IN VIVO LONG-TERM DURABILITY OF MATERIALS THAT COMPRISE IMPLANTED MEDICAL DEVICES

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Further, Together

MODERNIZING THE REGULATIONS FOR TODAY'S IMPLANT DURATION
RECENT PUBLICATION

ACS Macro Letters

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Longevity Expectations for Polymers in Medical Devices Demand New Approaches to Evaluating Their Biostability

K. A. Chaffin*

Cite This: *ACS Macro Lett.* 2020, 9, 1793−1798 Read Online

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ABSTRACT: Ten years after a new poly(dimethylsiloxane)urethane material was introduced as part of a long-term medical device implant, an unexpectedly high rate of in-service degradation was observed. The chemical signatures of molecular degradation in the materials were not identified during the comparatively short preclinical assessment of biostability. This outcome highlights the need to transform the assessment of biostability for new materials used in long-term implanted medical devices to protocols that rely more heavily on accelerated in vitro testing. The industry has over-relied on in vivo exposure to assess the stability of a material due to the perceived complexities associated with the accurate simulation of the biological environment. Strategically designed accelerated in vitro testing can provide important insights into the long-term biostability of materials: insights that cannot be readily gleaned through the in vivo studies that dominate current regulatory guidelines. Real-time validation of previously published accelerated data combined with clinical observations substantiates the accelerated approach and creates a compelling case for shifting the emphases in biostability assessment, especially for devices that have anticipated lifespans that exceed a decade.

- Regulatory guidance for the introduction of new materials into the long-term implantable space is outdated.
- Accelerated testing must be incorporated
- Real time validation of a hydrolytic accelerated test.

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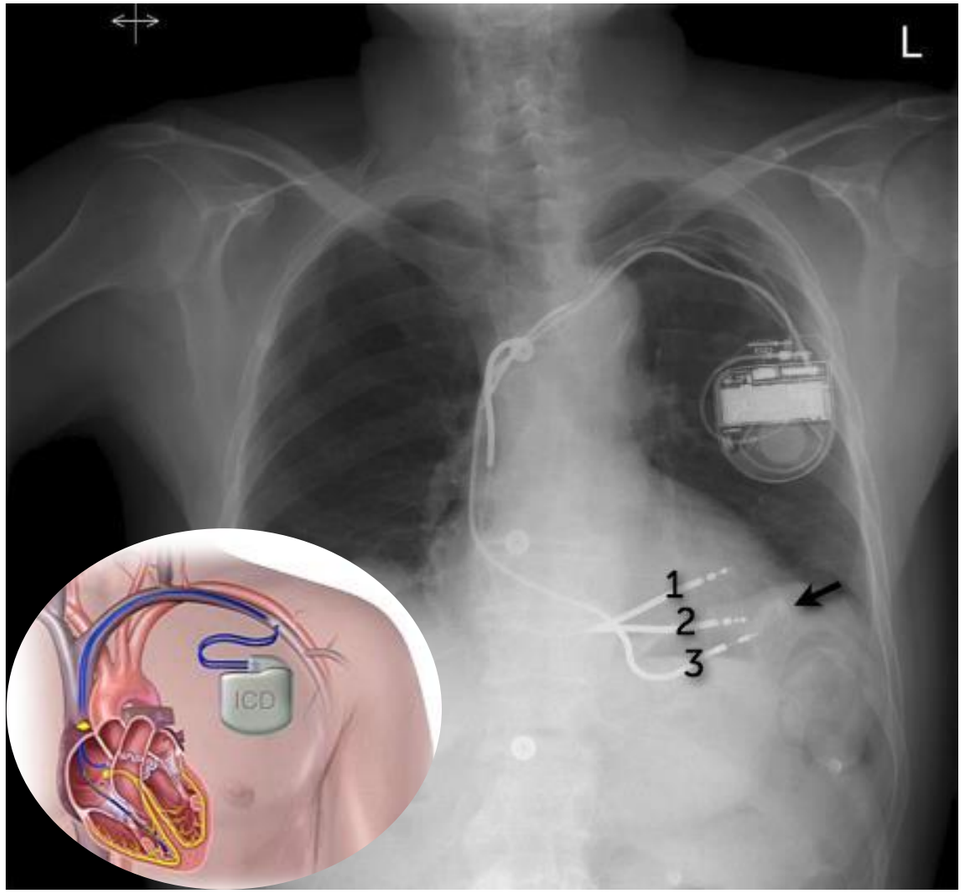
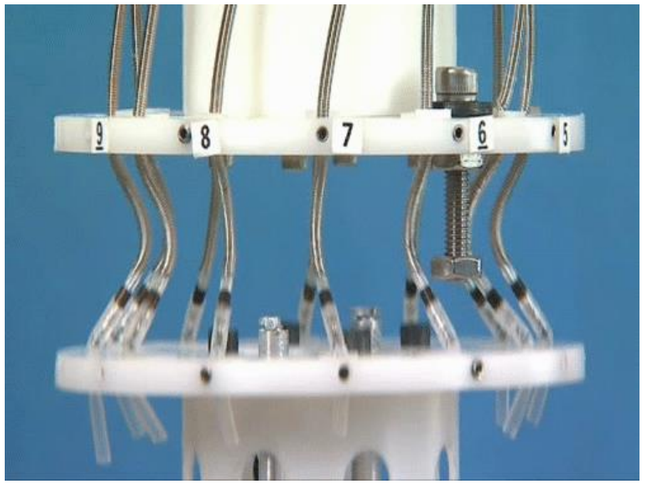
MANY MEDTRONIC PRODUCTS ARE IMPLANTED IN THE BODY FOR YEARS

CONSTANT MECHANICAL AND CHEMICAL ASSAULT





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EACH MATERIAL HAS A UNIQUE FAILURE MODE
ASSESSING THE TRADE OFF

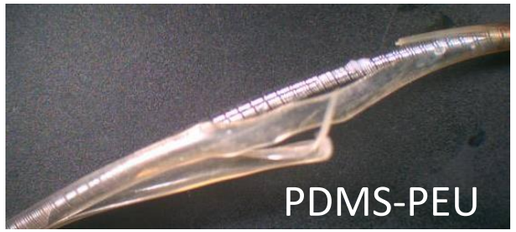
| Silicone
(Mechanical Failure)

- Chemical susceptibility to HYDROLYSIS
  - Ea = 120 kJ/mole
  - Bulk Reaction
- Low abrasion resistance
- Low tear resistance

| Poly(ether)urethane
(Superficial Oxidation)

- Chemical susceptibility to OXIDATION
  - Ea = 125 kJ/mole
  - Superficial Reaction
- High abrasion resistance
- High tear resistance

| PDMS-PU
(Hydrolysis)



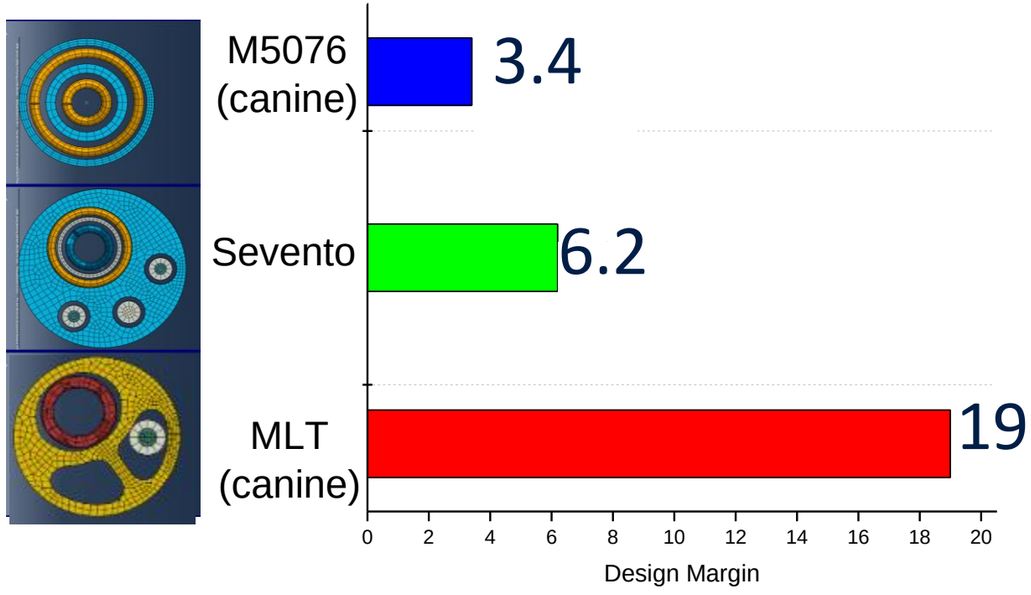
- Chemical susceptibility to HYDROLYSIS
  - Ea = 30 kJ/mole
  - Bulk Reaction
- Medium abrasion resistance at time=0
- Medium tear resistance at time=0

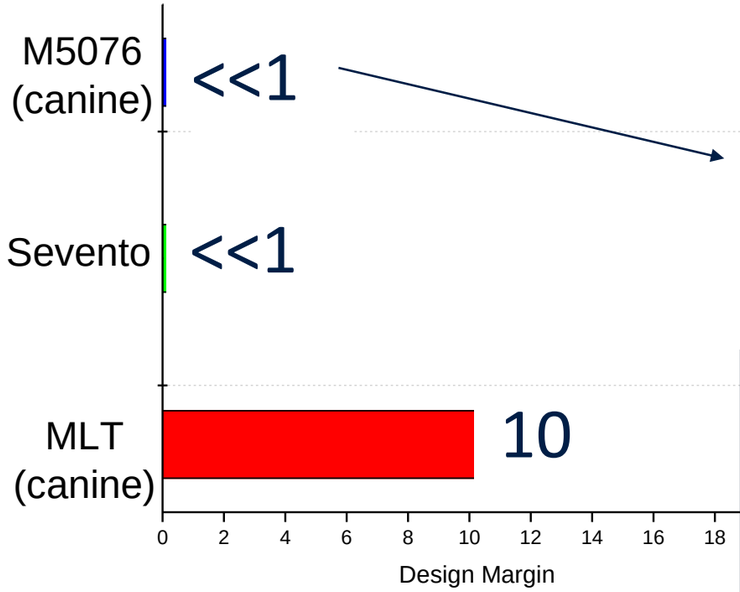
PREDICTING THE DURABILITY OF A DESIGN

PREDICTIVE ENGINEERING SCIENCE IS CRITICAL TO OUR SUCCESS

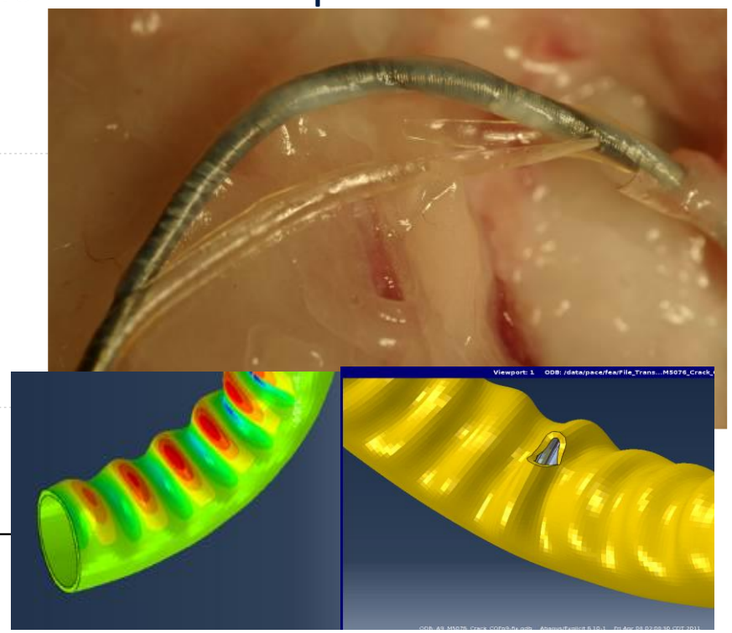
Accelerated Chemical Testing + Mechanical Testing + Modeling & Simulation → Reliability Prediction

Calculated Safety Factors*





5 year canine validated predictions



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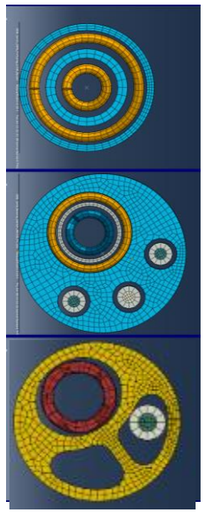
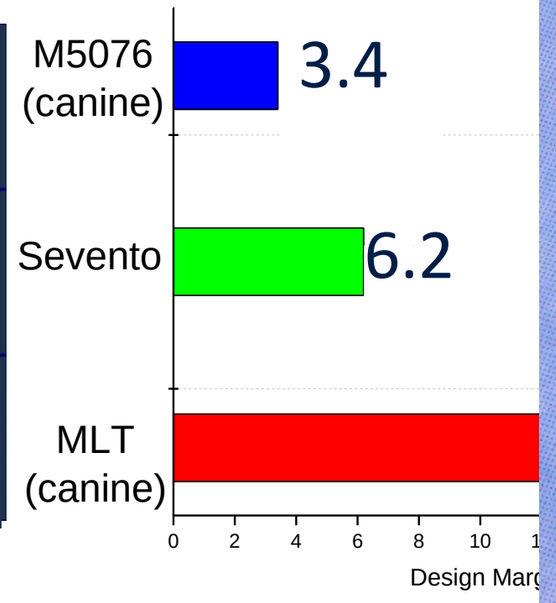
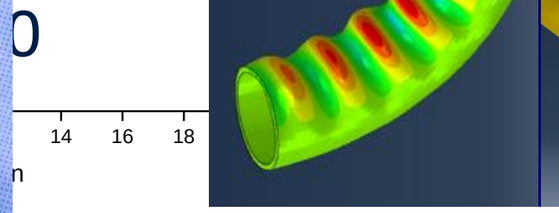
Calcul

Initial Material Properties





es at 5 years



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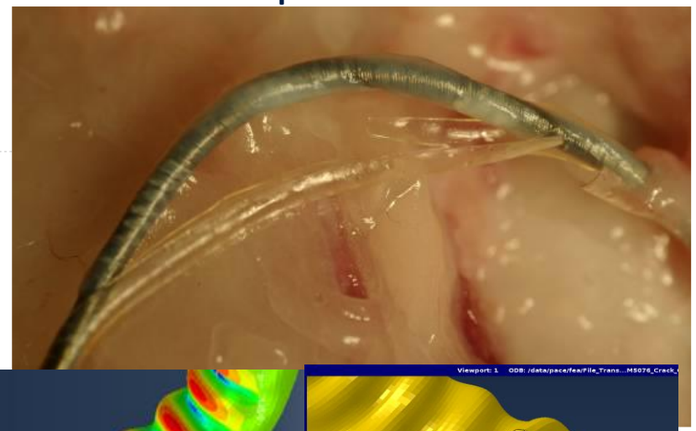

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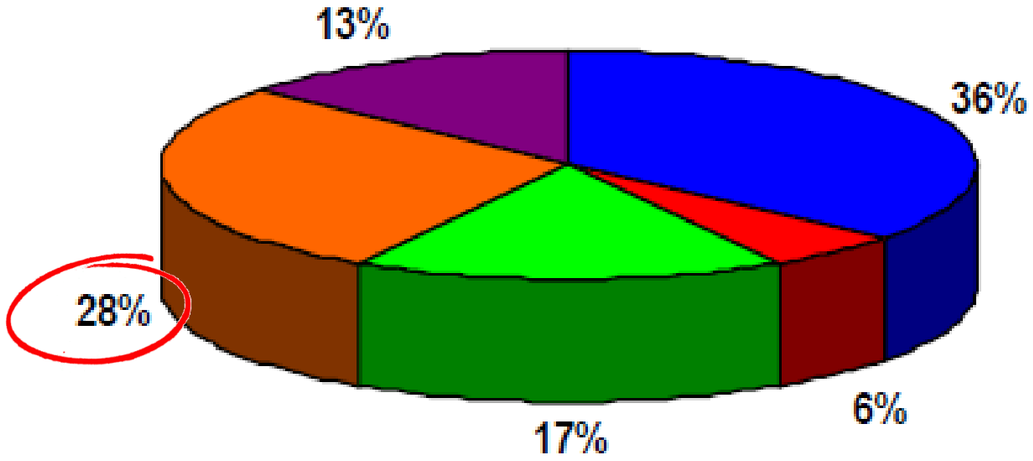
WHY DO MEDICAL DEVICES FAIL?
2/3 OF MATERIALS FAILURES ARE POLYMERS

Material failure is responsible for **~40 percent** of all FDA recalls on medical devices. **January 16, 2018**

FDA Analysis of Primary Recall Cause FY 2010-FY 2012



When considering the cases where materials have been cited as the secondary cause of recall, then materials are implicated in over **50%** of all medical device recalls!

