MedTech Monitor

Fox Rothschild LLP
ATTORNEYS AT LAW

DuVal & Associates
Drug, Device and Food Law

Hosted By:

Fox Rothschild LLP and DuVal & Associates

September 21, 2022

Observations on the Impact of the America Invents Act on Medical Device Patent Litigation

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Experienced, team-oriented partner specializing in Intellectual Property and Patent Law involving a wide range of technologies. Developed and led intellectual property practice, applying technical expertise with 20+ years of counseling, litigation, and prosecution experience to protect client assents and determine optimal U.S. diverse, well-development portfolio of clients on different types of intellectual property matters. Frequent speaker on intellectual property matters including training programs such as the U.S., Taiwan, and Azerbaijan. Mr. Sharifi has been active in the New York Intellectual Property Law Association, Iranian American Bar Association, and other associations.

Recognized for expertise and exception results with legal industry honors including Managing IP's IP Stars for 2014 through 2022; IAM Patent 1000 in 2015 through 2022; and International Law Office's Legal Choice Award for Patents, New York, 2015.

Disclaimer

- The information and discussion provided is not made on behalf of Fox Rothschild and should not be understood to be representative of the views of the law firm or its clients.
- The presentation does not take a position in favor of any party.
- Based on a conflict request, the mentioned parties are not represented by the firm.

Background

- In 2011, Congress enacted one of the most important patent legislations in U.S. history: the America Invents Act
- The legislation included many updates and revisions including important changes related to patent infringement litigation
- In 2010, Over 3000 patent infringement lawsuits were filed

Patent Power

- Roots of Patent Strength
  - Exclusion – Injunction
  - Damages
    - Reasonable Royalty
    - Lost Profit

Background – Patent Litigation

- In District Court patent infringement lawsuits, the patent is assumed valid in deference to the Patent Office.
- An accused infringer must prove by clear and convincing evidence that the patent is invalid.
- There is a perceived general sense of favorability towards the property owner, the patent owner.

Introduction of Inter Partes Review

- AIA enacted Inter Partes Review
  - Proceeding at Patent Office before the Patent and Trademark Appeal Board (PTAB)
  - Mix of litigation and prosecution – depositions, but no jury trial
  - Panel of three administrative judges with significant experience in patent law and technology experience
  - Lower standard both in proof and claim interpretation
- Reexamination and Inter Partes Reexamination existed previously but had not seen significant adoption as a litigation tool

IPR Key Features

- Key Features of Inter Partes Review (IPR)
  - Adversarial – not Ex Parte
  - Expert depositions and testimony
  - Trial – but no jury or live witnesses
  - One year time limit to file once patent infringement lawsuit is filed
  - The PTAB process will likely take 18-24 months. (based on enacted rules)
  - District courts commonly stay patent litigations pending IPR review

Original Premise

- Premise – Now that Inter Partes Review has been in effect as a tool for an observable period, what has been the impact or value?
- What is the observable impact and inferences in the context of medical device competitor cases?
  - Portfolio development
  - Strategy
  - Costs

Nevro – Boston Scientific

Spinal Cord Stimulation Therapy

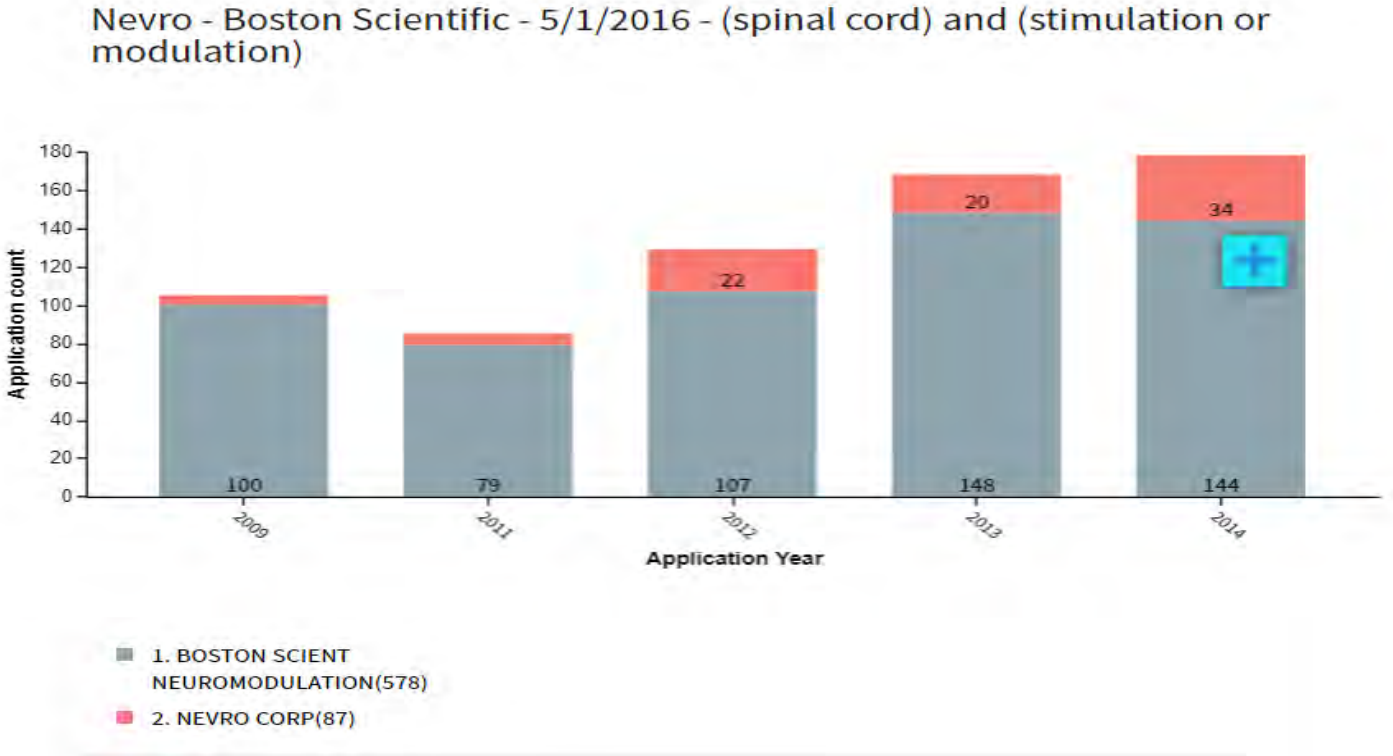
- Nevro obtained FDA approval of their paresthesia-free spinal cord stimulation (SCS) therapy, which treats pain with short electrical pulses. The therapy relieves pain by delivering electrical pulses to the spinal cord through small electrodes that are implanted near the spinal cord.
- FDA Approval of Senza® Spinal Cord Stimulation System Delivering HF10™ Therapy
- Nevro Press Release: Nevro's innovations in SCS, including the SENZA® system and HF10™ therapy, are covered by more than 75 issued U.S. and international patents.

