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Wolf, M., 2021. *Thrombogenciity Testing in the 21st Century: Time for Alternative Strategies for Medical Devices?*. [online] Fda.gov. Available at: <https://www.fda.gov/files/medical%20devices/published/Presentation--Thrombogenicity-Testing-in-the-21st-Century--Time-for-Alternative-Strategies-for-Medical-Devices-.pdf> [Accessed 2 March 2021].

Questions?

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