Most Common Reasons For Materials Failure

- Materials Selection /Design
- **In-service Degradation**
- Raw Material contamination
- Manufacturing incompatibility

References:

1..http://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cdrh/cdrhtransparency/ucm388442.pdf

2. https://www.mddionline.com/materials/mitigating-risks-materials-failures-medical-devices

3. http://exclusive.multibriefs.com/content/4-causes-of-failure-for-medical-devices/engineering

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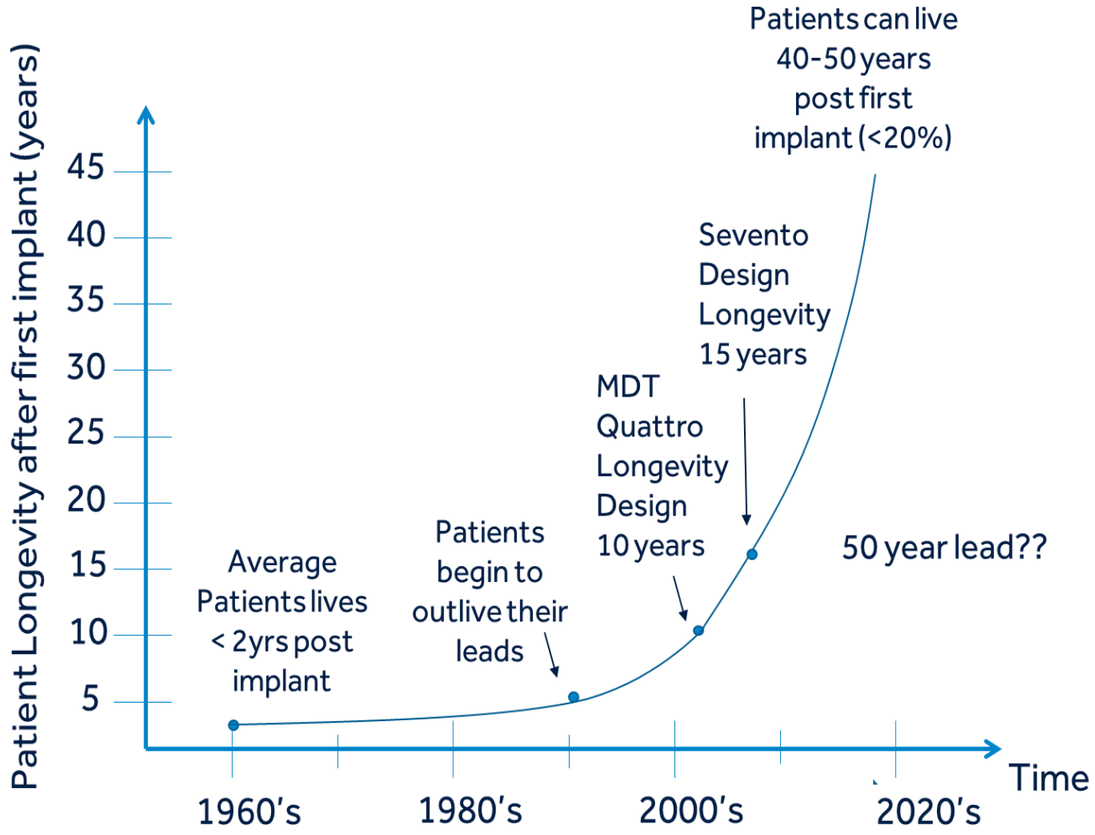
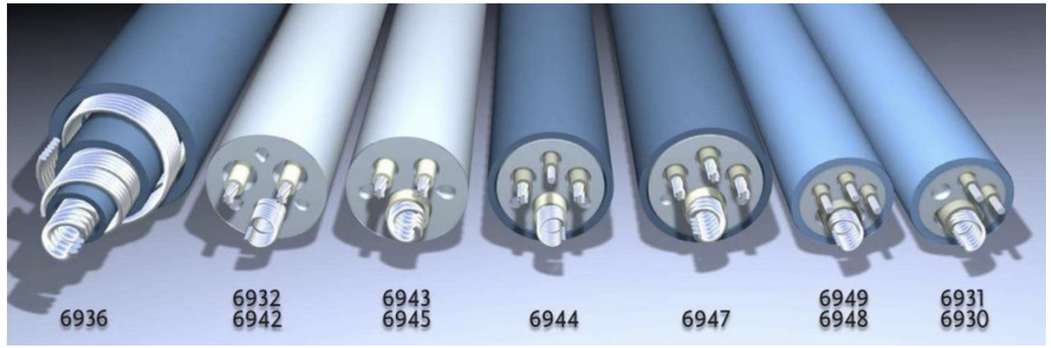
MATERIALS ARE BEING PUSHED TO THEIR LIMITS
EXPANDED LONGEVITY AND CONTINUED MINIATURIZATION

1 | Earlier diagnosis and modern therapies



2 | Miniaturization pushes material to limits



10 Fr (3.3 mm diameter) ⟶ 6.6 Fr (2.2 mm diameter)

We need materials that perform better than Poly(ether)urethane (94% at 14 yrs)

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WHAT IS BIOSTABILITY?
NOT TO BE CONFUSED WITH BIOCOMPATIBILITY

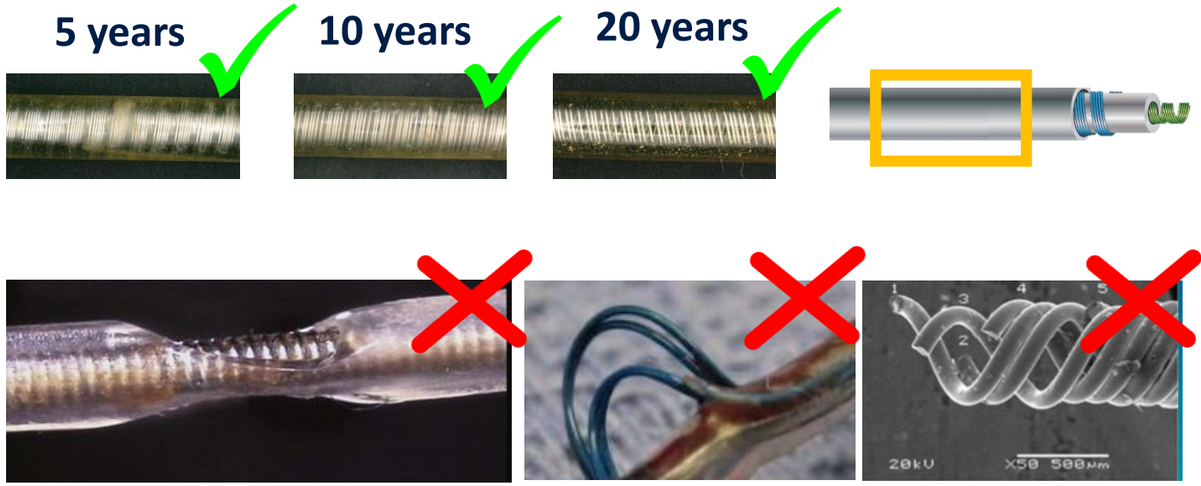
| Biostable:

‘To be resistant to the effects of the biological environment.’

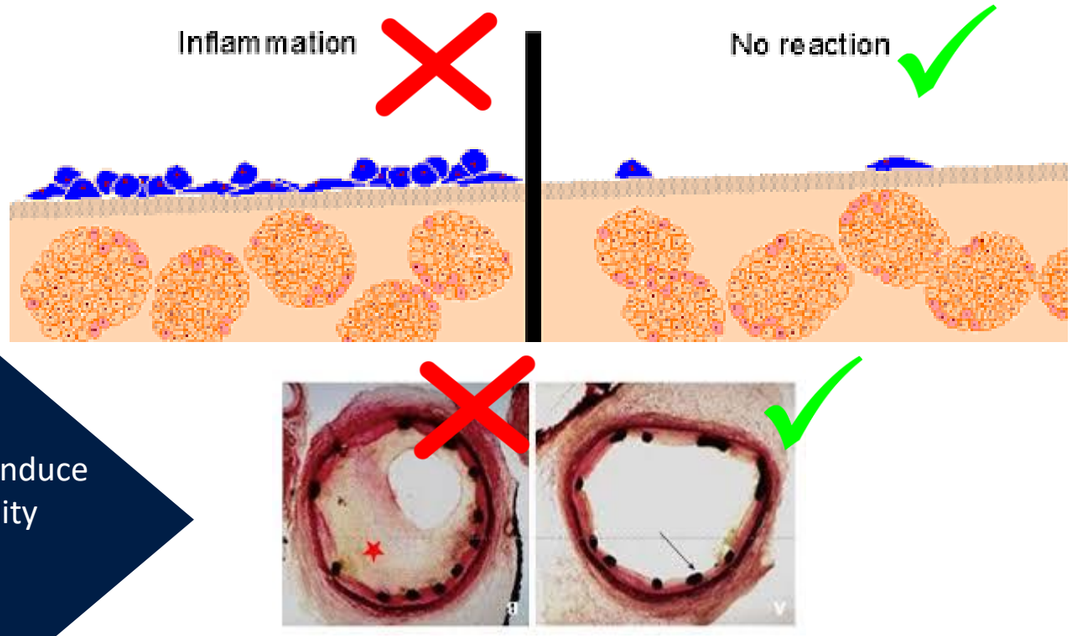
| Biocompatible:

‘The ability of a material to perform with an appropriate host response’

in vivo human exposure of cardiac lead



Changes can induce biocompatibility challenges



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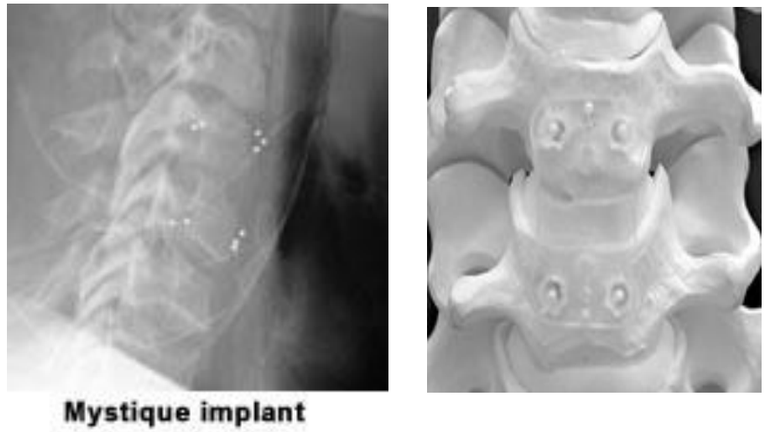
MOLECULAR WEIGHT AND PROPERTIES

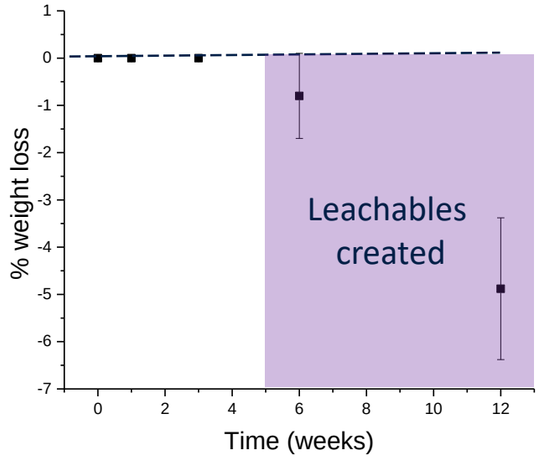
RESORBABLE POLYMERS TEACH US ABOUT THE RELATIONSHIP BETWEEN MECHANICAL PROPERTIES AND MOLAR MASS LOSS (REACTIONS PER CHAIN)

Polylactide Degradation



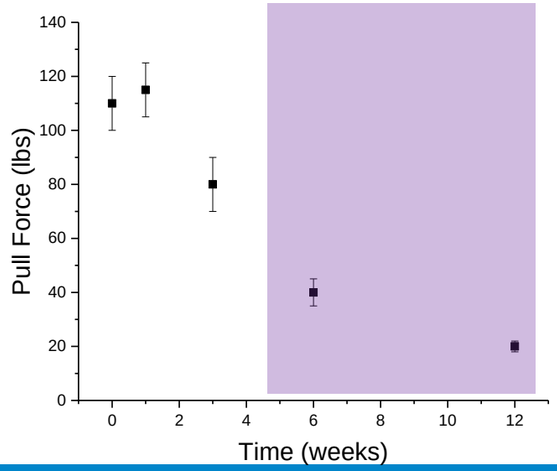
The MYSTIQUE Plate was made of HYDROSORB® PLDLA co-polymer. This co-polymer consists of 70 percent Poly (L-lactide) and 30 percent Poly (D,L-lactide).

Mass loss

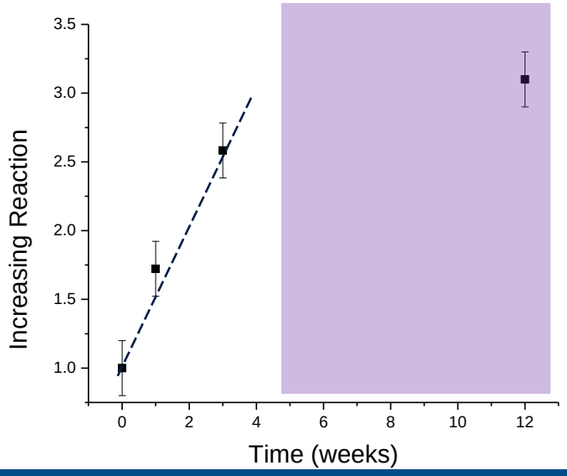


The mechanical properties were reduced by 50% (and the molar mass by >2.5 x) before leachables were created From the degradation reaction

Strength Loss



Number of reactions per polymer chair



Ref: Brkaric, *et al. J Spinal Disord Tech 2007 (20) 248-254.*

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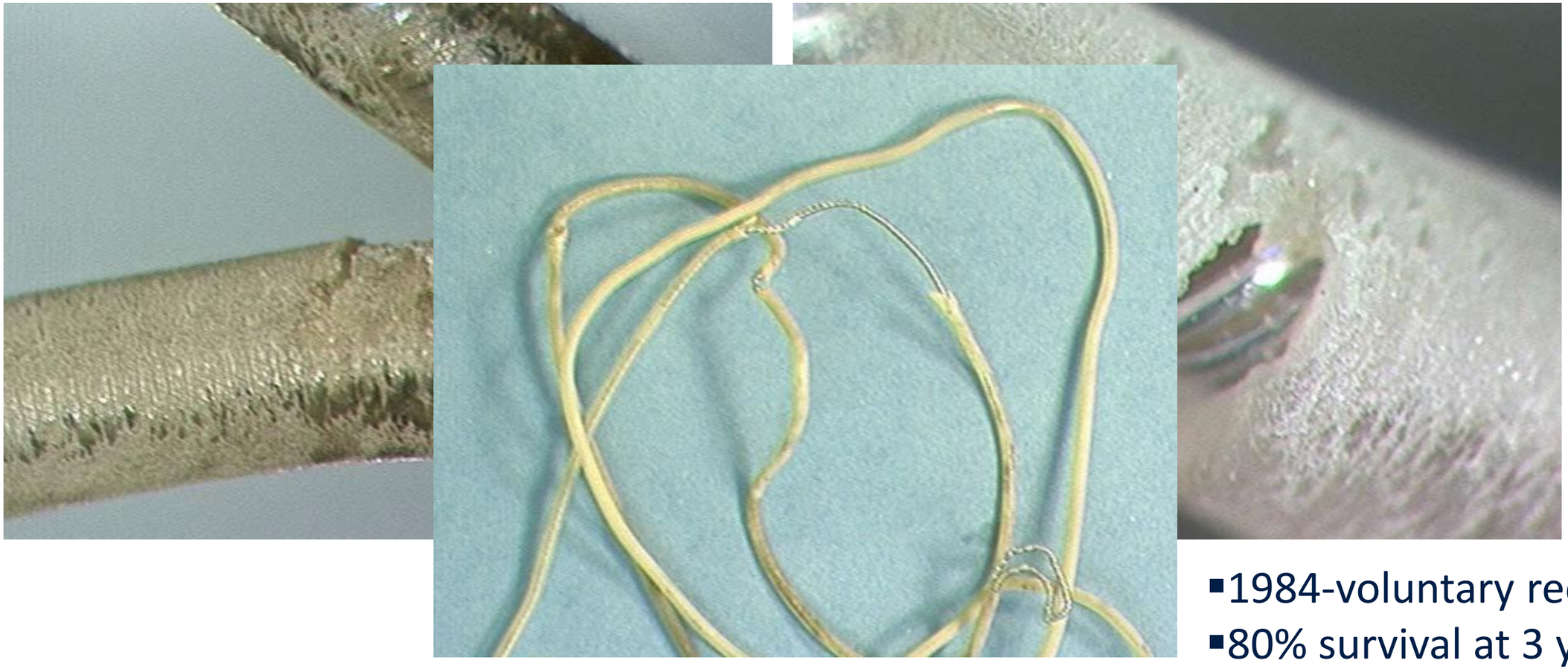
MEDTRONIC'S MOST CONSEQUENTIAL LEAD RECALL
ENVIRONMENTAL STRESS CRACKING AND METAL INDUCED OXIDATION



- 1984-voluntary recall
- 80% survival at 3 years end of life
- 30,123 leads
- Company size: $750 M annual revenue

https://urldefense.com/v3/__https://www.annalsthoracicsurgery.org/article/S0003-4975(10)62864-0/pdf__;!!NFcUtLLUcw!Drry0xN4vMi-PS5RJjo4tzl5dx82yfxmO1tRstaQmUx07anwvr2B0_aIFICyxvH1yM4U$

https://urldefense.com/v3/__https://www.gao.gov/assets/220/216942.pdf__;!!NFcUtLLUcw!BWNL_IT6eSM6-M1ofwJPcyKZJTrXnamRt82G10Me3W5B400YxP90p-m0AlDshu-mxCYf$

WE ESTABLISHED TESTING WITH THE GOAL OF PREVENTING BIOSTABILITY FAILURE

A FAILURE ANYWHERE IN THE INDUSTRY IS OUR CONCERN

Article

Human plasma α_2-macroglobulin promotes *in vitro* oxidative stress cracking of pellethane 2363-80A: *In vivo* and cor