Relative Financials

- Nevro – 2015
- Revenues - $69.6M
- Gross Profit - $41.5M
- Loss - $62.4M

- Boston Scientific – 2015
- Revenues - $7.4B

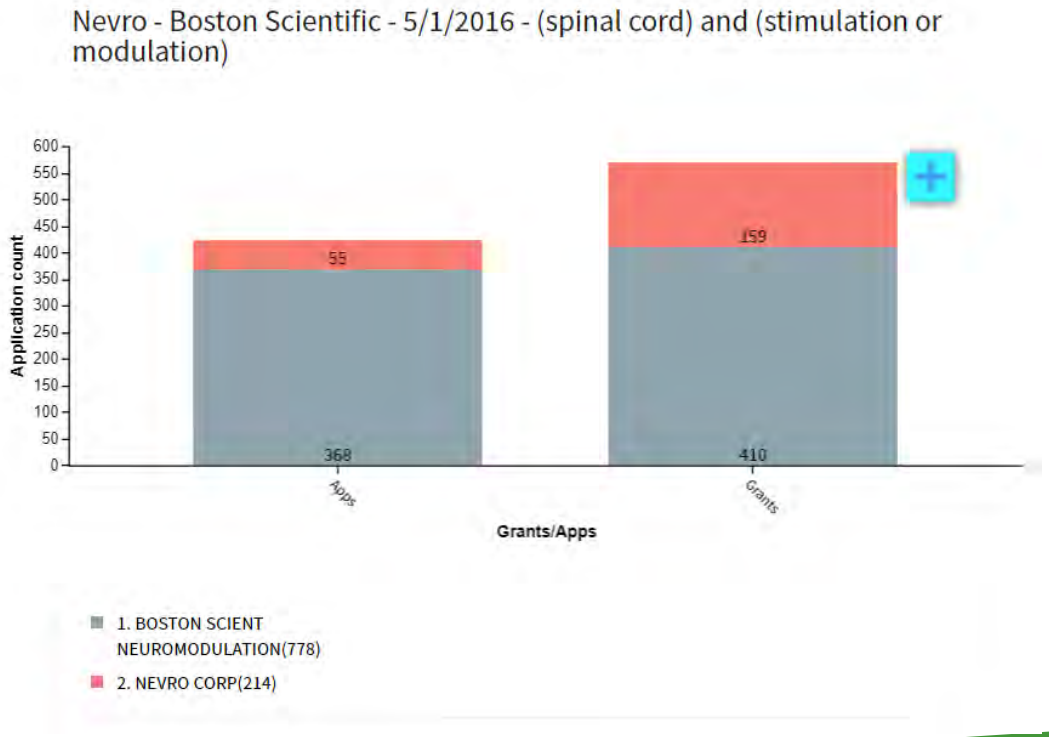
Relative Patent Positions



Relative Patent Positions

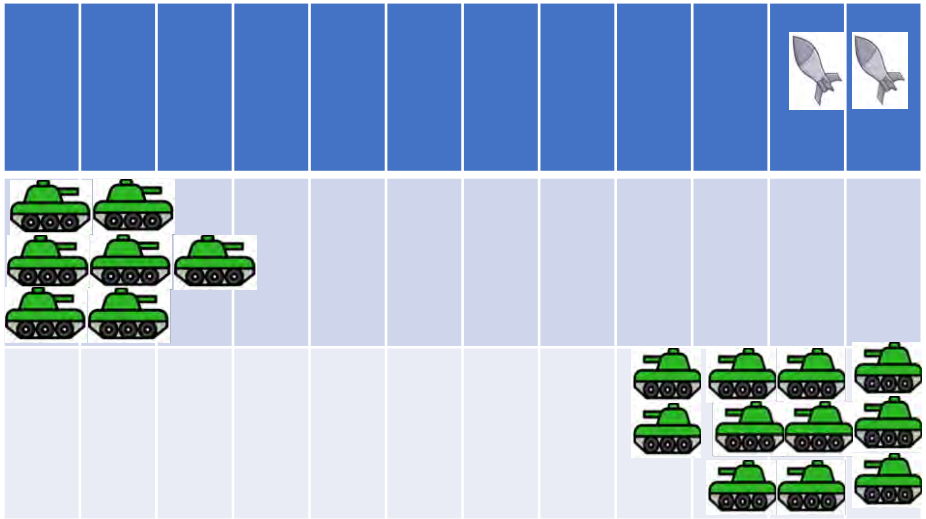
Issued Patents:
Nevro: 159
Boston Scientific: 410

Applications:
Nevro: 56
Boston Scientific 368



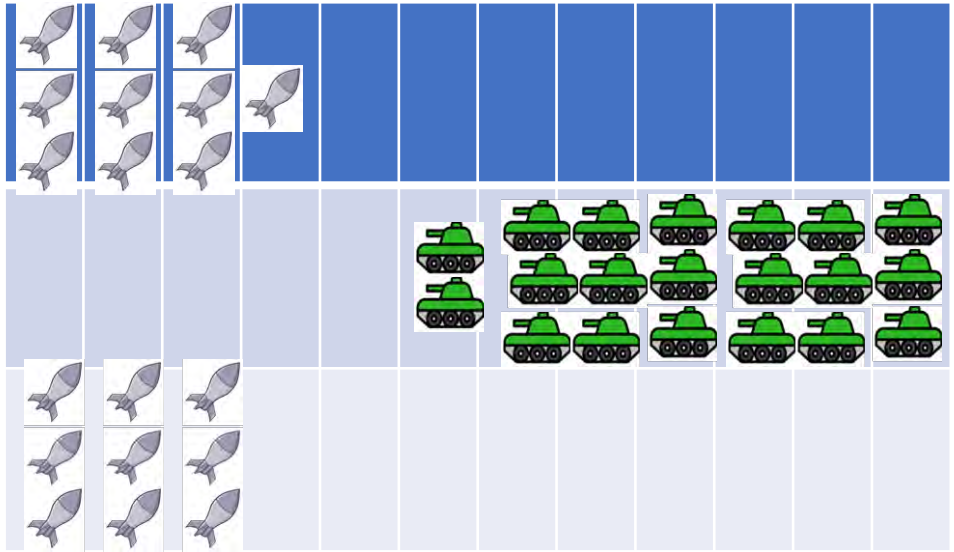
Litigation Maneuvers

- **May 2015** – Boston Scientific files IPR Petitions against one Nevro Patent
  - Nevro wins in Nov. 2015
- **Nov. 2016** – Nevro files patent Infringement suit against Boston Scientific relying on 7 Patents – N. D. Cal
- **Dec. 2016** – Boston Scientific files patent infringement suit against Nevro relying on 11 patents – D. Del



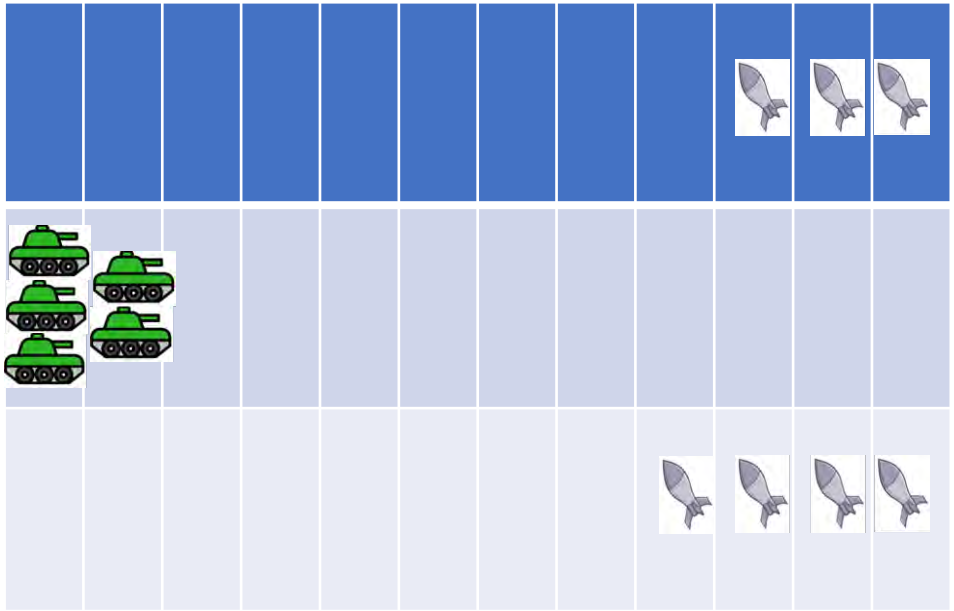
Litigation Maneuvers

- **2017** – Nevro files 10 IPR Petitions against Boston Scientific
- **2018** – Boston Scientific files patent infringement suit against Nevro relying on 20 patents – D. Del.
- **2019** – Nevro files 9 IPR Petitions against Boston Scientific



Litigation Maneuvers

- **2020** Boston Scientific files 3 more IPR Petition seeking to invalidate Nevro patents
- **Feb. 2021** Nevro files patent infringement suit against Boston Scientific relying on 5 patents – D. Del. (New Boston Scientific product Alpha)
- **Feb. 2022** – Boston Scientific files 4 IPR Petitions against Nevro



Scorecard

- IPR Scorecard (till close to settlement date)
  - Nevro 9 wins
  - Boston Scientific 8 wins

- Nov. 2021 – Delaware Jury awards Boston Scientific $20M

IPR Trend – Chronological Determinations

- Tale of two halves – first half (orange Nevro win, Yellow BSC win)

Boston Scientific Neuromodulation Corporation v. Nevro Corporation IPR2015-01203 (PTAB)	5/14/2015	Terminated	11/30/2015	Patentee Won
Boston Scientific Neuromodulation Corporation v. Nevro Corp. IPR2015-01204 (PTAB)	5/14/2015	Terminated	11/30/2015	Patentee Won
Nevro Corp. v. Boston Scientific Neuromodulation Corporation et al IPR2017-01811 (PTAB)	7/21/2017	Terminated	4/2/2018	Patentee Won
Nevro Corp. v. Boston Scientific Corp. IPR2017-01920 (PTAB)	8/11/2017	Terminated	5/3/2018	Joined/Consolidated
Nevro Corp. v. Boston Scientific Corp. IPR2017-01831 (PTAB)	7/21/2017	Terminated	9/20/2018	Patentee Won
Nevro Corp. v. Boston Scientific Neuromodulation Corporation et al IPR2018-00143 (PTAB)	11/2/2017	Terminated	9/21/2018	Patentee Won
Nevro Corp. v. Boston Scientific Neuromodulation Corporation et al IPR2018-00147 (PTAB)	11/2/2017	Terminated	1/7/2019	Patentee Won
Nevro Corp. v. Boston Scientific Neuromodulation Corporation et al IPR2018-00141 (PTAB)	11/3/2017	Terminated	1/7/2019	Patentee Won
Nevro Corp. v. Boston Scientific Neuromodulation Corporation et al IPR2018-00148 (PTAB)	11/3/2017	Terminated	1/7/2019	Patentee Won
Nevro Corp. v. Boston Scientific Neuromodulation Corporation et al IPR2018-00175 (PTAB)	11/10/2017	Terminated	1/7/2019	Patentee Won

IPR Trend – Chronological Determinations

- Second Half (orange Nevro win, Yellow BSC win – blue mixed)

Nevro Corp. v. Boston Scientific Neuromodulation Corporation et al IPR2017-01899 (PTAB)	7/31/2017	Terminated	2/22/2019	Patent Challenger Won
Nevro Corp. v. Boston Scientific Neuromodulation Corp. et al IPR2019-01216 (PTAB)	7/10/2019	Terminated	7/13/2020	Patent Challenger Won
Nevro Corp. v. Boston Scientific Neuromodulation Corp. IPR2019-01315 (PTAB)	7/18/2019	Terminated	7/13/2020	Patent Challenger Won
Nevro Corp. v. Boston Scientific Neuromodulation Corp. IPR2019-01318 (PTAB)	7/15/2019	Terminated	1/19/2021	Mixed
Nevro Corp. v. Boston Scientific Neuromodulation Corp. IPR2019-01341 (PTAB)	7/18/2019	Terminated	1/19/2021	Mixed
Nevro Corp. v. Boston Scientific Neuromodulation Corporation et al IPR2017-01812 (PTAB)	7/21/2017	Terminated	2/16/2021	Mixed
Nevro Corp. v. Boston Scientific Neuromodulation Corp. IPR2019-01284 (PTAB)	7/10/2019	Terminated	3/23/2021	Patent Challenger Won
Boston Scientific Corp. et al v. Nevro Corp. IPR2021-00295 (PTAB)	12/7/2020	Terminated	7/13/2021	Patentee Won
Boston Scientific Corp. et al v. Nevro Corp. IPR2020-01562 (PTAB)	9/8/2020	Terminated	3/14/2022	Patent Challenger Won
Nevro Corp. v. Boston Scientific Neuromodulation Corp. IPR2019-01340 (PTAB)	7/18/2019	Terminated	7/25/2022	Patent Challenger Won
Nevro Corp. v. Boston Scientific Neuromodulation Corp. IPR2019-01313 (PTAB)	7/15/2019	Terminated	8/10/2022	Patent Challenger Won
Boston Scientific Corp. et al v. Nevro Corp. IPR2020-01563 (PTAB)	9/8/2020	Terminated	8/25/2022	Mixed

Nevro’s view of Nov. 2021 Jury Award

- Nevro Press release: The jury awarded Boston Scientific $20 million (Nov. 2021). “This decision has no commercial implications or would otherwise impose any restrictions on any current or future Nevro products, and the jury award is an amount of money that will not have a material impact on Nevro's business.”
- “’We disagree with the finding by the jury and plan to appeal,’” said Kashif Rashid, Nevro's General Counsel.”
- “Nevro's Chairman and CEO, Keith Grossman, stated: "It is important to put this lawsuit into the proper context. The suit regarding lead patents by Boston Scientific was in retaliation for the 2016 lawsuit Nevro filed to stop Boston Scientific from launching a 10kHz spinal cord stimulation system, which would blatantly and directly infringe Nevro's core intellectual property. This lawsuit has absolutely no implications on Nevro's commercial efforts for current or planned products, and is directed to manufacturing methods implemented by our third-party supplier. Nevro will continue to be the exclusive provider of HFX with 10 kHz Therapy, which the FDA determined to be superior to Boston Scientific's SCS therapy.”

https://nevro.com/English/us/investors/investor-news/investor-news-details/2021/Nevro-Announces-Update-in-Patent-Litigation-with-Boston-Scientific/default.aspx

Parties Settle

- Settlement Announced – August 1, 2022
  - Boston Scientific agrees to pay Nevro $85M
- Nevro Corp. (NYSE: NVRO) and Boston Scientific Corp. (NYSE: BSX) announced today that they have reached a settlement in their ongoing intellectual property litigations that gives Boston Scientific the freedom to operate using the features and capabilities embodied in its current line of products for frequencies below 1,500 Hz, and gives Nevro the freedom to operate using the features and capabilities embodied in its current line of products.
- Nevro will grant Boston Scientific a worldwide, non-exclusive, non-transferable license to practice paresthesia-free therapy at frequencies below 1,500 Hz and a covenant not to sue for any features embodied in any current Boston Scientific products for frequencies below 1,500 Hz. Boston Scientific also will grant Nevro a worldwide, non-exclusive, non-transferable license under Boston Scientific's asserted patent families and a covenant not to sue for any features embodied in any current Nevro products.
- This settlement concludes all of the existing litigations between Nevro and Boston Scientific, and includes a net payment from Boston Scientific to Nevro of $85 million.
- https://nevro.com/English/en/about/newsroom/newsroom-details/2022/Nevro-and-Boston-Scientific-Announce-the-Settlement-of-Their-Ongoing-Intellectual-Property-Litigations/default.aspx

Align Technology – 3Shape Intraoral Scanner Systems

- Align Technology

- 2017 Revenues $1.5B

- 3Shape

- 2018 $60m (third party site)