Q. H.
Urbar

Articles

The in vivo auto-oxidation of p by

Kenr
Page

Article

Glass Wool–H_2O_2/$CoCl_2$ test sy biodegradative stress cracking

Qinghong Z

Stokes, K., Urbanski, P. and Cobi
Cracking and Metal Catalyzed Oxi
Polyuretl

Ten-Year Experienc
Insulation

10 Ans D'Expérience D'Électro

Guidance for Industry

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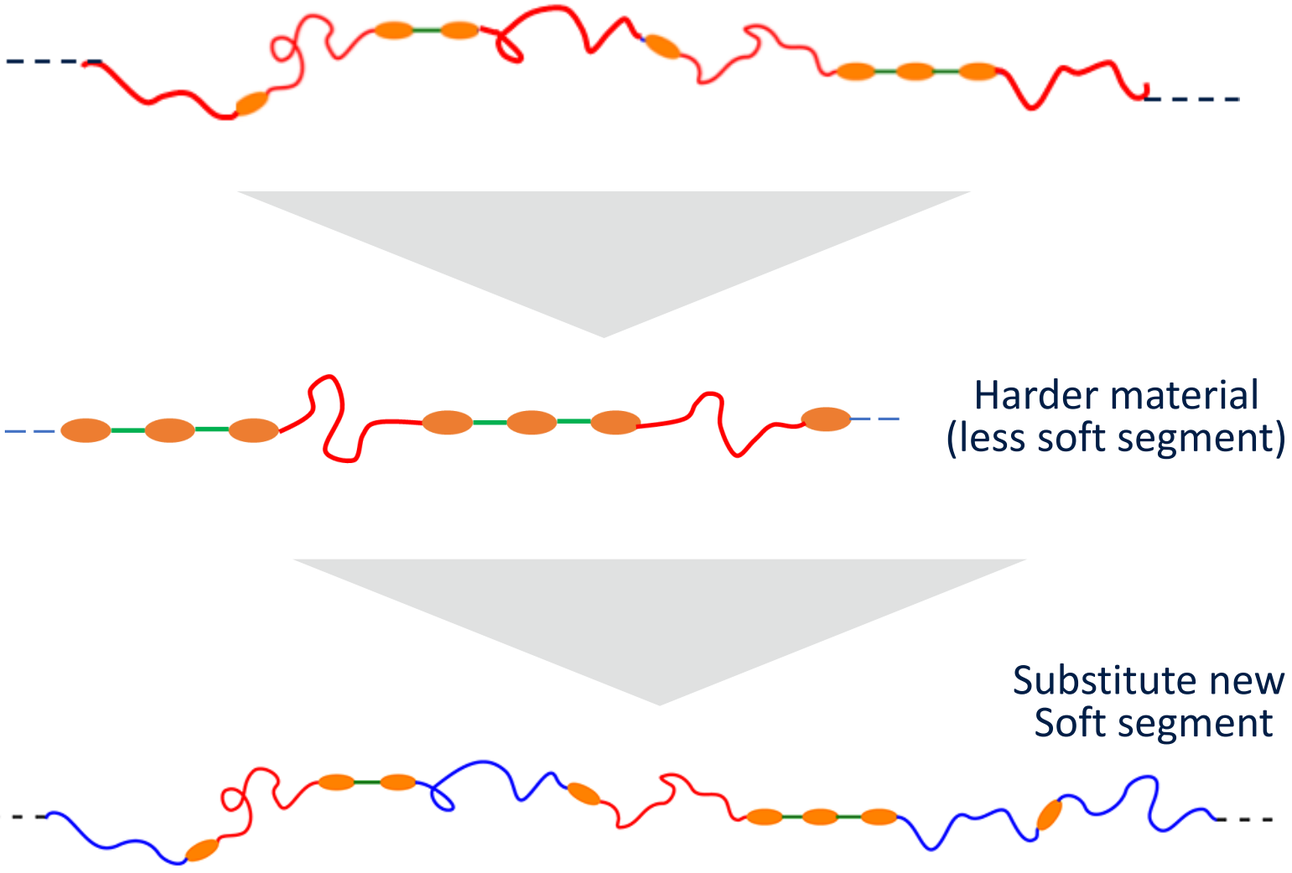
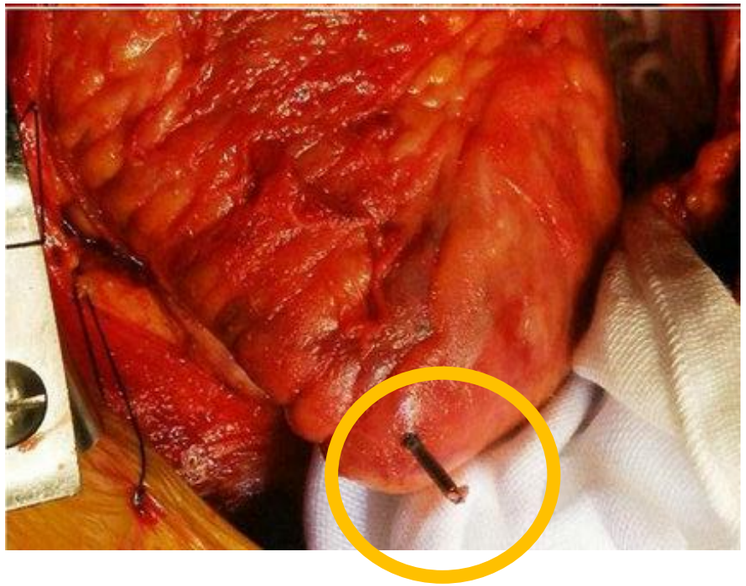
NEW PRIMARY LEAD INSULATION MATERIALS
DRIVE TOWARD NEW SOFT MATERIALS TO SUPPORT MINIATURIZATION

The Soft Segments (red) were responsible for degradation





PDMS-URETHANES
COPOLYMER PERFORMANCE IS NOT ADDITIVE

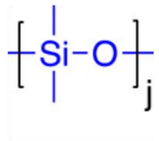
Silicone
- Flexibility
- Biostability

Polyurethane
- Lubricity
- Durability

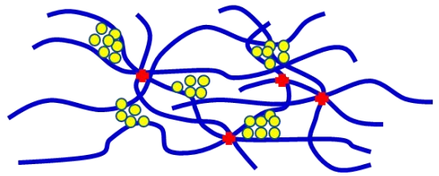
50x the abrasion Resistance of silicone!

PMDS-Urethane: Poly(ether) urethane with some of the soft segment substituted out and replaced with PDMS

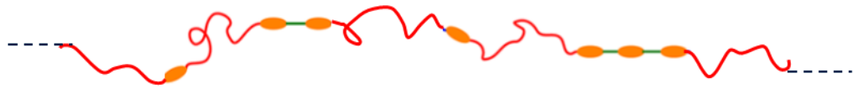
Silicone



Cross Linker



Poly(ether)urethane (PEU)



What does the regulatory guidance say about testing this material's suitability??

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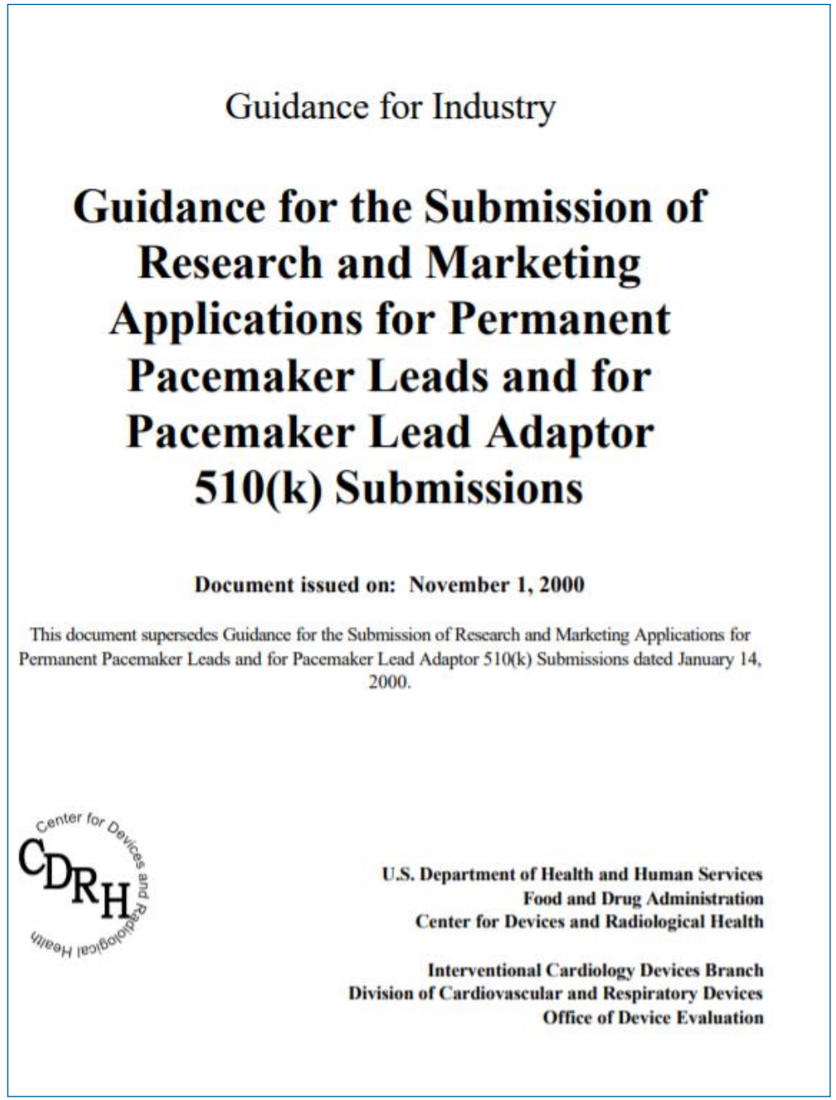
STANDARDS GUIDING NEW MATERIAL INTRODUCTION



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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Interventional Cardiology Devices Branch
Division of Cardiovascular and Respiratory Devices
Office of Device Evaluation

Authored 2000

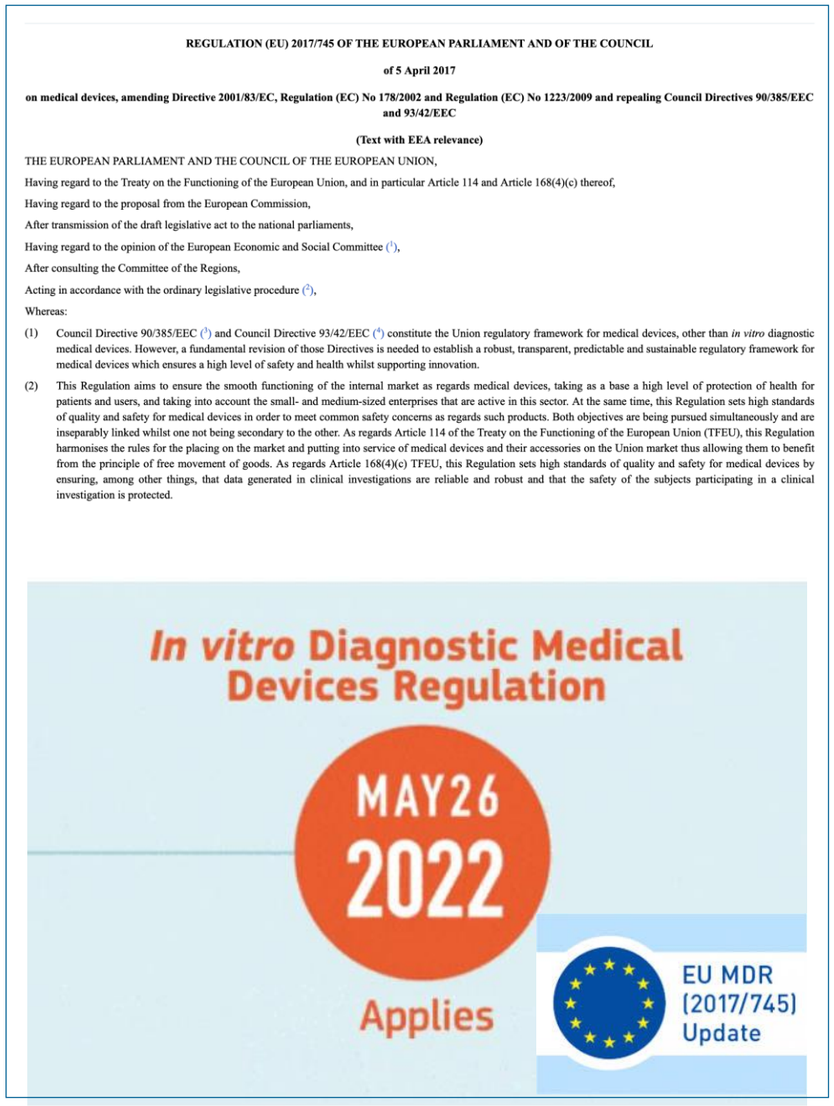
American National Standard

ANSI/AAMI/ISO 10993-13:2010

Biological evaluation of medical devices — Part 13: Identification and quantification of degradation products from polymeric medical devices

AAMI
Association for the Advancement of Medical Instrumentation

Authored 2010



REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 5 April 2017

on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 and Article 168(4)(c) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee (1),

After consulting the Committee of the Regions,

Acting in accordance with the ordinary legislative procedure (2),

Whereas:

(1) Council Directive 90/385/EEC (3) and Council Directive 93/42/EEC (4) constitute the Union regulatory framework for medical devices, other than *in vitro* diagnostic medical devices. However, a fundamental revision of those Directives is needed to establish a robust, transparent, predictable and sustainable regulatory framework for medical devices which ensures a high level of safety and health whilst supporting innovation.

(2) This Regulation aims to ensure the smooth functioning of the internal market as regards medical devices, taking as a base a high level of protection of health for patients and users, and taking into account the small- and medium-sized enterprises that are active in this sector. At the same time, this Regulation sets high standards of quality and safety for medical devices in order to meet common safety concerns as regards such products. Both objectives are being pursued simultaneously and are inseparably linked whilst one not being secondary to the other. As regards Article 114 of the Treaty on the Functioning of the European Union (TFEU), this Regulation harmonises the rules for the placing on the market and putting into service of medical devices and their accessories on the Union market thus allowing them to benefit from the principle of free movement of goods. As regards Article 168(4)(c) TFEU, this Regulation sets high standards of quality and safety for medical devices by ensuring, among other things, that data generated in clinical investigations are reliable and robust and that the safety of the subjects participating in a clinical investigation is protected.

In vitro Diagnostic Medical Devices Regulation

MAY26 2022 Applies

EU MDR (2017/745) Update

Authored 2017

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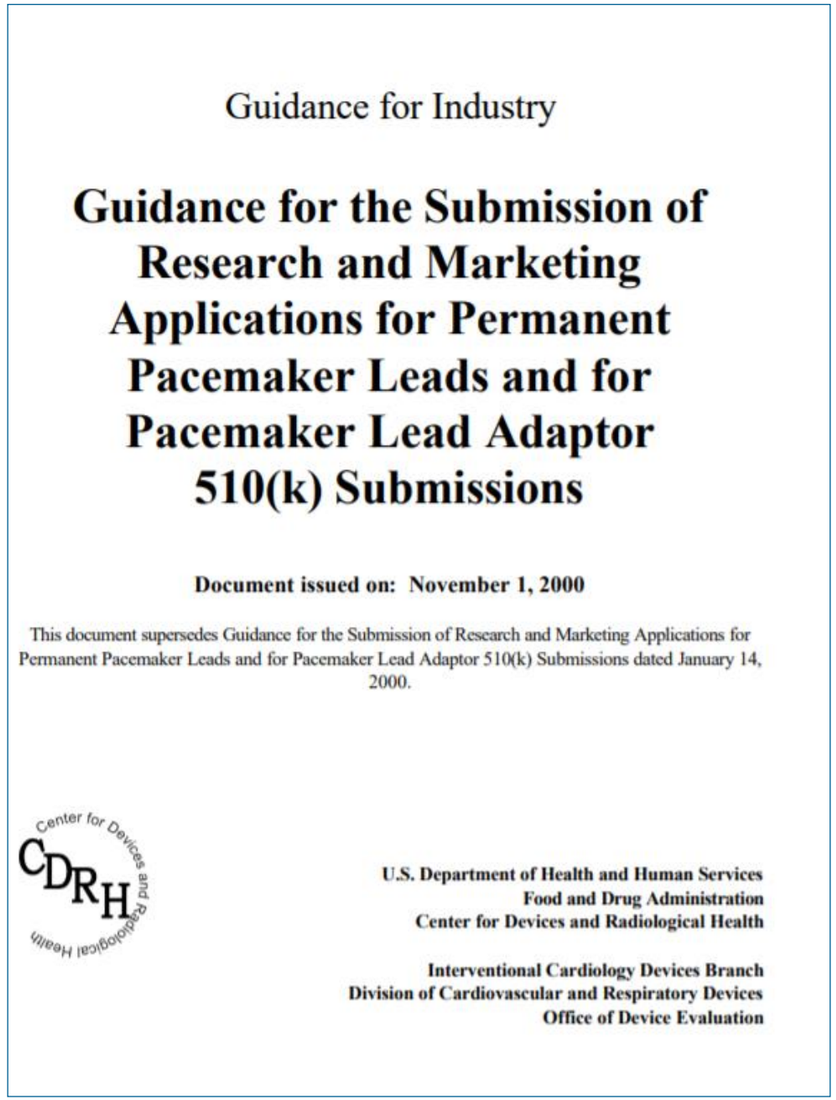

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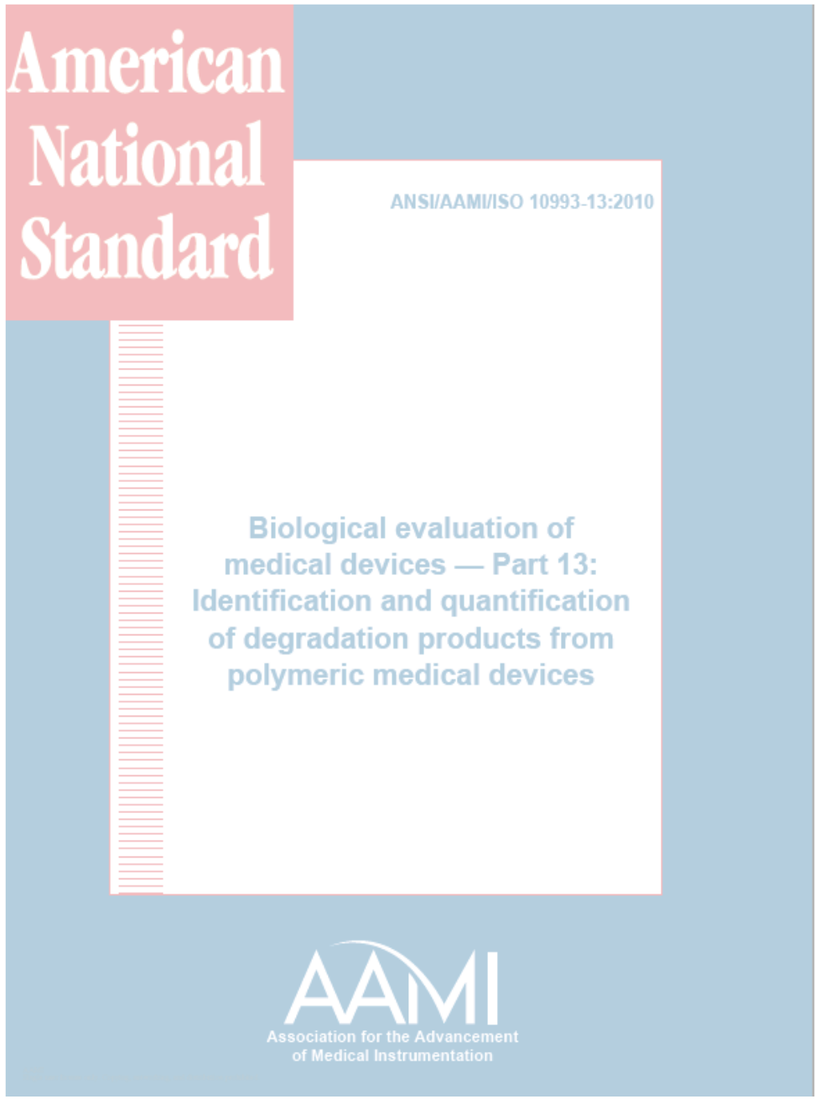