Align Technology – Tech Field

- Align Technology's –
  - Invisalign

  - iTero Oral Scanner

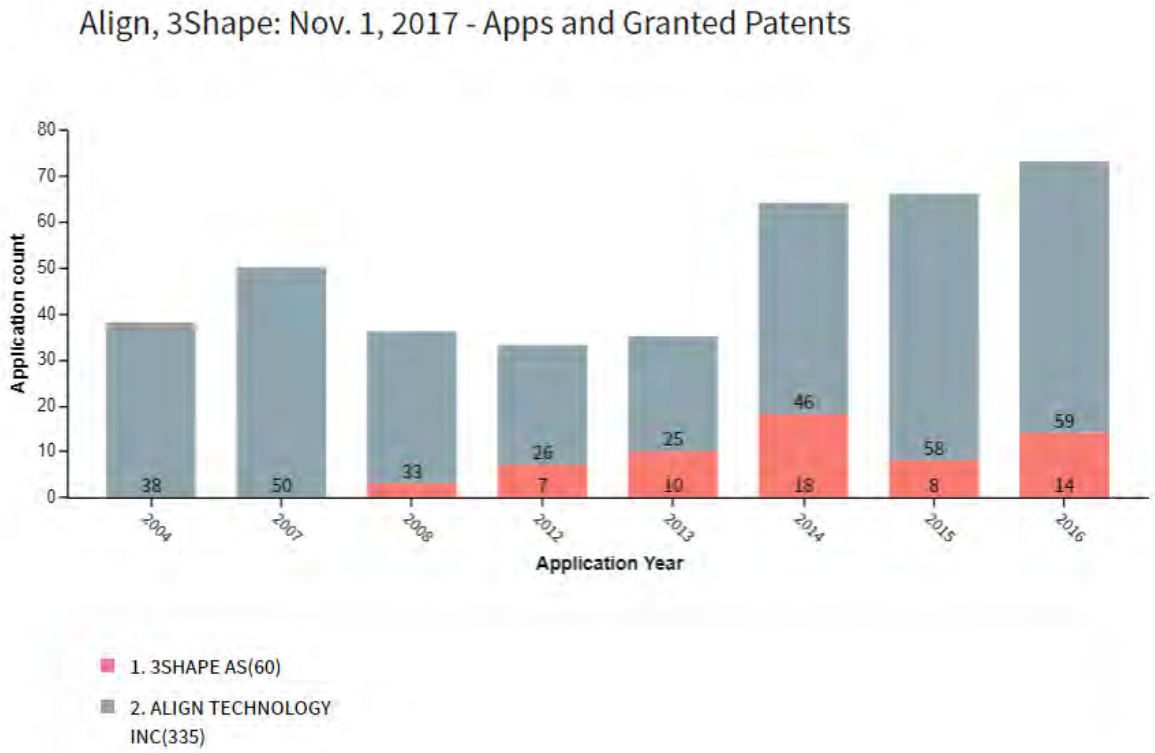
3Shape - Product

- 3Shape – TRIOS Intraoral Scanners

Background

- Align's key patents covering Invisalign's design and manufacturing expired in October 2017, and many of its remaining related patents were to expire by 2019
- 3Shape implemented a feature that allowed an open system – permitted dentists to use the 3Shape TRIOS scans with the Invisalign System
- Align sought to have 3Shape eliminate the open system. Align's Dominance of Clear-Teeth-Straightener Market Tested (1) (bloomberglaw.com)