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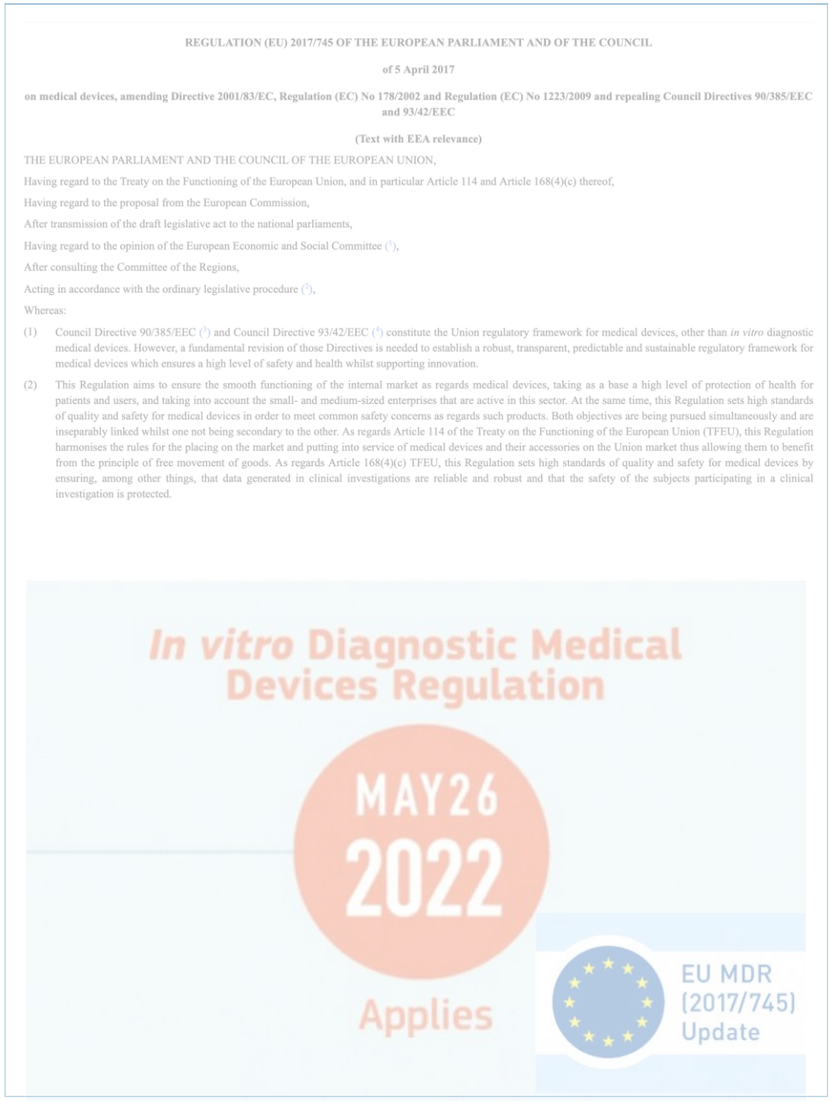

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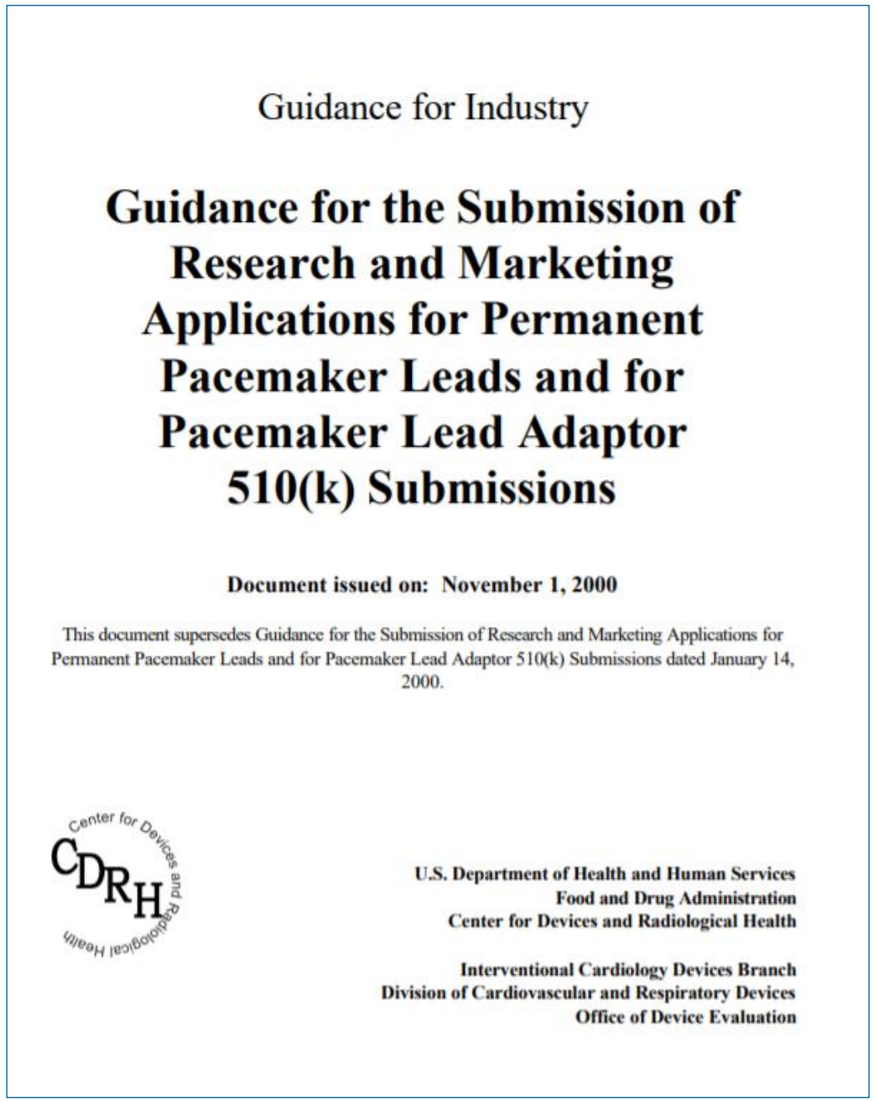
GUIDANCE FOR LEADS IS BASED ON POLY(ETHER)URETHANE PREDICATE



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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Interventional Cardiology Devices Branch
Division of Cardiovascular and Respiratory Devices
Office of Device Evaluation

Case 1:
Pellethane® 2363-Equivalent Pacemaker System with alternate vendors to Pellethane

No ***In Vitro*** Work Required

Case 2:
Polyurethane Components Replacement Protocol to characterize new polyurethane materials

In Vitro Work Required

Option A: Implant leads in animal hearts to obtain data on 20 leads at the end of 2 two years ·

Option B: Implant leads in animal hearts with intent of obtaining data on 20 leads after six months · AND Accelerated Testing – ESC and MIO testing

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STANDARDS GUIDING NEW MATERIAL INTRODUCTION

Guidance for Industry

Guidance for the Submission of Research and Marketing Applications for Permanent Pacemaker Leads and for Pacemaker Lead Adaptor 510(k) Submissions

Document issued on: November 1, 2000

This document supersedes Guidance for the Submission of Research and Marketing Applications for Permanent Pacemaker Leads and for Pacemaker Lead Adaptor 510(k) Submissions dated January 14, 2000.

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Interventional Cardiology Devices Branch
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Office of Device Evaluation

Authored 2000

American National Standard

ANSI/AAMI/ISO 10993-13:2010

Biological evaluation of medical devices — Part 13: Identification and quantification of degradation products from polymeric medical devices

AAMI
Association for the Advancement of Medical Instrumentation

Authored 2010

REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 5 April 2017

on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 and Article 168(4)(c) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee (1),

After consulting the Committee of the Regions,

Acting in accordance with the ordinary legislative procedure (2),

Whereas:

(1) Council Directive 90/385/EEC (3) and Council Directive 93/42/EEC (4) constitute the Union regulatory framework for medical devices, other than *in vitro* diagnostic medical devices. However, a fundamental revision of those Directives is needed to establish a robust, transparent, predictable and sustainable regulatory framework for medical devices which ensures a high level of safety and health whilst supporting innovation.

(2) This Regulation aims to ensure the smooth functioning of the internal market as regards medical devices, taking as a base a high level of protection of health for patients and users, and taking into account the small- and medium-sized enterprises that are active in this sector. At the same time, this Regulation sets high standards of quality and safety for medical devices in order to meet common safety concerns as regards such products. Both objectives are being pursued simultaneously and are inseparably linked whilst one not being secondary to the other. As regards Article 114 of the Treaty on the Functioning of the European Union (TFEU), this Regulation harmonises the rules for the placing on the market and putting into service of medical devices and their accessories on the Union market thus allowing them to benefit from the principle of free movement of goods. As regards Article 168(4)(c) TFEU, this Regulation sets high standards of quality and safety for medical devices by ensuring, among other things, that data generated in clinical investigations are reliable and robust and that the safety of the subjects participating in a clinical investigation is protected.

***In vitro* Diagnostic Medical Devices Regulation**

MAY26 2022 Applies

EU MDR (2017/745) Update

Authored 2017

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EVALUATION PERFORMED TO THE CURRENT STANDARDS

Biological evaluation of medical devices — Part 13: Identification and quantification of degradation products from polymeric medical devices

Real Time Test Duration = 12 months

Accelerated conditions: 70 °C for 60 days

4.1.1 Test design

In accordance with ISO 10993-9, degradation tests shall be used to generate, identify and/or quantify degradation products. If degradation is observed in an accelerated test, identification and quantification of the degradation products can provide sufficient information for risk analysis. If identification and quantification of degradation products from the accelerated test do not provide sufficient information for the risk analysis, real-time testing shall be performed. The sequence of steps that shall be followed is described in detail in this part of ISO 10993.

The FDA does NOT recognize this part of the standard

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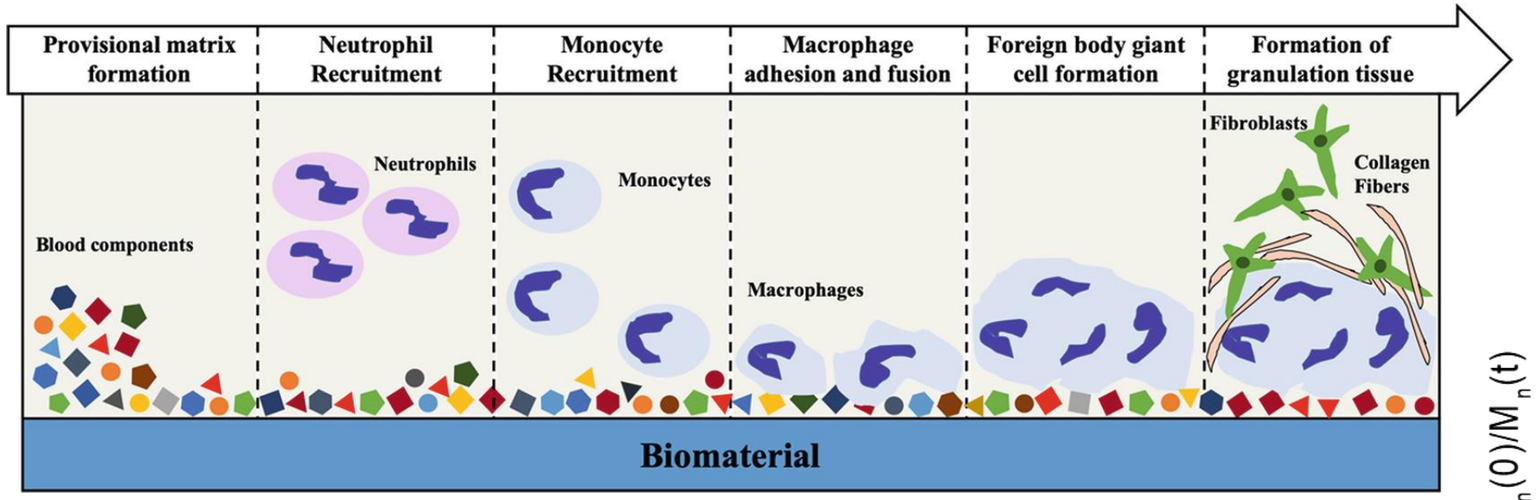
IN VIVO DATA MAKES EXTRAPOLATION DIFFICULT

WE CAN DO BETTER THAN TREATING THE BODY AS A BLACK BOX

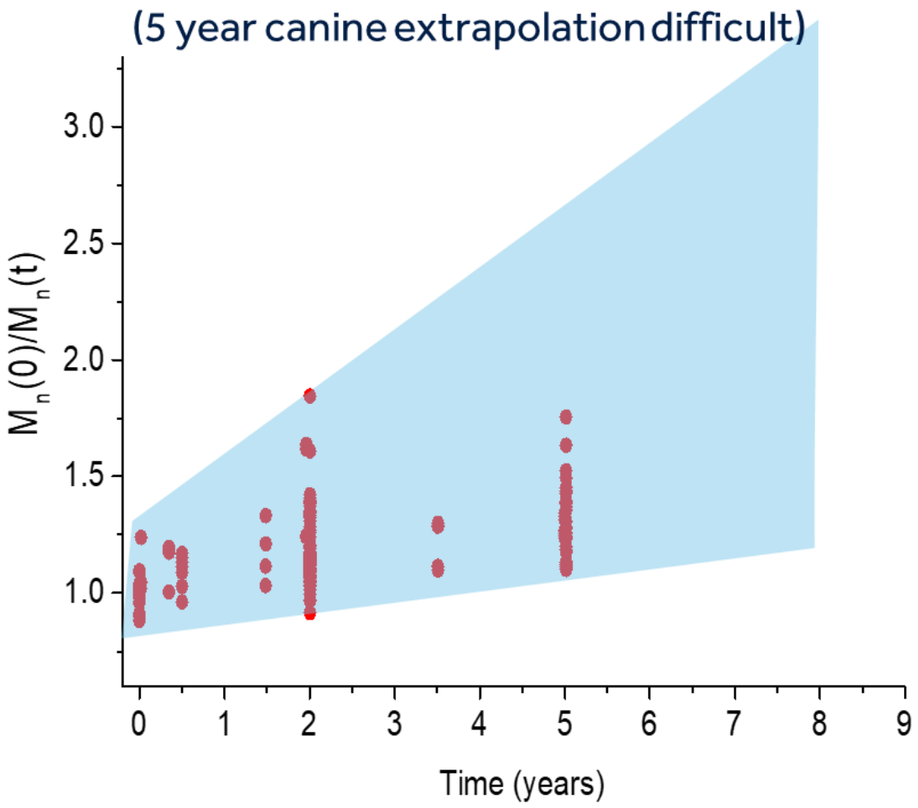
A mysterious *in vivo* environment and over reliance on *in vivo* data



Ref: Frazão et al. Biomimicked Biomaterials 2020 (1250) p 978-981.

High Variation, Low N

(5 year canine extrapolation difficult)



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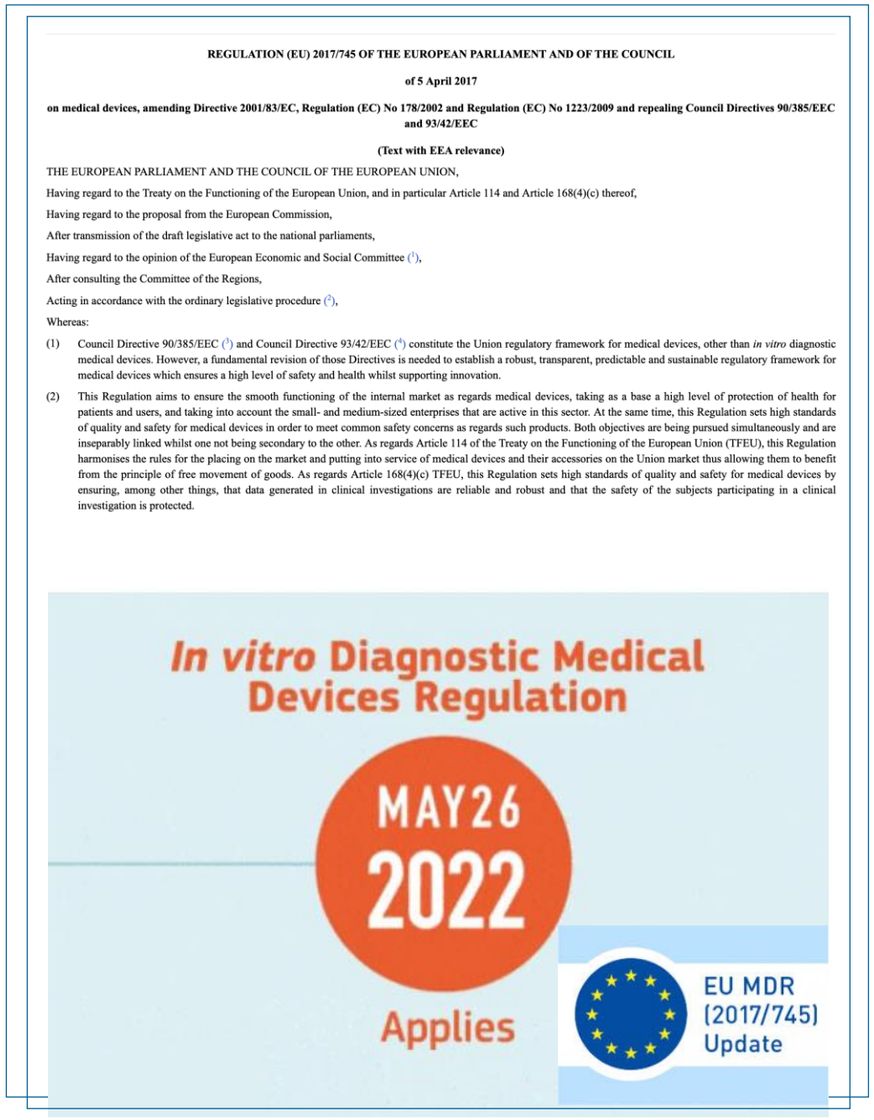
EVALUATION PERFORMED TO THE CURRENT STANDARDS



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EU MDR: European Union Medical Device Regulation

- 11 references to end-of-life performance
- Product surveillance requirements
- No explicit guidance

Accelerated Chemical Testing

+

Mechanical Testing

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WE ARE TAKING THE LEAD IN DEFINING THE STANDARDS
CONTINUING TO DO WHAT WE HAVE DONE

RETURN TO ISSUE | < PREV **ARTICLE** NEXT >

Influence of Water on the Structure and Properties of PDMS-Containing Multiblock Polyurethanes

Kimberly A. Chaffin*†, Adam J. Buckalew†, James L. Schley†, Xiangji Chen†, Matthew Jolly†, Julie A. Alkatout†, Jennifer P. Miller†, Darrel F. Untereker†, Marc A. Hillmyer*‡, and Frank S. Bates*§

RETURN TO ISSUE | < PREV **ARTICLE** NEXT >

Polyether Urethane Hydrolytic Stability af

Kimberly A. Chaffin*†, Xiangji Chen†, Lori McNamara†, Frank S. Bates*‡, ar

Abrasion and fatigue resistance of
containing multiblock polyuretha
accelerated water exposure at eleva
temperature

Kimberly A. Chaffin [a, b], Charles L. Wilson [a, c], Adam K. Himes [a, c], James W. Dawson [a, c], Tarek D. Haddad [a, c], Adam J. Buckalew [a, b], Jennifer P. Miller [a, c], Darrel F. Untereker [a, b], Narendra K. Simha [a, b]