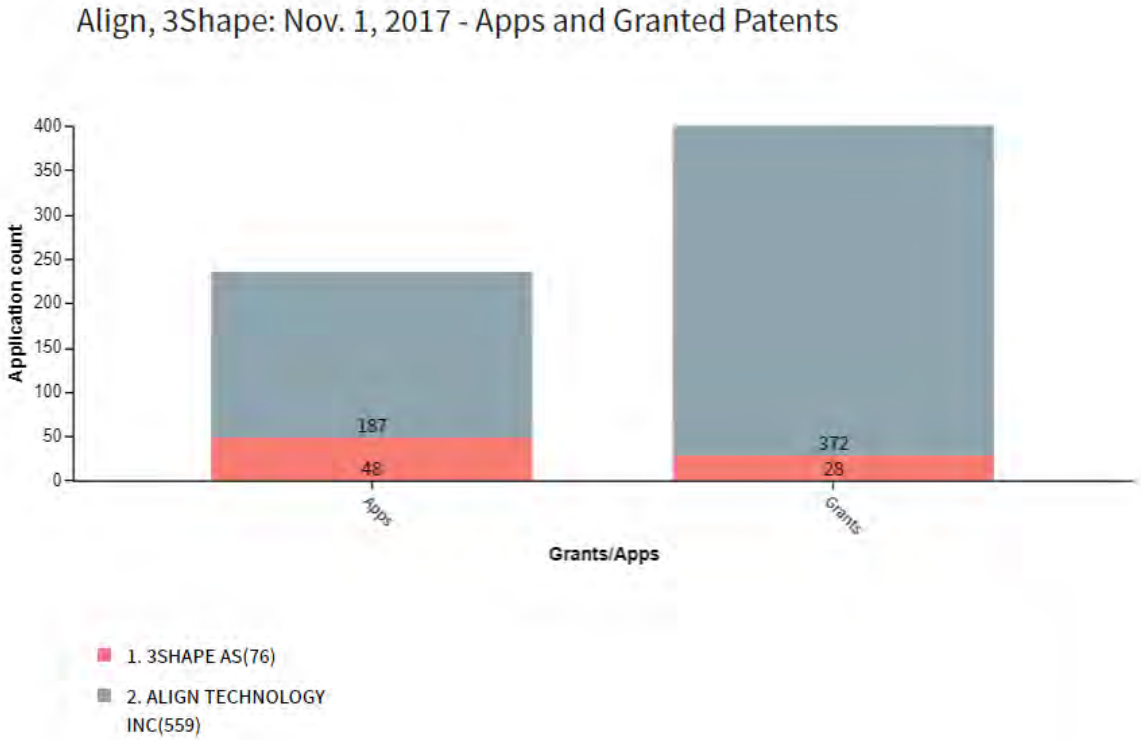
Relative Patent Position



Relative Patent Position

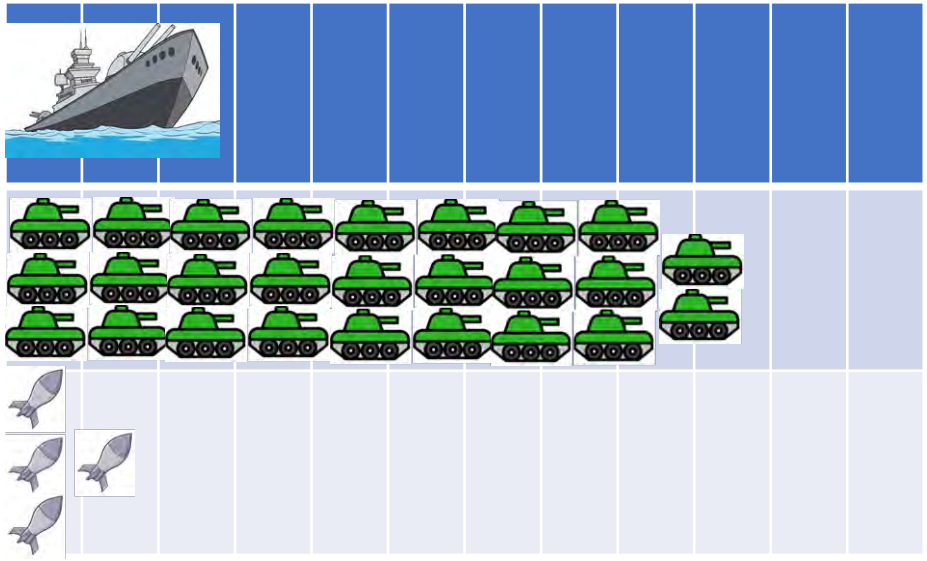
Align: 187 Apps;
372 Granted Patents

3Shape: 48 Apps;
28 Granted Patents



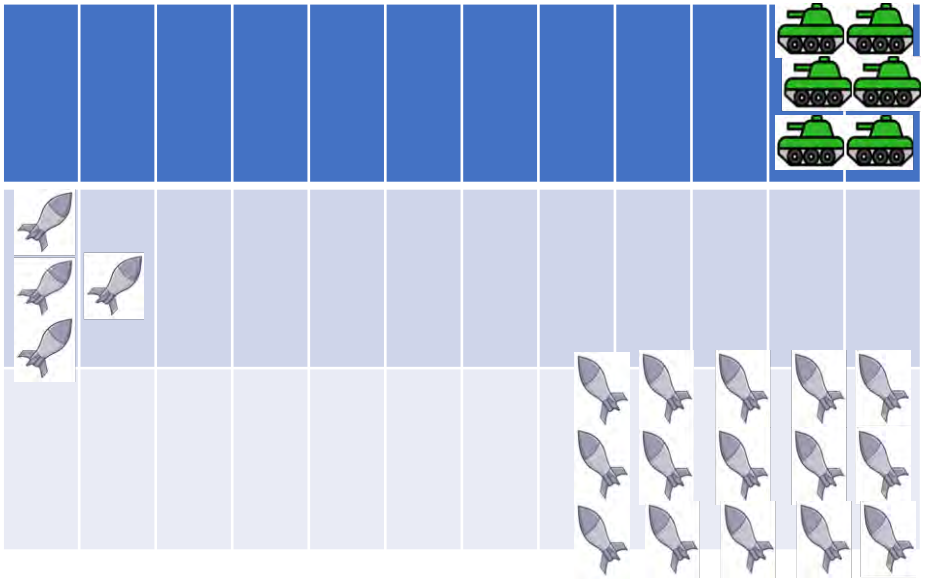
Litigation Maneuvers

- **November 2017** – Align Technology files two complaints in the USITC and requesting an exclusion order – Align asserted 11 patents
- **November 2017** – Align also files four patent infringement lawsuits in the District of Delaware – asserting infringement of a total of 26 patents
- **November 2017** – Align files 4 IPR Petitions seeking to invalidate 4 3Shape patents



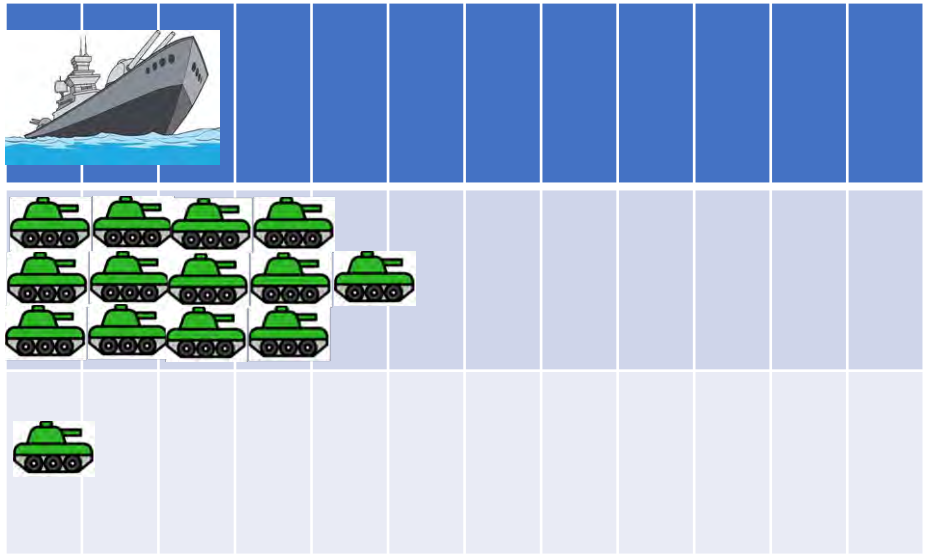
Litigation Maneuvers

- **Mid-2018** –3shape files two patent infringement lawsuits in District of Delaware – asserting infringement of a 6 patents
- **November 2018** – Align files 4 IPR Petitions seeking to invalidate 4 3Shape patents
- **November 2018** – 3Shape files 15 IPR Petitions seeking to invalidate 12 Align patents



Litigation Maneuvers

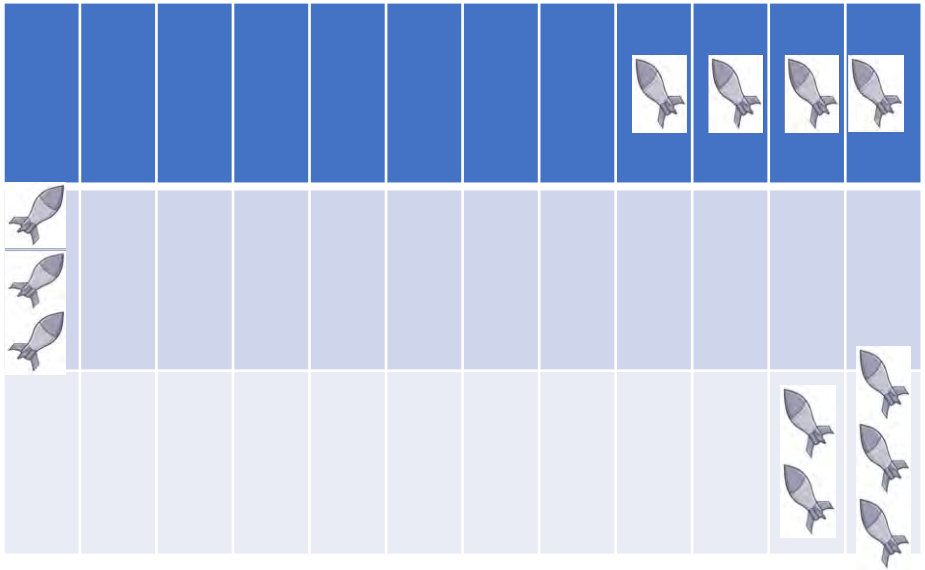
- **December 2018** – Align files another ITC case seeking exclusion order using 5 patents
- **December 2018** – Align files two patent infringement suits in DDE asserting 13 patents
- **November 2019** – Align files a patent infringement suit in DDE asserting 1 patent



Litigation Maneuvers

- **December 2019** – 3Shape files 4 IPR Petitions seeking to invalidate 2 Align patents
- **June 2020** – Align files 3 IPR Petitions seeking invalidate one 3 Shape patent

- **September 2020** - 3Shape files 5 IPR Petitions against 3 Align patents



Litigation Maneuvers

- **October 2020** – Align files patent infringement suit in the Western District of Texas asserting 3Shape infringes 13 Align patents
- **November 2020** – 3Shape files patent infringement suit in the District of Delaware asserting Align infringes 7 3Shape patents
- **From June 2021 and November 2021** 3Shape filed 5 IPR Petitions against 5 Align patents and Align files 9 IPR Petitions against 4 3Shape patents

IPR Scorecard

1. IPR Scorecard up to February 2022:
    1. Align won 8 IPR
    2. 3Shape had won 18 IPRs (3Shape also won 2 ITC and 3 DDE)

Settlement

- February 2022 – Align and 3Shape announce settlement
  - Settlement Terms Confidential
- “Align said customers of its Invisalign may continue using scans from 3Shape’s Trios 2 and 3 intraoral scanners for Invisalign case submissions in certain places outside the U.S., China, and Japan.”
- “Jakob Just-Bomholt, chief executive officer of 3Shape, called the pact ‘fair and equitable’ and said in a press statement that it ends ‘four years of legal infights.’” Align, 3Shape Settle Antitrust, IP Disputes Over Clear Aligners (bloomberglaw.com)

Observations

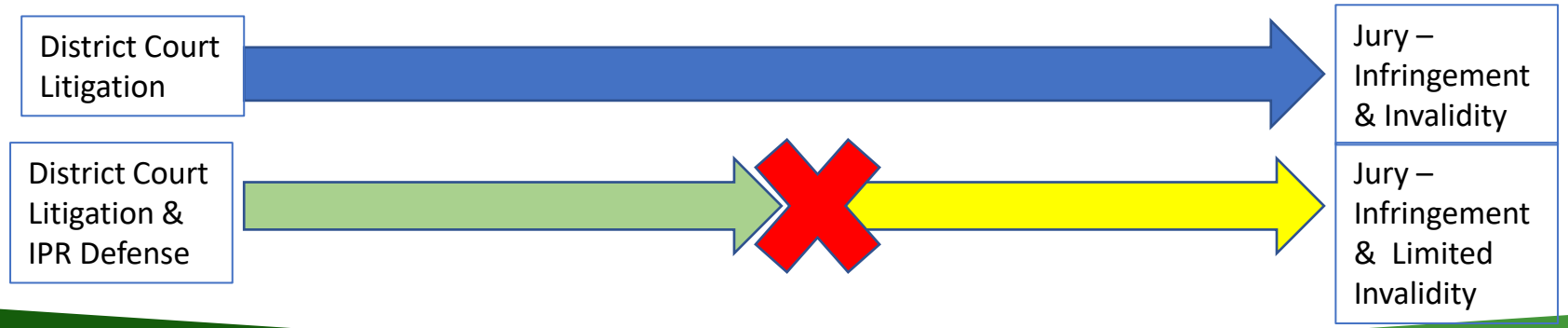
- Key Observations:
  - IPR has been embraced as a critical counter-offensive tool in patent litigation wars involving competitors
  - In these examples, in competitive patent battles, used as a tool to “level” the battlefield
  - Impact on litigation costs
  - Speeds up case resolution