Longevity expectations for polymers in medical devices demand new approaches to evaluating their biostability

Vater

K. A. Chaffin
Corporate Science and Technology,
Medtronic, plc. Minneapolis, MN 55432
kim.chaffin@medtronic.com

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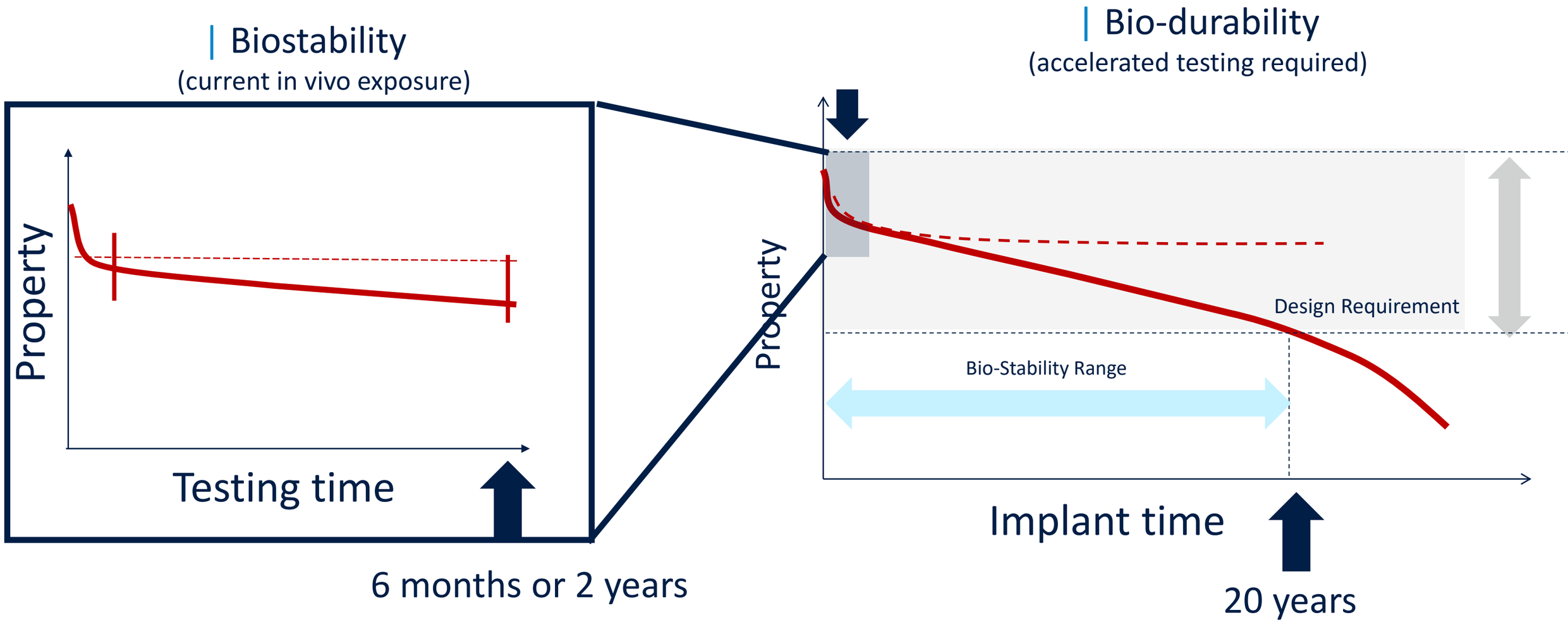
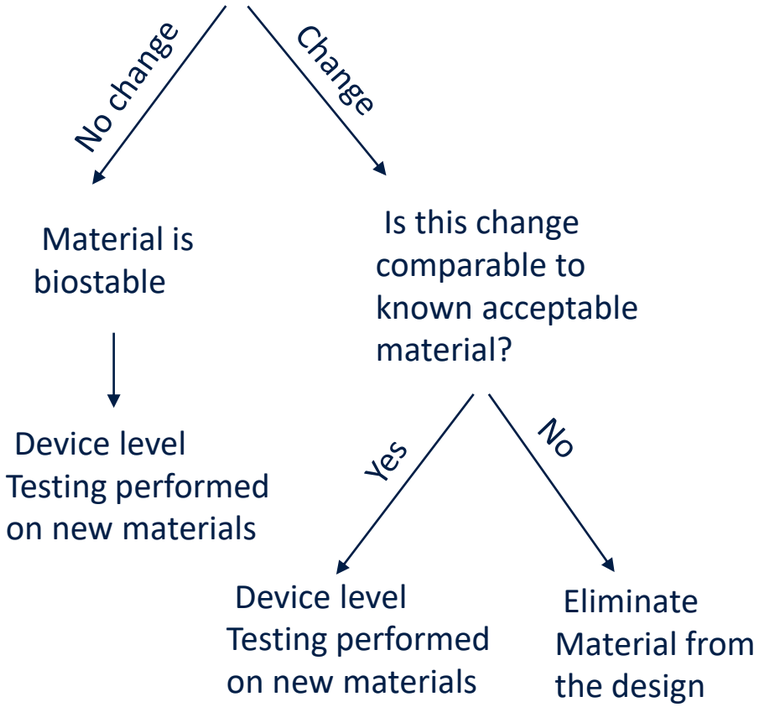
WE MUST SHIFT OUR DEFINITION OF BIOSTABILITY
MODERN DAY LONGEVITIES DEMAND THIS SHIFT



MISTAKES THAT OCCUR WHEN USING HISTORICAL BIOSTABILITY ASSESSMENT
WHEN MODERN DEVICE LONGEVITY IS DEMANDED IN THE APPLICATION

Current Regulatory Guidance

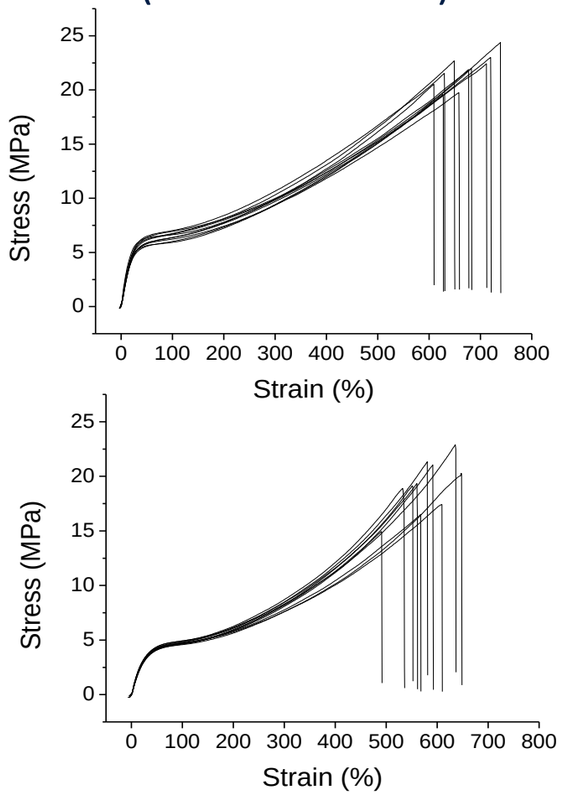
- Expose the material to some extreme condition
- Assess properties



New Material

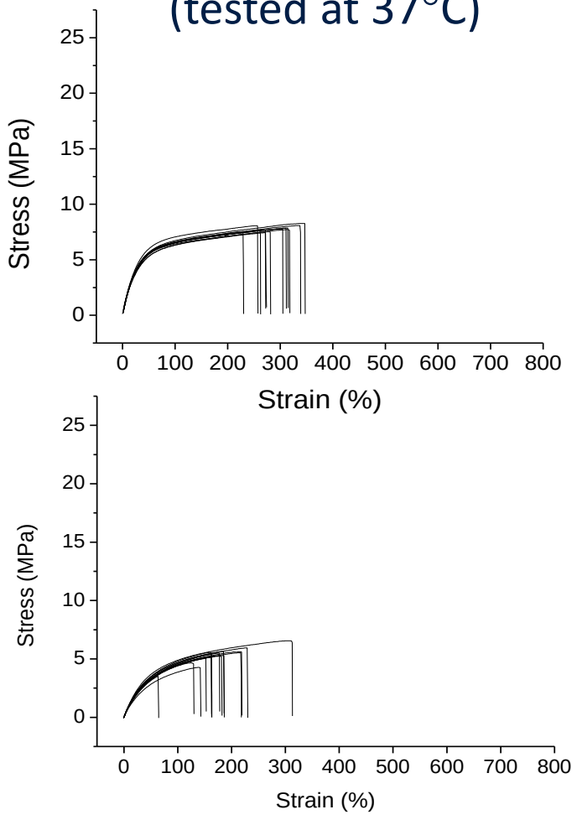
Poly(ether)Urethane Control

Initial Hydrated
(tested at 37°C)



Extreme Condition

85°C in Buffered Saline
(tested at 37°C)



Ref: Chaffin *et al. Macromolecules* 2012, 45, 22, 9110-9120
Chaffin *et al. Macromolecules* 2014, 47, 15, 5220-5226

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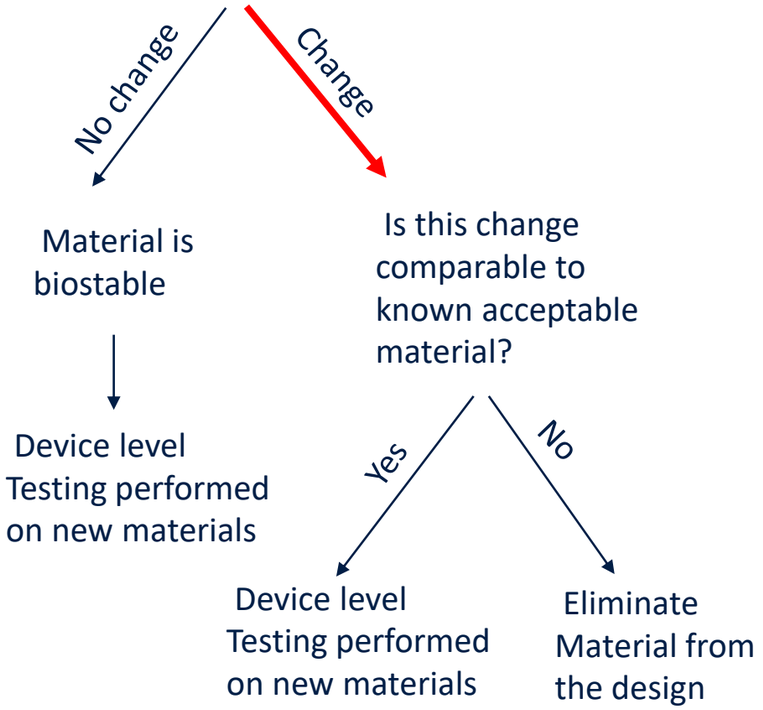

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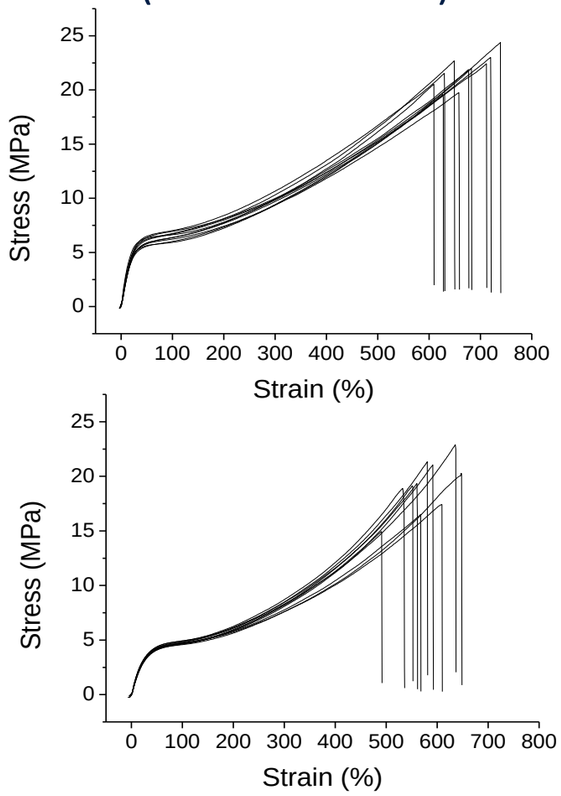

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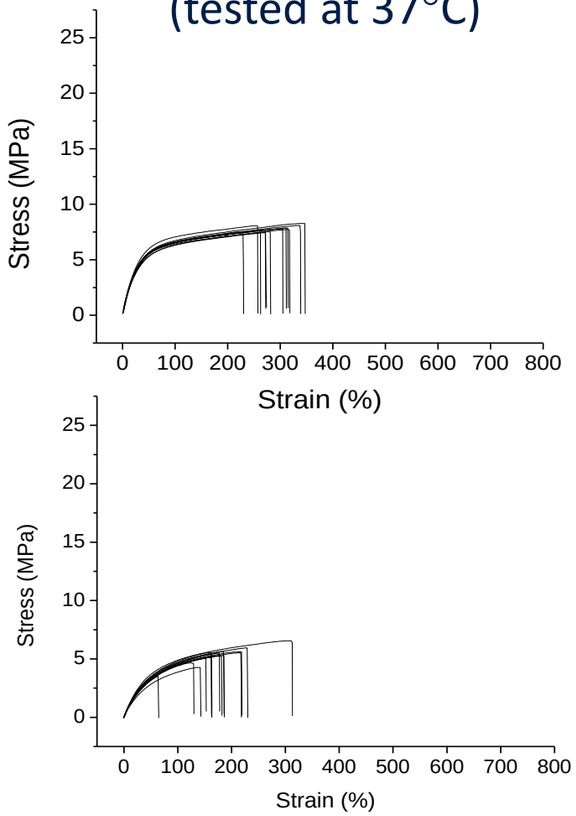

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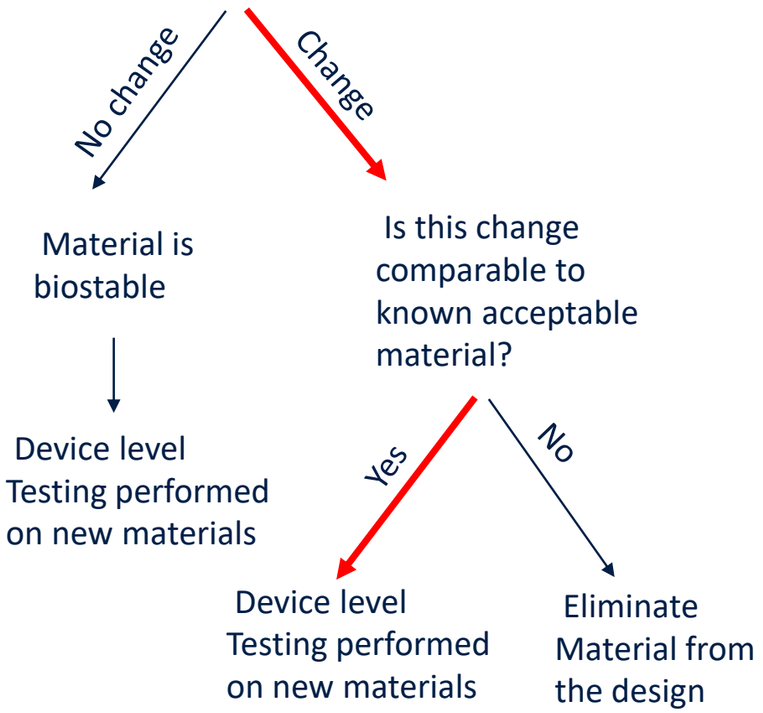

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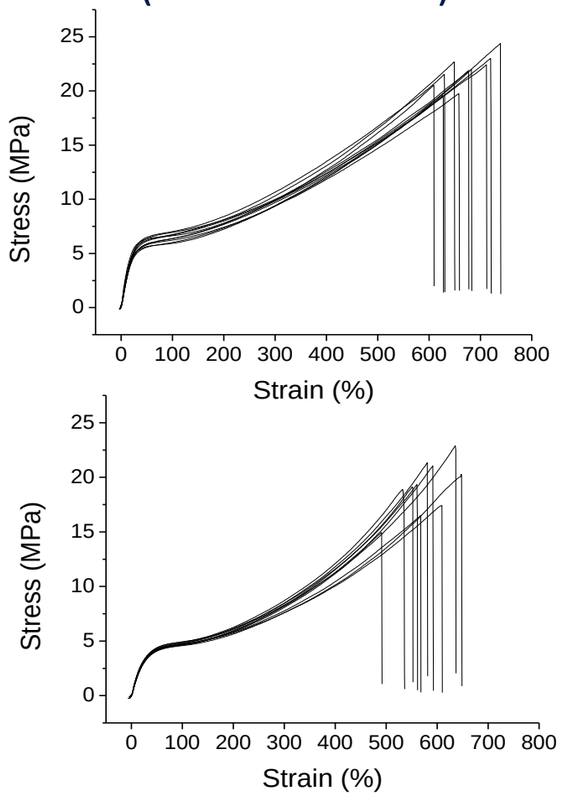

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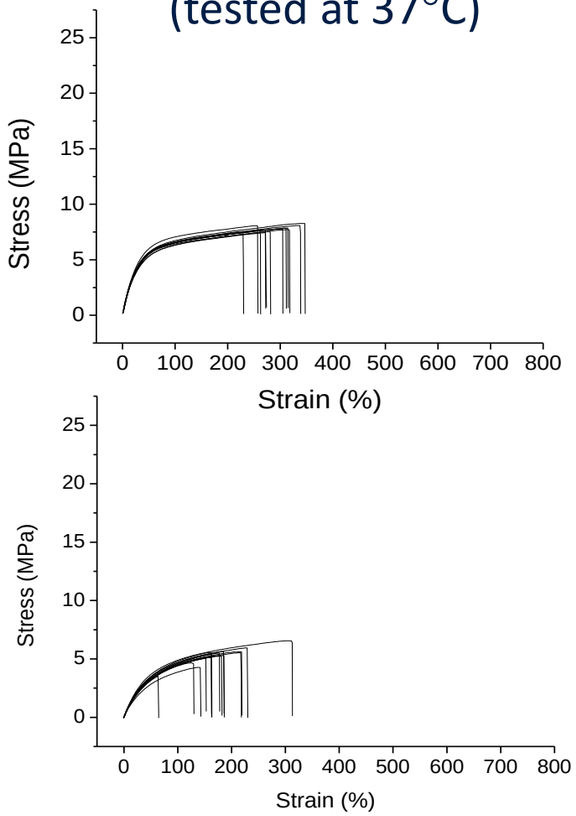

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Current Regulatory Guidance

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Use the Chat feature

Which is the better performing material?