Meaning to Patent Portfolio and De-risking

- Strengthens or weakens patent system?
  - IPR can be filed at any time (subject to one year rule)
  - Patent Office has limited time to conduct “initial” patent prosecution
  - IPR results in a second level (deeper) study of patentability, years later in the context of commercial developments – Patents that survive are viewed differently in assessing litigation case

Meaning to Patent Portfolio and De-risking

- De-risk
  - Block the likelihood of being invalidated in an IPR
    - Patent count may not be a great metric
    - Quality –
      - Better understanding of prior technology landscape
      - Formulate non-obviousness positions
        - Test results in some situations but not all



Meaning to Patent Portfolio and De-risking

- Diversify continuations through continuation applications
- Use continuations for backup invalidity positions
- Keep priority chain open for consideration during increase in commercial activity
- Develop top-down portfolio development strategy and use analytics and research to strengthen portfolio

Thank You

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FDA Enforcement: Negotiating Your Way Forward From a Difficult Starting Place

Medtech Monitor Conference

September 21, 2022

Bryan Feldhaus, Vice President, Legal-Regulatory & Compliance

DuVal & Associates, P.A.

DuVal & Associates
Drug, Device and Food Law

Our Panelists/Speakers

- **Dr. Stephanie Redmond**
  - Co-Founder, Vice President & COO, Dr. Stephanie's Supplements

Dr. Redmond will share her experiences and strategies in responding to enforcement activity from the Food & Drug Administration and the Federal Trade Commission, including reliance on First Amendment protections in promotional claims.

Our story....

"I was frustrated that there were no products available that contained ***enough of*** or ***the right*** active ingredients.

Using medical research and with a team of the top Endocrinologists in the USA, I formulated my own products.

My products offer the most effective combination of ingredients, ***at high enough doses***, with fewer pills, and from one trusted source.

You can feel confident you are getting natural supplements that are truly worth taking.† "

Doctor Stephanie

FDA Warning Letter – Painful Lessons

FDA's point: ingredient claims are considered product claims

On your "Diabetes Doctor Blood Sugar 24 Hour" product page on your website:

- "Studies have shown cassia cinnamon [ingredient in product] at high doses can reduce fasting blood sugars by 25mg/dL
- "Milk Thistle [ingredient in product] ... has been clinically proven to fight resistance for significant benefits on blood sugar health"
  - o "Lower fasting blood sugars by 11%"
  - o "Lower insulin needs by 14%"
  - o "Lower HbA1C by 1.5%"
  - o "Lower abnormal liver enzymes in patients with non-alcoholic fatty liver disease"
  - o "Lower protein in the urine (marker of kidney damage) in patients with diabetic kidney disease"
- "Bilberry [ingredient in product] ...shown improved retinal (eye) circulatory health in adults with diabetic retinopathy after 6 months"
- "Banaba [ingredient in product] acts as a natural insulin sensitizer to support healthy blood sugar and A1C . ...[B]anaba can reduce blood sugars by 30%, and A1C by 0.65%"

Updated Ingredient Section on Website

Banaba Clinical Evidence Links

Clinical Trial > J Ethnopharmacol. 2003 Jul;87(1):115-7. doi: 10.1016/s0378-8741(03)00122-3.

Antidiabetic activity of a standardized extract (Glucosol) from Lagerstroemia speciosa leaves in Type II diabetics. A dose-dependence study

William V Judy [*], Siva P Hari, W W Stogsdill, Janet S Judy, Yousry M A Naguib, Richard Passwater

Affiliations + expand

PMID: 12787964 DOI: 10.1016/s0378-8741(03)00122-3

Abstract

The antidiabetic activity of an extract from the leaves of Lagerstroemia speciosa standardized to 1% corosolic acid (Glucosol) has been demonstrated in a randomized clinical trial involving Type II diabetics (non-insulin-dependent diabetes mellitus, NIDDM). Subjects received a daily oral dose of Glucosol and blood glucose levels were measured. Glucosol at daily dosages of 32 and 48mg for 2 weeks showed a significant reduction in the blood glucose levels. Glucosol in a soft gel capsule formulation showed a 30% decrease in blood glucose levels compared to a 20% drop seen with dry-powder filled hard gelatin capsule formulation (P<0.001), suggesting that the soft gel formulation has a better bioavailability than a dry-powder formulation.

https://pubmed.ncbi.nlm.nih.gov/12787964/

We shared the clinical evidence for our claims

> J Complement Integr Med. 2016 Dec 1;13(4):413-420. doi: 10.1515/jcim-2016-0031.

DLBS3233, a combined bioactive fraction of Cinnamomum burmanii and Lagerstroemia speciosa, in type-2 diabetes mellitus patients inadequately controlled by metformin and other oral antidiabetic agents

Askandar Tjokroprawiro, Sri Murtiwi, Raymond R Tjandrawinata

PMID: 27451997 DOI: 10.1515/jcim-2016-0031

Abstract

BackgroundDLBS3233, a combined bioactive fraction of Cinnamomum burmanii and Lagerstroemia speciosa, has preclinically demonstrated its beneficial effects on glucose and lipid metabolism through the upregulation of insulin-signal transduction. This study evaluated the clinical efficacy of an add-on therapy with DLBS3233 in type-2 diabetes mellitus subjects inadequately controlled by metformin and other oral antidiabetes. MethodsThis was an open and prospective clinical study for 12 weeks of therapy, involving type-2 diabetes mellitus patients who had been treated with two oral antidiabetic agents for at least 3 months prior to screening, yet, with HbA1c level was still beyond 7.0 %. DLBS3233 was given orally at the dose of 100 mg once daily in addition to their baseline oral antidiabetes medication. The primary end point was the reduction of HbA1c level; and the secondary end points were changes of fasting and 1-h postprandial glucose, homeostatic model assessment-insulin resistance, adiponectin, and lipid profile, from their respective baseline. Results After 12 weeks of treatment, the HbA1c level was reduced by 0.65±1.58 % (p=0.001) from baseline (9.67±2.11 %); while the 1-h-PG level was reduced by -1.45±3.89 mmol/L (p=0.021) from baseline (15.29±4.49 mmol/L). Insulin sensitivity, lipid profile and adiponectin level were improved to a considerable extent. DLBS3233 did not adversely affect body weight, liver, and renal function. Most adverse events observed were tolerably mild and they all had been resolved by the end of the study. ConclusionsThe add-on oral antidiabetes therapy with DLBS3233 at the dose of 100 mg once daily helped type-2 diabetes mellitus patients to improve their glycemic control, enhance insulin sensitivity, lipid profile, and adiponectin level. In addition, DLBS3233 treatment concomitantly with other oral antidiabetic agents was proven safe and tolerable in type-2 diabetes subjects.

https://pubmed.ncbi.nlm.nih.gov/27451997/

Cassia Cinnamon Clinical Evidence Link

Review > Ann Fam Med. Sep-Oct 2013;11(5):452-9. doi: 10.1370/afm.1517.