New Material

Poly(ether)Urethane Control

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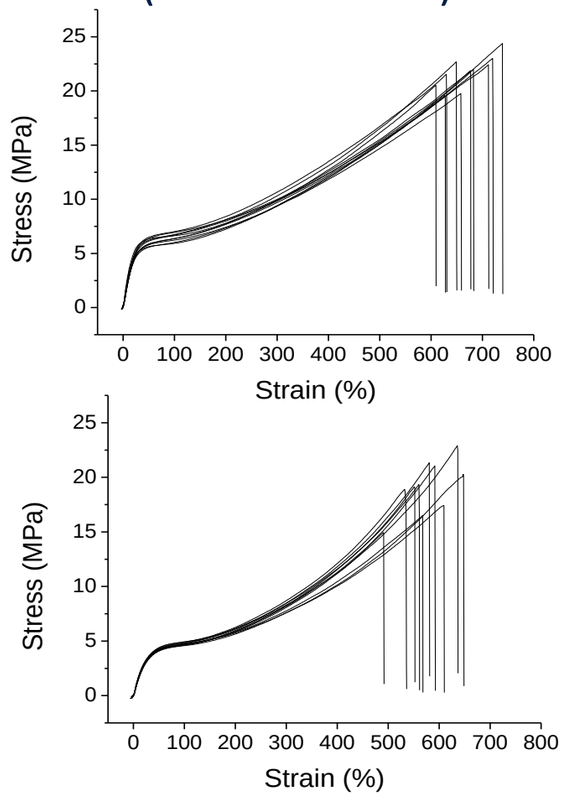

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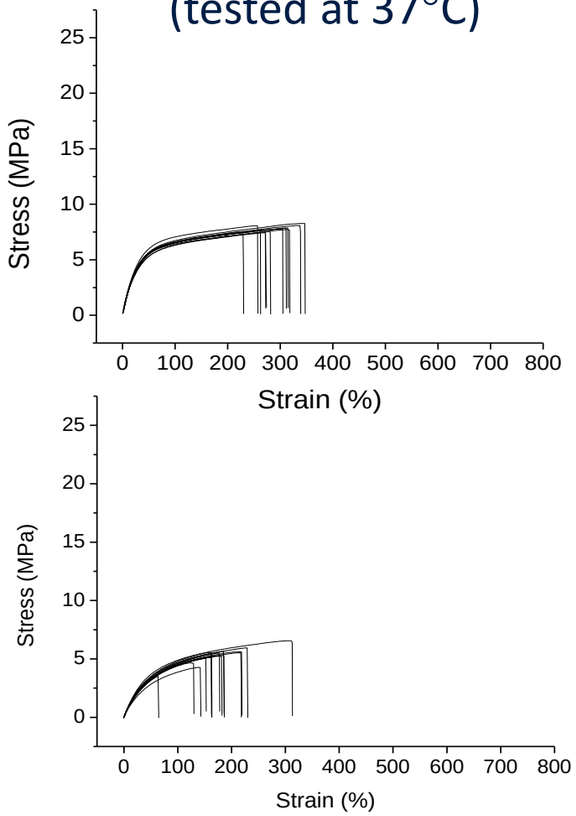

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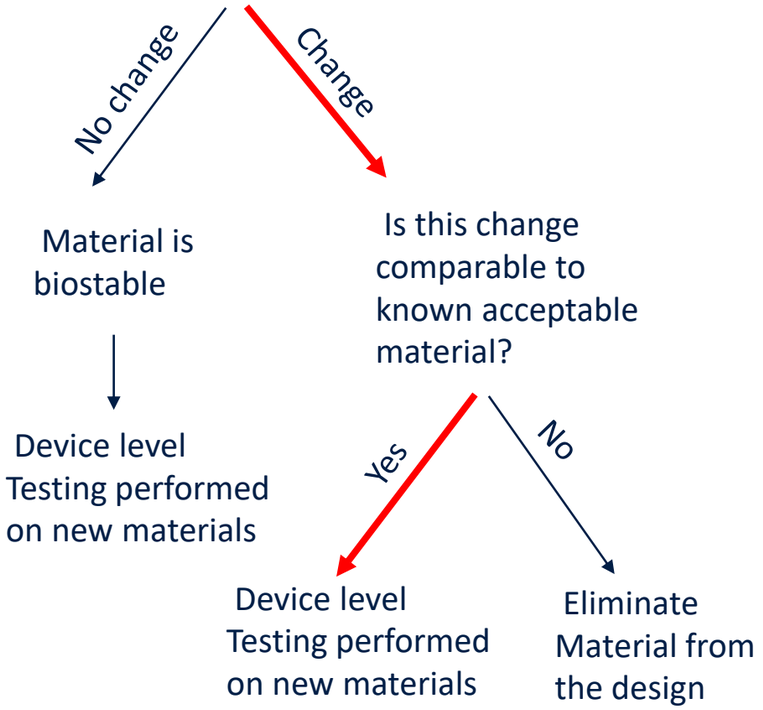

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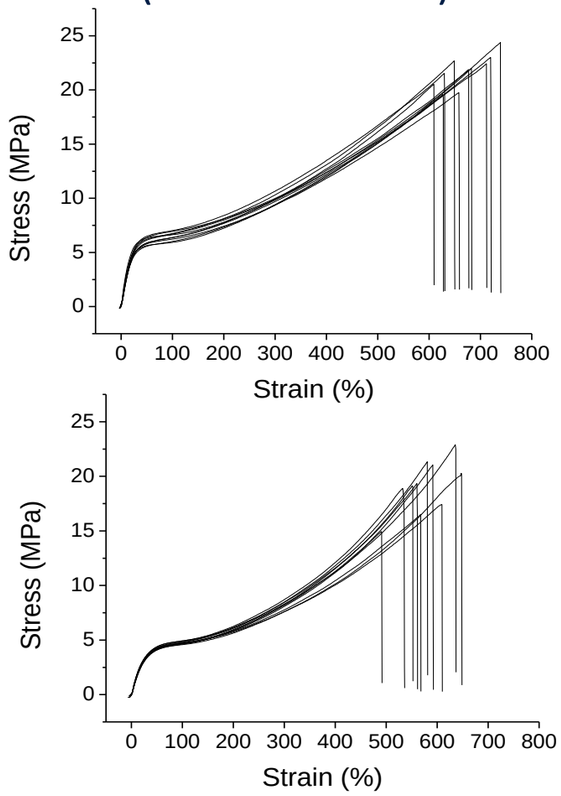

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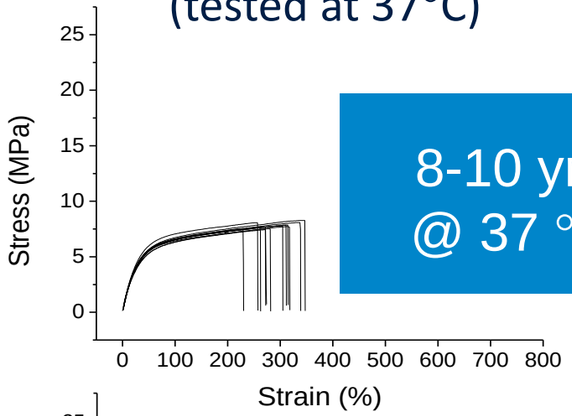
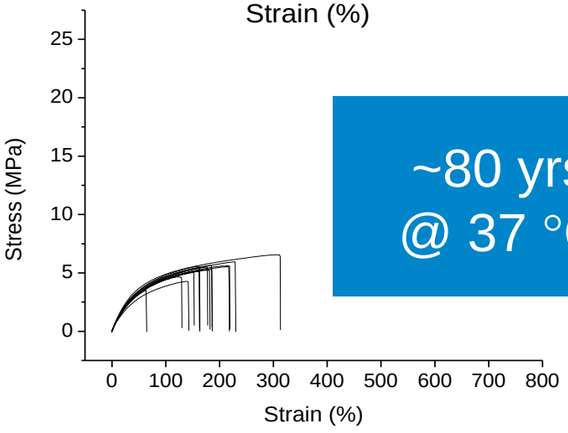


8-10 yrs @ 37 °C



~80 yrs @ 37 °C

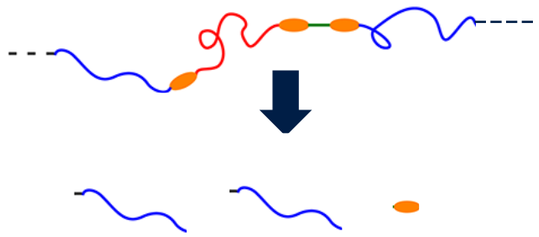
Ref: Chaffin *et al. Macromolecules* 2012, 45, 22, 9110-9120
Chaffin *et al. Macromolecules* 2014, 47, 15, 5220-5226

HISTORICAL METHODS DO NO ELUCIDATE A TIMEFRAME FOR DEGRADATION

ERROR IS SIGNIFICANT WHEN APPLYING THESE METHODS TO MODERN DEVICE LONGEVITIES

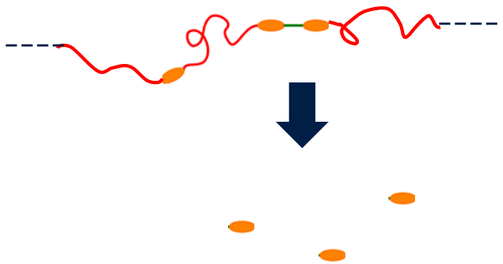
| Which bond matters

New Material (PDMS-PEU)



Siloxane + Urethane Hydrolysis

Poly(ether)Urethane Control



Urethane Hydrolysis

| Activation Energy

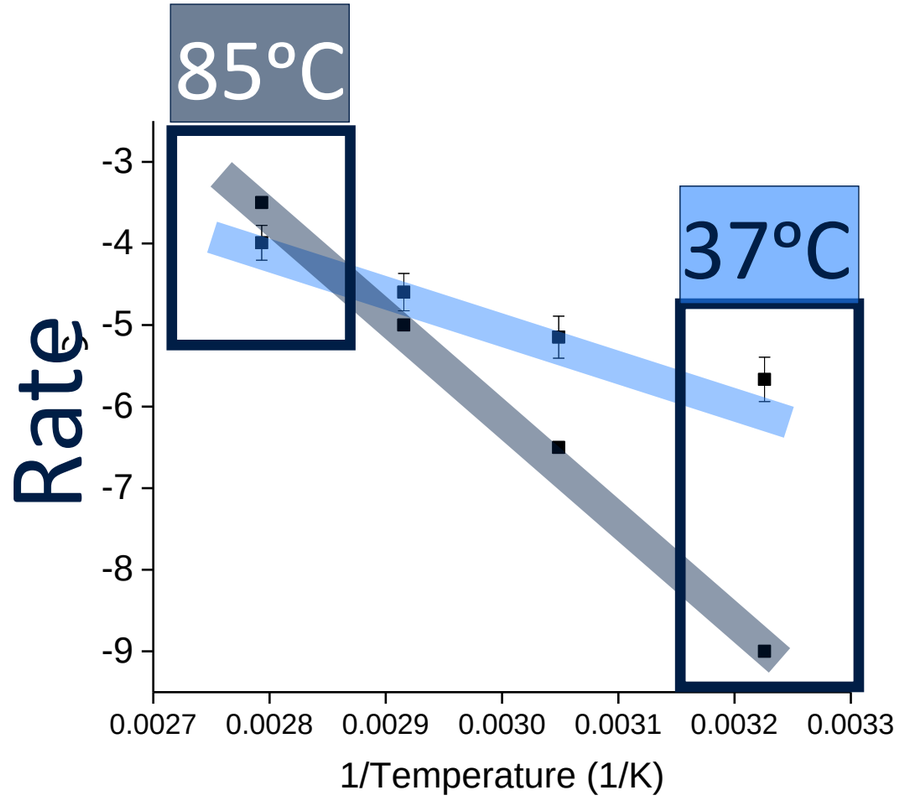
E_A = 30 KJ/MOLE

Reaction needs only a little energy to proceed

E_A = 90 KJ/MOLE

Reaction needs LOTS of energy to proceed

| The reaction rate (k)



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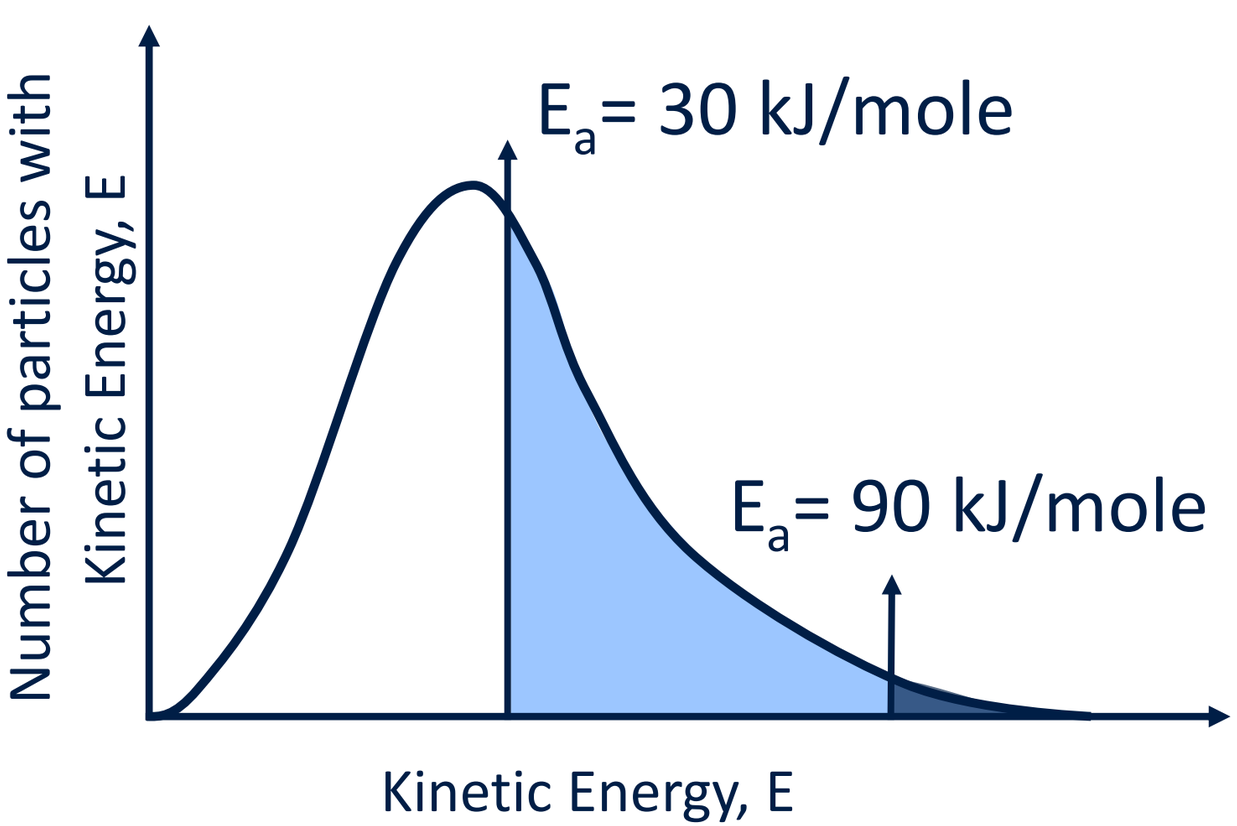
A DEEP LOOK AT THE ACTIVATION ENERGY AND TEST TEMPERATURE

THE ENERGY REQUIRED FOR REACTION

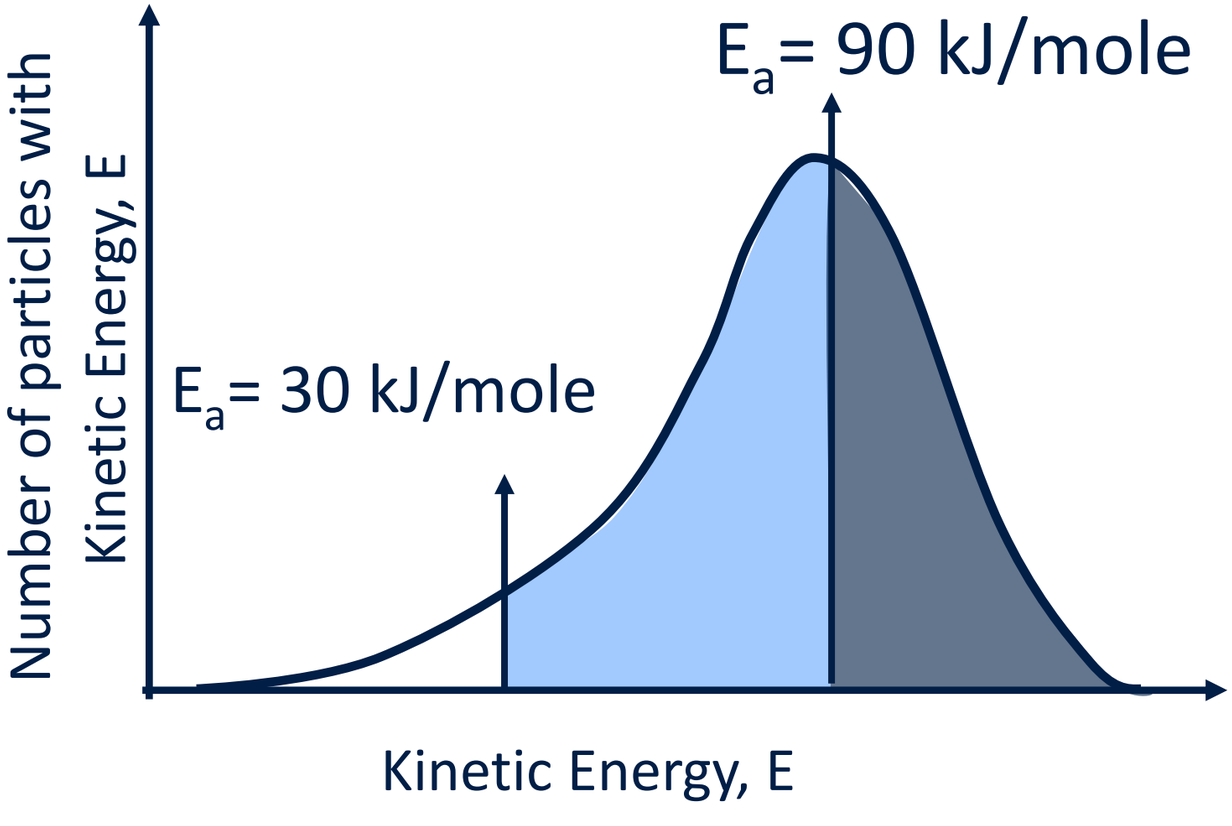
New Material (PDMS-PEU)

Poly(ether)Urethane Control

| 37 °C Reaction



| 85 °C Reaction



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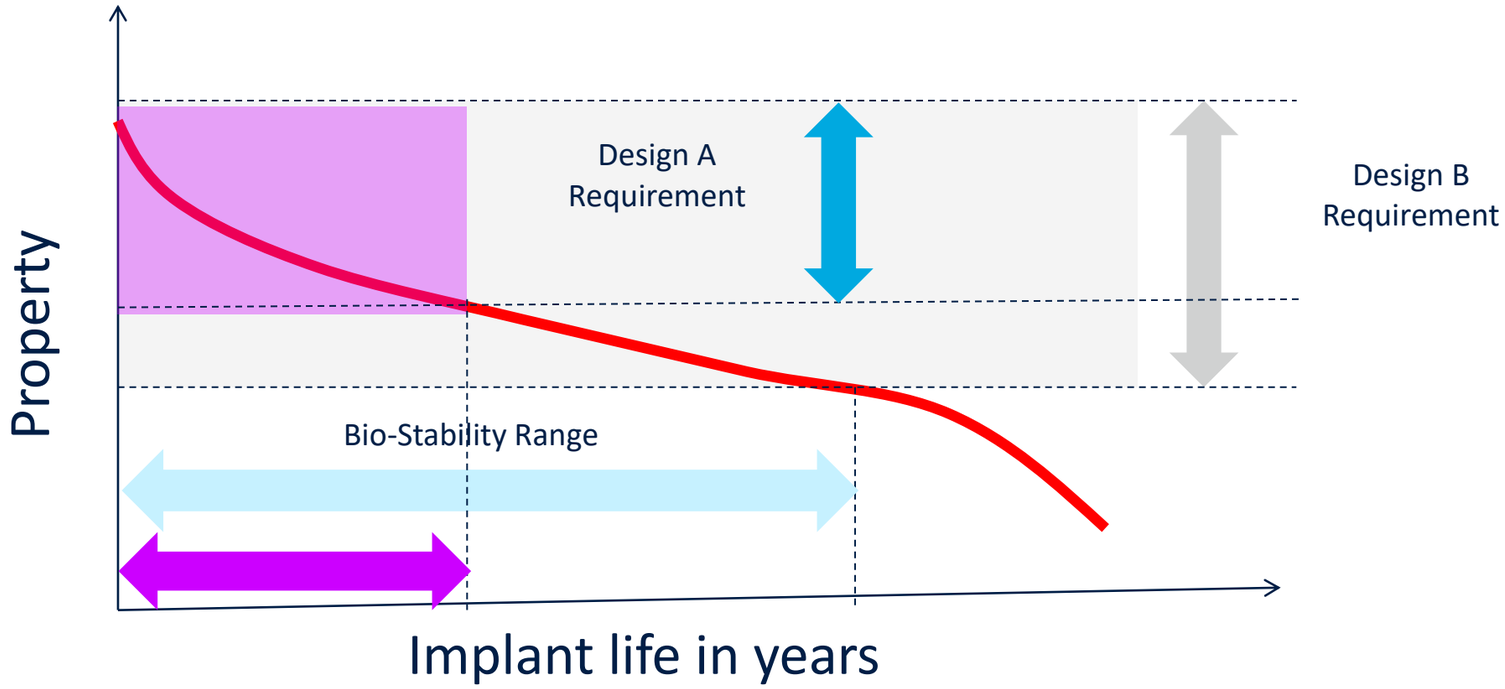
BIOSTABILITY FOR TODAY'S LONGEVITIES
REQUIRES QUANTITATIVE ACCELERATED PREDICTIVE TESTING



New requirements

- Properties can change but change must be understood
- Design requirements (in vivo loads) must be known with greater certainty
- Chemical reactions must be accelerated quantitatively
- Acceleration methods must be validated
- The characteristic failure mode of the material must be understood
- Animal models take on less prominent role

ACCELERATING QUANTITIVELY
PREDICTING EXTENT OF REACTION AT LONG TIMES

1. Determine the reaction (What bonds?)

Hydrolysis

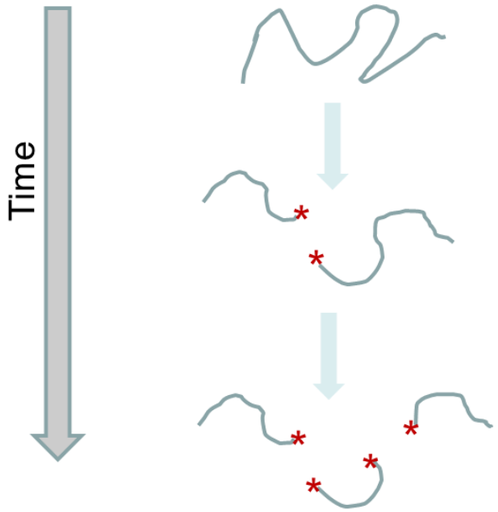
Polymer + $H_2O \rightarrow$ 2 Short Polymers

Oxidation

Polymer + $O_2 \rightarrow$ 2 Short Polymers

Ref: Chaffin *et al. Macromolecules* 2012, 45, 22, 9110-9120

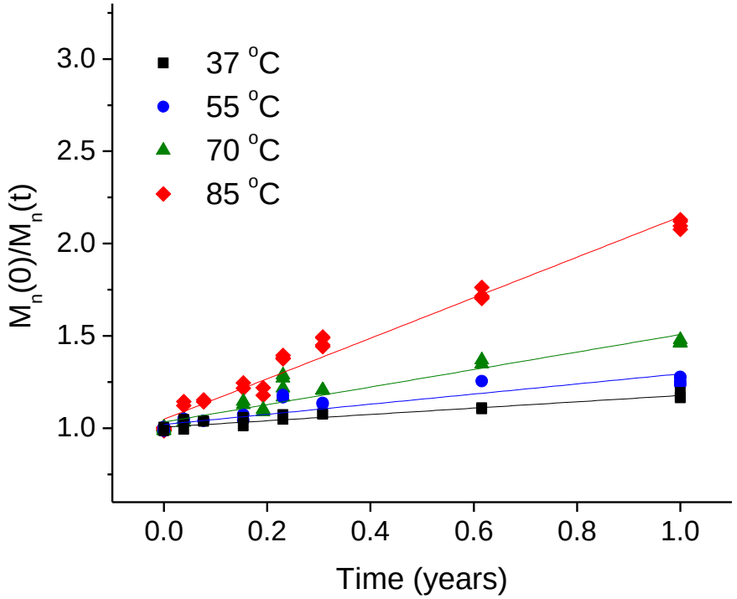
2. Measure the rate (reaction per time)



Chain length = Molecular Weight = M_n

The number of chemical reactions is inversely proportional to chain length

3. Accelerate the reaction (the same bond as at 37 °C)



Determine the effect of temperature on rate (i.e. the activation energy (E_A))

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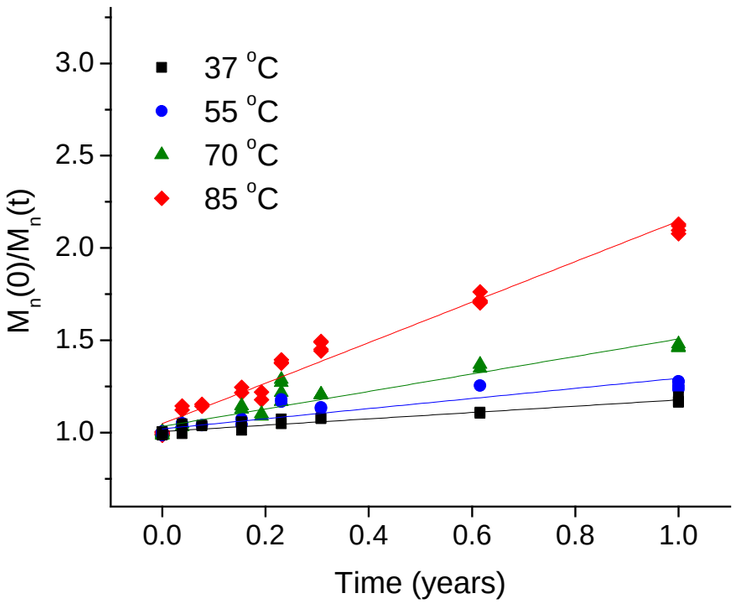
PREDICTING THE EXTENT OF REACTION AT 37 °C
ARRHENIUS RELATIONSHIP

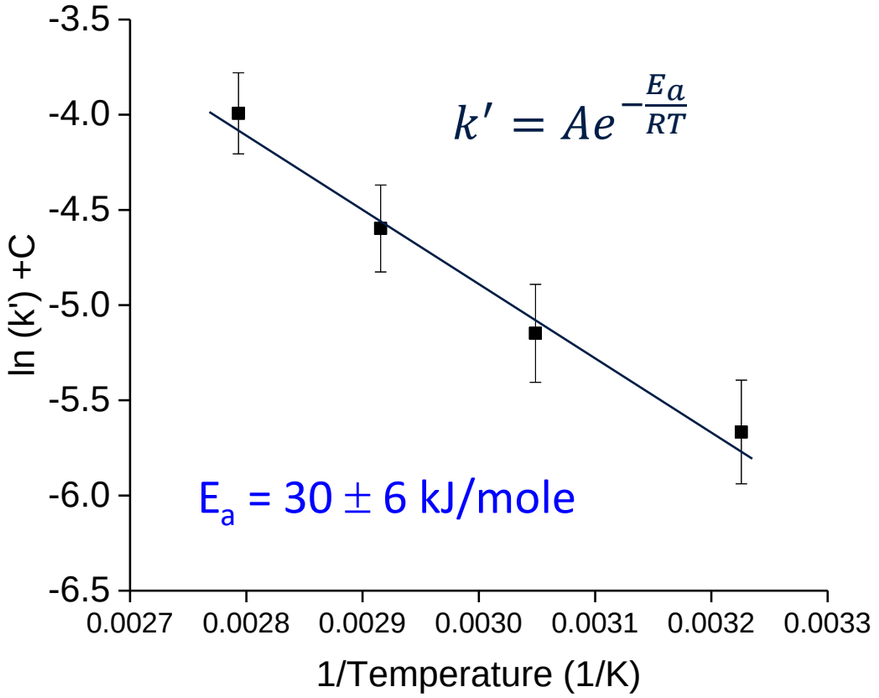
| Reaction Rate
(Increases with Temperature)

The slope of the line is the rate of reaction (k)



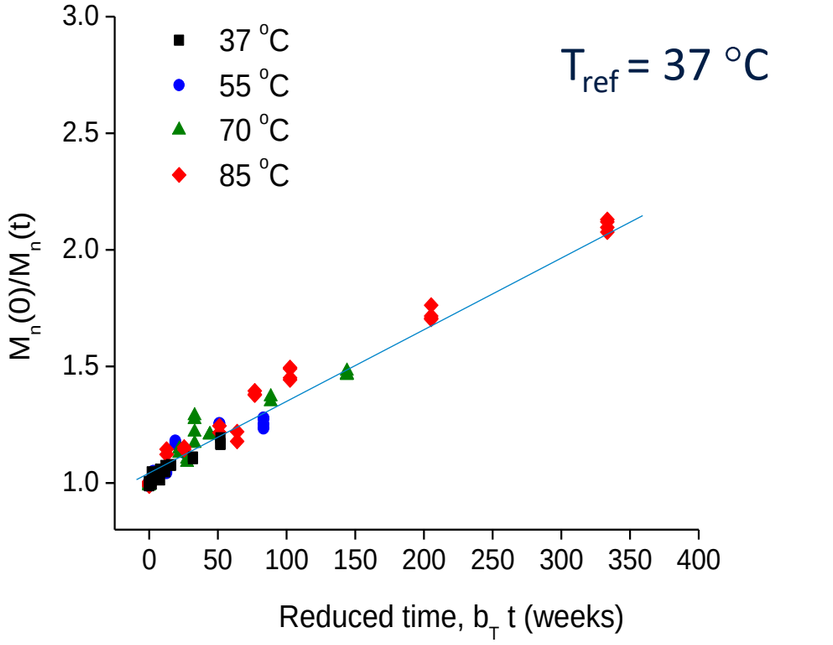
| Activation Energy
(A single activation energy)

$$k' = Ae^{-\frac{E_a}{RT}}$$



| Reduced Time
(1 year predicts ~ 7 year performance)

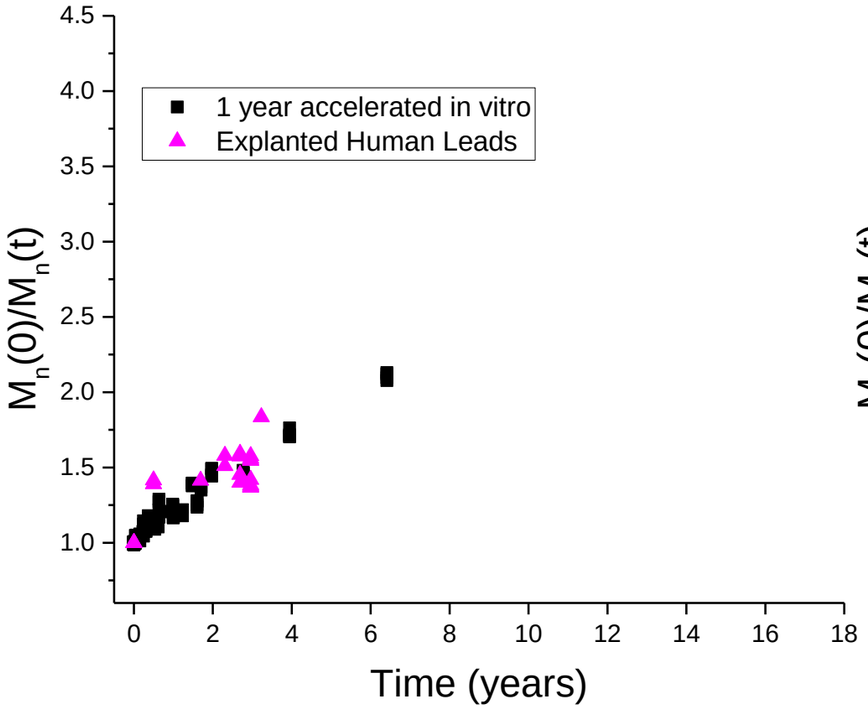
$$t_{\mathrm{ref}} = \mathrm{b_T}\, t \quad \text{where} \quad \mathrm{b_T} = e^{\frac{E_a}{R}\left(\frac{1}{\mathrm{T_{ref}}}+\frac{1}{\mathrm{T}}\right)}$$



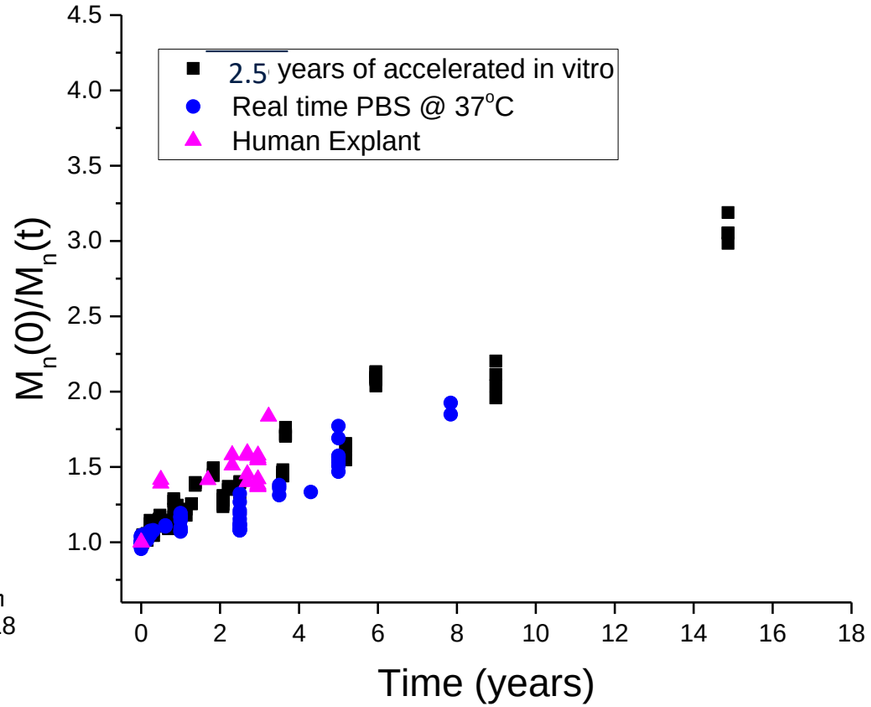
Ref: Chaffin *et al. Macromolecules* 2012, 45, 22, 9110-9120

USING ACCELERATED DATA TO PREDICT REACTION AT BODY TEMPERATURE
VALIDATING ACCELERATED PREDICTIONS

| Validated with human data
(1 year accelerated dataset)



| Validated with real time in vitro
(2.5 yr accelerated dataset)



| Quantitative Acceleration (Successful)

- Predictive capability is consistent with modern longevities
- Reactions must be understood
- Acceleration protocols must be validated.