Cinnamon use in type 2 diabetes: an updated systematic review and meta-analysis

Robert W Allen [*], Emmanuelle Schwartzman, William L Baker, Craig I Coleman, Olivia J Phung

Affiliations + expand

PMID: 24019277 PMCID: PMC3767714 DOI: 10.1370/afm.1517

Free PMC article

Abstract

Purpose: Cinnamon has been studied in randomized controlled trials (RCTs) for its glycemic-lowering effects, but studies have been small and show conflicting results. A prior meta-analysis did not show significant results, but several RCTs have been published since then. We conducted an updated systematic review and meta-analysis of RCTs evaluating cinnamon's effect on glycemia and lipid levels.

Methods: MEDLINE, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched through February 2012. Included RCTs evaluated cinnamon compared with control in patients with type 2 diabetes and reported at least one of the following: glycated hemoglobin (A1c), fasting plasma glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), or triglycerides. Weighted mean differences (with 95% confidence intervals) for endpoints were calculated using random-effects models.

Results: In a meta-analysis of 10 RCTs (n = 543 patients), cinnamon doses of 120 mg/d to 6 g/d for 4 to 18 weeks reduced levels of fasting plasma glucose (-24.59 mg/dL; 95% CI, -40.52 to -8.67 mg/dL), total cholesterol (-15.60 mg/dL; 95% CI, -29.76 to -1.44 mg/dL), LDL-C (-9.42 mg/dL; 95% CI, -17.21 to -1.63 mg/dL), and triglycerides (-29.59 mg/dL; 95% CI, -48.27 to -10.91 mg/dL). Cinnamon also increased levels of HDL-C (1.66 mg/dL; 95% CI, 1.09 to 2.24 mg/dL). No significant effect on hemoglobin A1c levels (-0.16%; 95%, CI -0.39% to 0.02%) was seen. High degrees of heterogeneity were present for all analyses except HDL-C (I^2) ranging from 66.5% to 94.72%).

Conclusions: The consumption of cinnamon is associated with a statistically significant decrease in levels of fasting plasma glucose, total cholesterol, LDL-C, and triglyceride levels, and an increase in HDL-C levels; however, no significant effect on hemoglobin A1c was found. The high degree of heterogeneity may limit the ability to apply these results to patient care, because the preferred dose and duration of therapy are unclear.

https://pubmed.ncbi.nlm.nih.gov/24019277/

FDA Warning Letter – Painful Lessons

FDA alleged the term "insulin resistance" is considered a violation

On your Amazon.com storefront product page for your "Diabetes Doctor Blood Sugar 24 Hour" product:

- "Diabetes Doctor Daily Support – 7 in 1 Blend for Daily Diabetes Needs and High Blood Sugar Regulation - Target Insulin Resistance and Sensitivity, Organ Health ..."
- "REVOLUTIONARY BLEND AND HIGH DOSES: ... natural ingredients needed for daily Diabetes support and blood sugar regulation"
- "COMBAT INSULATION RESISTANCE: Diabetes Doctor's powerful blend of Cinnamon, Banaba, Magnesium, and Chromium helps promote healthy insulin function ..."

Using the word "Diabetes" in any context (i.e. Diabetes Support) is an alleged violation

"Blood Sugar Regulation" is an alleged overt violation – not approved internally & listings managed by 3rd parties

FDA Warning Letter – Competitive Claims

Products (Amazon Listings & Packaging)

About this item

- FULL SPECTRUM OF BENEFITS TO PEOPLE WITH BLOOD SUGAR CONCERNS: (1) Promotes normal blood sugar levels, (2) Promotes weight loss, (3) Reduces absorption of sugars & other carbohydrates, (4) Promotes healthy insulin sensitivity & production, (5) Promotes healthy cholesterol, heart, blood vessels & circulation, and (6) Promotes healthy energy.
- HOW GLUCOCIL WORKS: Not many people know that there are 3 Essentials for keeping your blood sugar normal: (1) Reduce sugar absorption from food, (2) Reduce the liver's sugar production, and (3) Increase the body's use of sugar for energy. Target any one of the 3 Essentials and you'll improve your blood sugar levels. But target all 3 Essentials together, and you'll help keep your levels within the normal range. ONLY GLUCOCIL TARGETS ALL 3 ESSENTIALS FOR NORMAL BLOOD SUGAR.
- EXTRA STRENGTH SOFTGELS (*2,250mg OF ACTIVE INGREDIENTS PER SERVING): Doctor formulated, proprietary blood glucose management blend, 14 clinically researched ingredients based on more than 100 published research studies, including human clinical studies on Glucocil's proprietary mulberry leaf extract, which was shown to instantly lower peak post-meal elevations by up to 44%.
- OVER 1 MILLION BOTTLES SOLD: The Simple Secret of Targeting All 3 Essentials for Normal Blood Sugar + Support Overall Wellness for Enjoying Life More, since 2008, made in a registered GMP facility in USA, 100,000+ Facebook fans.
- DIRECTIONS: For the first 3 days, take 1 softgel with lunch and 1 softgel with dinner. After 3 days, take 2 softgels with lunch and 2 softgels with dinner. As with any nutritional supplement, talk with your doctor before using Glucocil.

Compare with similar items

Consider a similar item

Nature Made Diabetes Health Pack, 60 Packets

Visit the Nature Made Store

4.4 out of 5 stars 1,420 ratings | 28 answered questions

Special Ingredients	Docosahexaenoic acid, Fish Oil
Brand	Nature Made
Item Form	Packets
Color	A
Ingredients	Acetate, Beta Carotene, Ascorbic Acid, Cholecalcifero, dl-Alpha Tocopheryl Acetate, Phytonadione, Thiamin Mononitrate, Riboflavin, Niacin, Pyridoxine Hydrochloride,...