Ref: Chaffin *ACS Macro Lett.* ***2020****, 9, 12, 1793-1798*

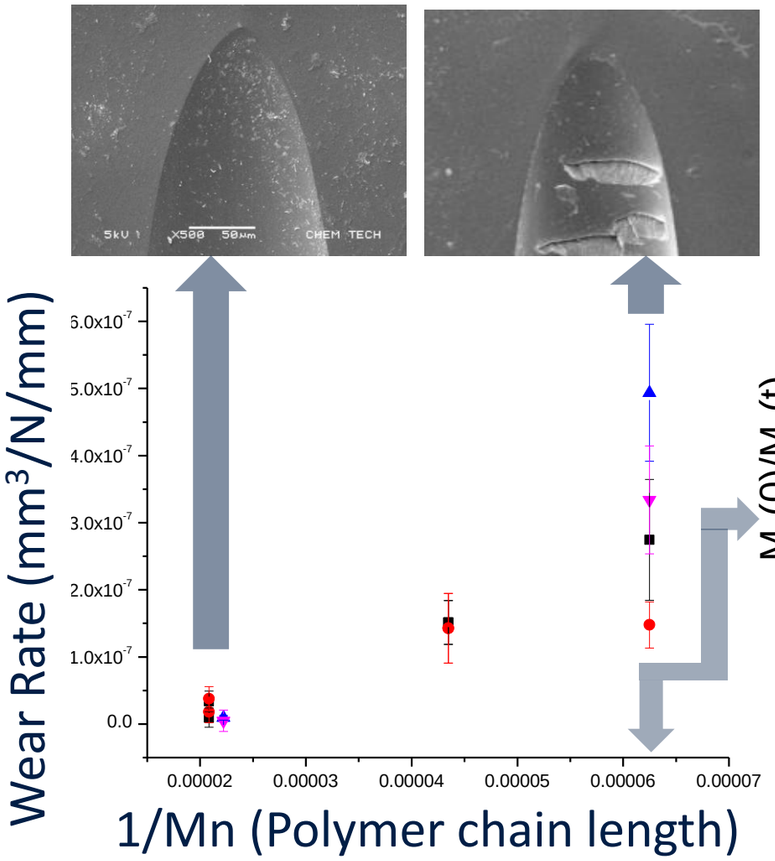
MECHANICAL PROPERTIES CAN BE EVALUATED AFTER ACCELERATED CHEMISTRY

INTEGRATE ALONG TIME ACCESS TO UNDERSTAND LONG TERM PERFORMANCE

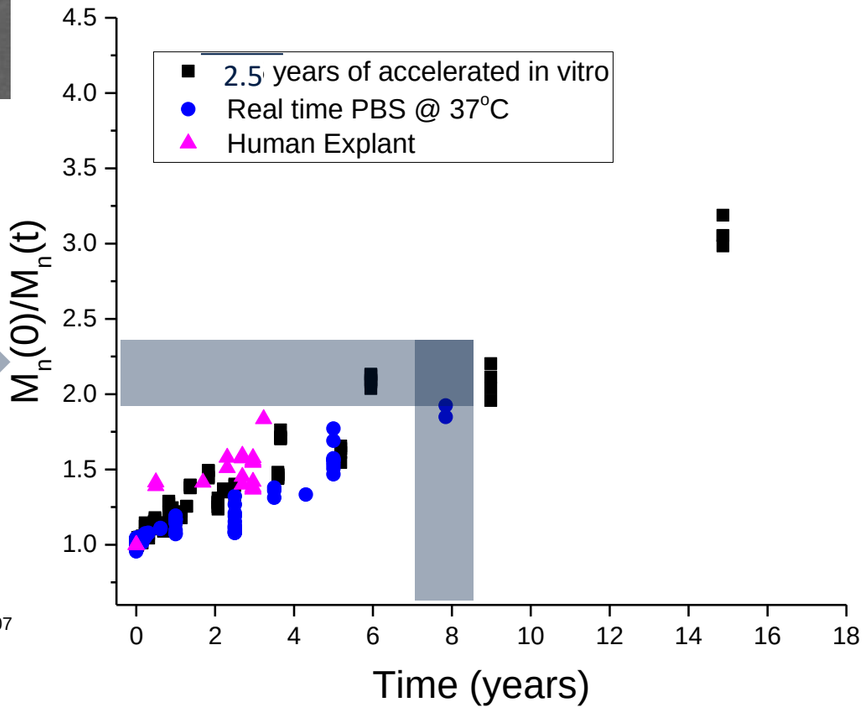
| Characteristic Failure Mode

(chronically implanted cardiac leads)

| Abrasion/Wear



| Longevity Prediction



Ref: Chaffin *et al. Biomaterials* 2013, 34, 33, 8030-8041

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MECHANICAL PROPERTIES CAN BE EVALUATED AFTER ACCELERATED CHEMISTRY
INTEGRATE ALONG TIME ACCESS TO UNDERSTAND LONG TERM PERFORMANCE

Characteristic Failure Mode
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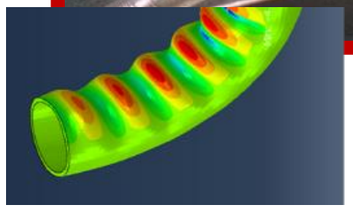
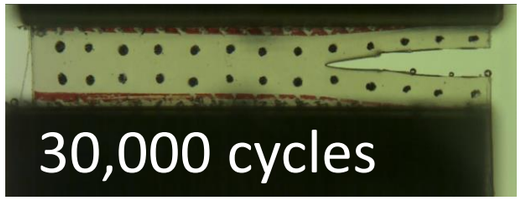
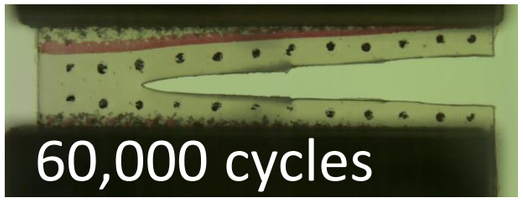
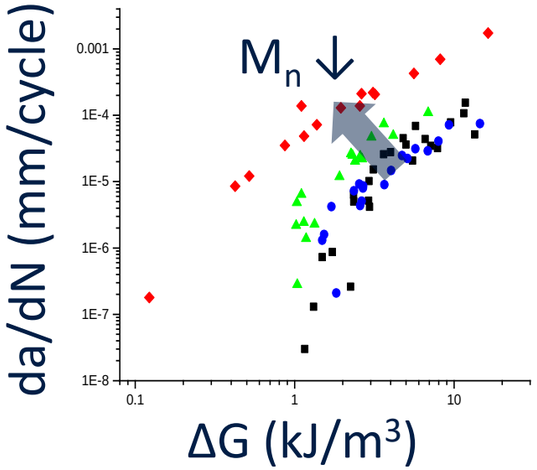


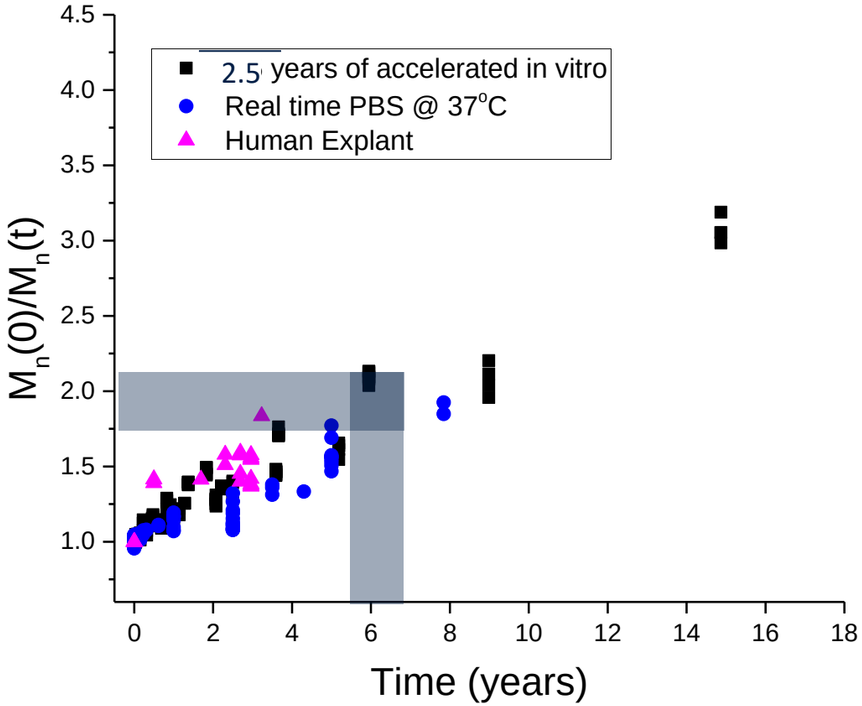
Crack Propagation







Longevity Prediction



Ref: Chaffin *et al. Biomaterials* 2013, 34, 33, 8030-8041

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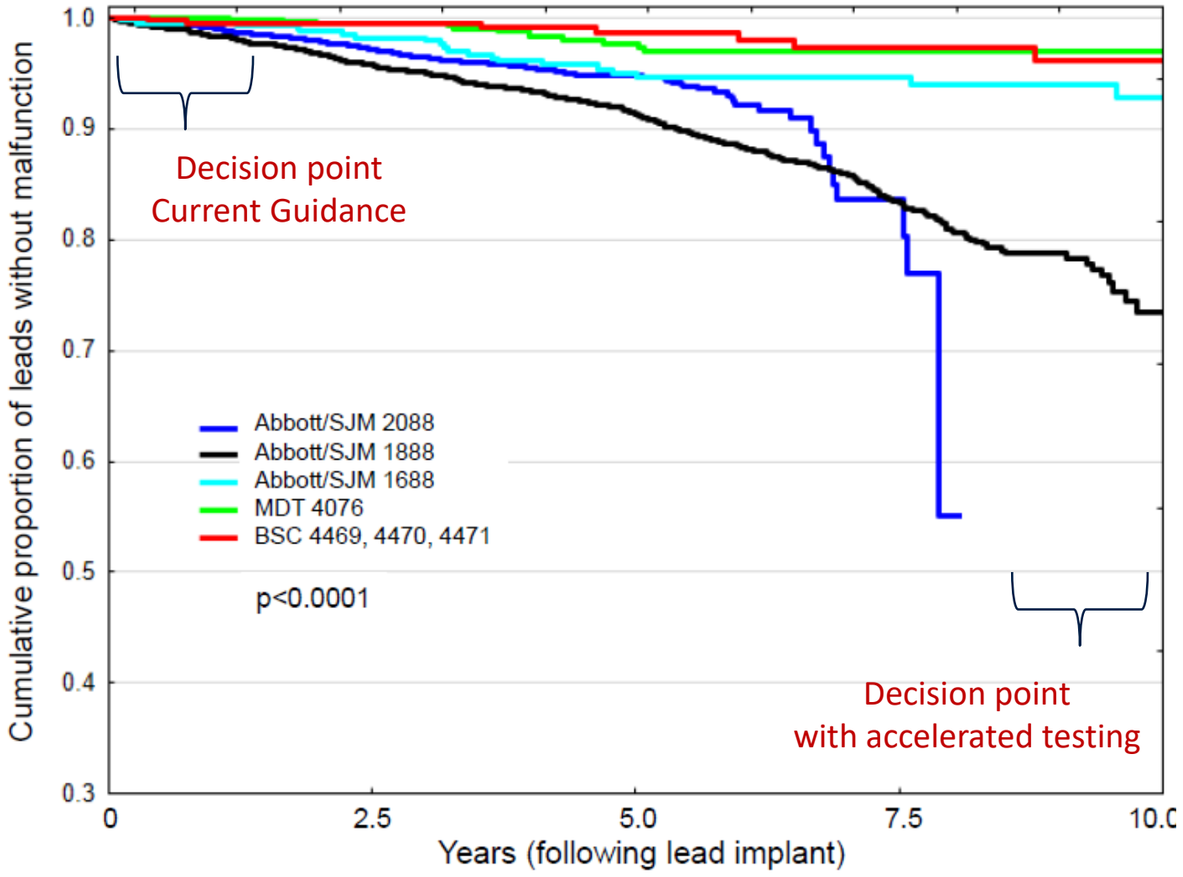
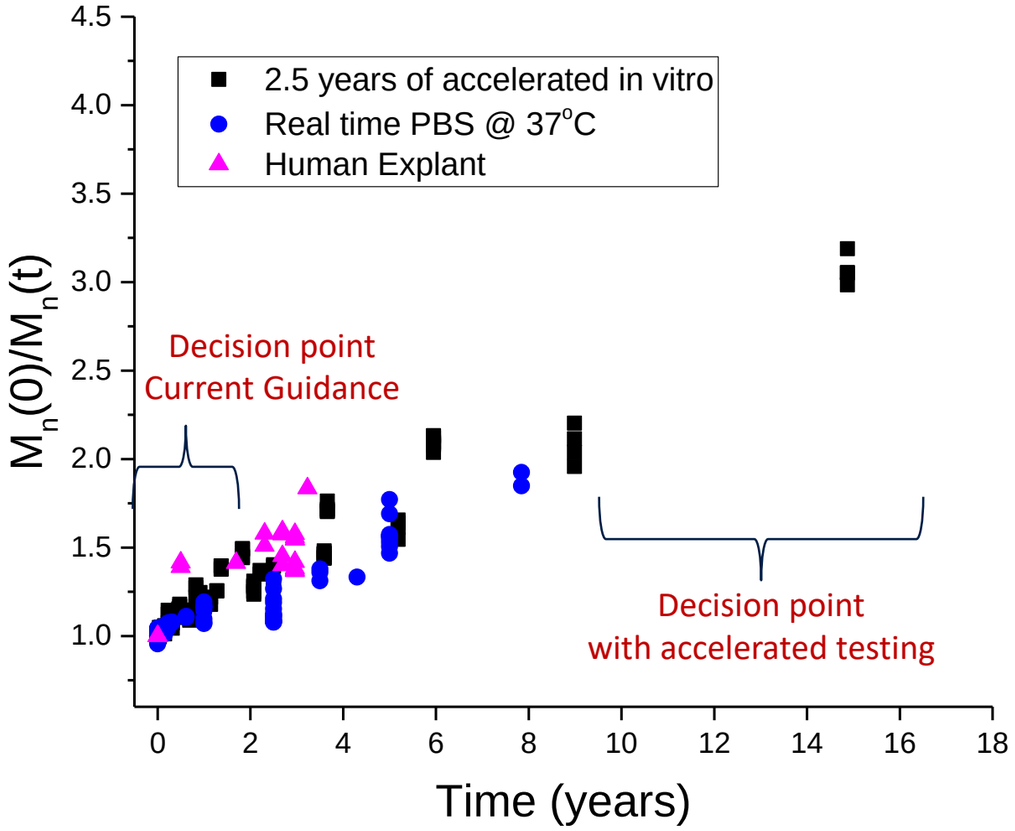
HUMAN LEAD PERFORMANCE (LOW VOLTAGE)
A RETROSPECTIVE ANALYSIS OF 8,000 CARDIAC LEADS

Human Lead Performance



Ref: El-Chami, et al *Heart Rhythm*, **2019**, 16,572-578.

Carefully planned accelerated testing predicts long term biostability



Ref: Chaffin *ACS Macro Lett.* ***2020****, 9, 12, 1793-1798*

SUMMARY OF MATERIAL BIOSTABILITY

ACCELERATED TESTING IS A KEY ELEMENT OF MODERN MATERIAL INTRODUCTION

- Modern Materials react slowly
  current guidance will not reveal change
- Carefully planned accelerated testing
  provide insight into long term biostability
- In vivo Reactions
  can be isolated and understood
- Bio-durability
  A material can change if the performance consequence is understood

QUESTIONS?
THOUGHTS?

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BACKUP SLIDES

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Further, Together

PEER REVIEWED PAPERS PUBLISHED TO DATE ON PDMS-PU STABILITY
CONFERENCE PROCEEDINGS AND POSTERS EXCLUDED (20 YEARS)

- ✓ **Kinetic Aspects of Hydrolytic Resistance of Avcotan and Biomer Segmented Polyurethanes** INT J POLYM MATER , vol. 46, no. 3-4, pp. 655-661, 2000
- ✓ **Long-term in vivo biostability of poly(dimethylsiloxane)/poly(hexamethylene oxide) mixed macrodiol-based polyurethane elastomers** Biomaterials 2004 Sep;25(20):4887-900.
- ✓ ***In vivo* biostability of polysiloxane polyether polyurethanes: Resistance to biologic oxidation and stress cracking** Journal of Biomedical Materials Research Part A Volume 77A, Issue 3, pages 580–589, 1 June 2006
- ✓ **Influence of Water on the Structure and Properties of PDMS-Containing Multiblock Polyurethanes** *Macromolecules*, **2012**, *45* (22), pp 9110–9120 (MDT)
- ✓ **Abrasion and fatigue resistance of PDMS containing multiblock polyurethanes after accelerated water exposure at elevated temperature** Biomaterials, Volume 34, Issue 33, November 2013, Pages 8030-8041(MDT)
- ✓ **Polyether Urethane Hydrolytic Stability after Exposure to Deoxygenated Water** *Macromolecules*, **2014**, *47* (15), pp 5220–5226 (MDT)
- ✗ **Limitations of predicting *in vivo* biostability of multiphase polyurethane elastomers using temperature-accelerated degradation testing** J. Biomed Mater Res Part B **2015**, 103 (1) pp 159-168. (SJM)
- ✓ **Hydrolytically stable polyurethanes** J. Polym. Sci. A Polym. Chem 2015 15(53):1-4 (Akron)
- ✓ **Long term *in vitro* hydrolytic stability of thermoplastic polyurethane** J Biomed Mater Res A. 2015 103(12):3798-806 (BSX)
- ✗ **The biostability of cardiac lead insulation materials as assessed from long-term human implants** J Biomed Mater Res B Appl Biomater. 2016 104(2):411-21 (SJM)
- ✓ **Comparison of the clinical explants and accelerated hydrolytic aging to improve biostability assessment of silicone-based polyurethanes** J Biomed Mater Res Part A 2016 104A (7) 1805-1816 (SJM) (report a 22% drop in molar mass between 2-3 years)
- ✓ **Simultaneous Improvement of Oxidative and Hydroitic Resistance of Polycarbonate Urethanes Based on Polydimethylsiloxane/Poly(hexamethylene carbonate) Mixed Macrodiols** Biomacromolecules 2018, 19, 2137-2145

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PARTIAL LIST

Influence of Water on the Structure and Properties of PDMS-Containing Multiblock Polyurethanes
Macromolecules 2012, 45, 22, 9110-9120

Polyether Urethane Hydrolytic Stability after Exposure to Deoxygenated Water
Macromolecules 2014, 47, 15, 5220-5226

Abrasion and fatigue resistance of PDMS containing multiblock polyurethanes after accelerated water exposure at elevated temperature
Biomaterials 2013, 34, 33, 8030-8041

Longevity expectations for polymers in medical devices demand new approaches to evaluating their biostability Recommended for publication with minor correction, ACS Viewpoints

OPTIM: COMBINES THE TOUGHNESS OF PEU WITH THE CHEMICAL STABILITY OF SILICONE: *STUDIES AFTER 10 YEARS OF IMPLANT TIME*

Silicone
- Flexibility
- Biostability

Polyurethane
- Lubricity
- Durability

50x the abrasion Resistance of silicone!

Copolymer properties are NOT additive!

High Voltage

Journal of Cardiovascular Electrophysiology
THE OFFICIAL JOURNAL OF THE WORLD SOCIETY OF ARRHYTHMIAS
World Society of Arrhythmias

ORIGINAL ARTICLE

Long-term performance and lead failure analysis of the Durata defibrillation lead compared to its previous model, the recalled Riata defibrillation lead

Thomas Kleemann MD, Florian Nonnenmacher MD, Margit Strauss MD ... See all authors

First published: 22 July 2019 | https://doi.org/10.1111/jce.14087 | Citations: 3

Low Voltage

Comparative Study > Heart Rhythm. 2019 Apr;16(4):572-578.

doi: 10.1016/j.hrthm.2018.10.024. Epub 2018 Oct 24.

Long-term performance of a pacing lead family: A single-center experience

Mikhael F El-Chami [1], Birju Rao [2], Anand D Shah [2], Carolyn Wood [2], Michael Sayegh [2], Patrick Zakka [2], Krista Ginn [2], Lauren Pallotta [2], Bryanna Evans [2], Michael H Hoskins [2], David Delurgio [2], Michael Lloyd [2], Jonathan Langberg [2], Angel R Leon [2], Faisal M Merchant [2]

Affiliations + expand

PMID: 30366161 DOI: 10.1016/j.hrthm.2018.10.024

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