See more

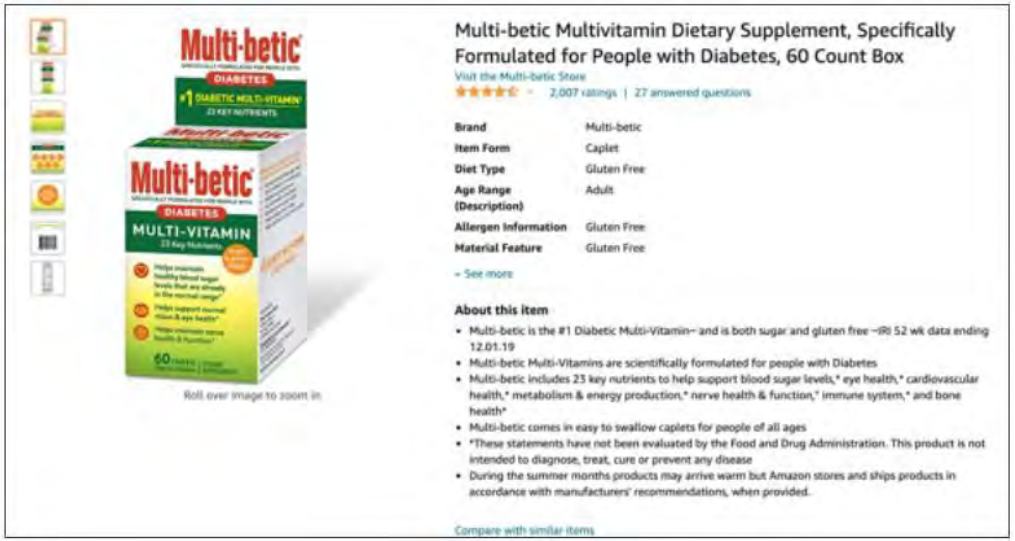
About this item

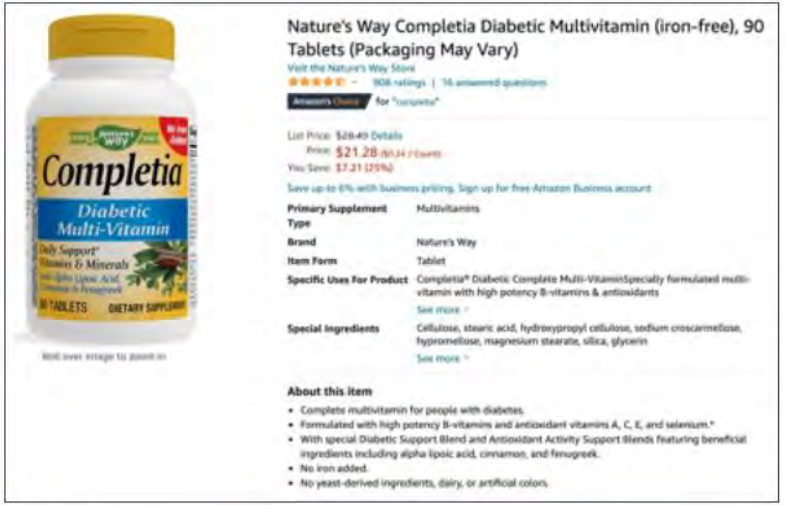
- Each box contains 60 packets of multi-vitamin and mineral supplements for diabetics.
- Provides essential vitamins and minerals for daily nutritional support
- Contains A comprehensive combination of key vitamins, minerals, and other supplements including EPA and DHA omega-3 fatty acids, which help support A healthy heart
- Nature Made diabetes health pack is scientifically formulated to provide daily nutritional support for people with diabetes or prediabetes
- During the summer months products may arrive warm but Amazon stores and ships products in accordance with manufacturers' recommendations, when provided.

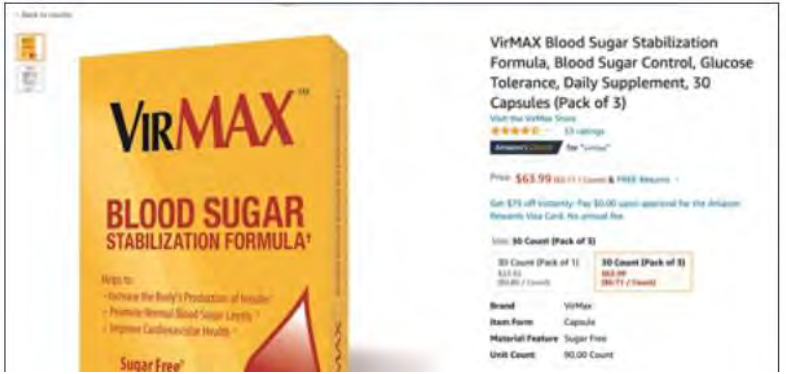
Compare with similar items

FDA Warning Letter – Competitive Claims

Products
(Amazon Listings & Packaging)



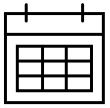




Take Home Lessons

- Never assume its OK… even if other (bigger) companies are doing it
- Need checks & balances with legal as you grow, fast
- FDA has a LOT of power & discretion in their interpretation
- Underestimated the impact this would have on retail partnerships & “eternal” restrictions on Amazon

Timeline of Events



FDA U.S. FOOD & DRUG ADMINISTRATION

- **9/9/2021 – Warning letter issued**
- 9/22/2021 - Submitted Official Response to FDA/FTC
- 10/11/2021 – Follow-Up Prompt sent to FDA/FTC
- 10/28/2021 – Second Follow-Up Prompt sent to FDA/FTC
- 11/9/2021 – Amazon listing restricted/removed permanently
- **1/19/2022 – FDA Close-Out Letter Issued**

Dr. Stephanie's™

All-Natural Supplements

#1 BEST SELLING BLOOD SUGAR SUPPORT IN-STORES!

Tested to be Trusted™

CVS pharmacy®

Walmart

Walgreens

Kroger®

Our Panelists/Speakers

- **Todd Bailey**
  - President & CEO, Premier Biotech (by video)
- **Dr. Larry Masterson**
  - Director of Product Operations & Development

Todd and Larry will share the story of going from a seemingly unregulated and FDA-exempt medical device product portfolio to a disagreement with FDA over the status of these products, and then negotiating enforcement discretion with FDA to obtain FDA 510(k) clearance for their products.

FDA regulations in the Drugs of Abuse Detection Industry:

navigating compliance and leading changes

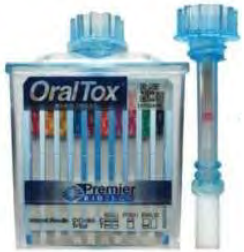
Dr. Larry R. Masterson

Director of Product Operations and Development

September 21, 2022

Premier BIOTECH

Established in 2009, founded by Todd Bailey (CEO, owner)



[redacted]

OralTox

- Pre/continued employment & reasonable suspicion
- Forensics/corrections/law enforcement
- Clinical/treatment

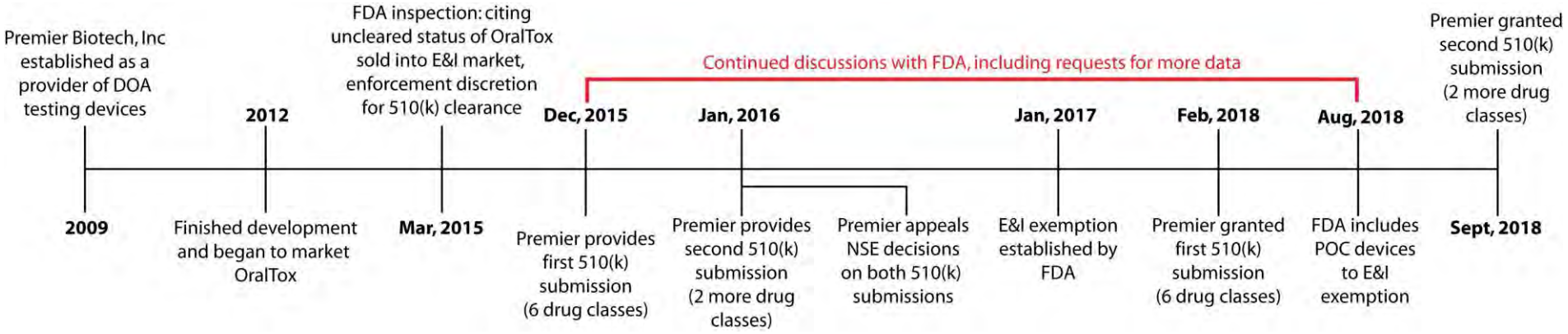
[redacted]

BioCup/BioDip

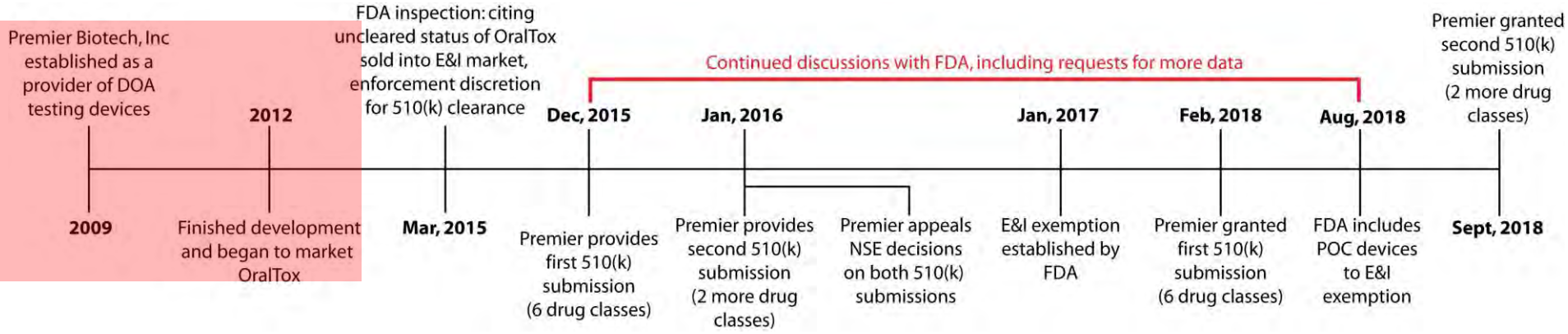
- Pre/continued employment & reasonable suspicion
- Forensics/corrections/law enforcement
- Clinical/treatment

Oral Detect

- Road side DOA testing by law enforcement



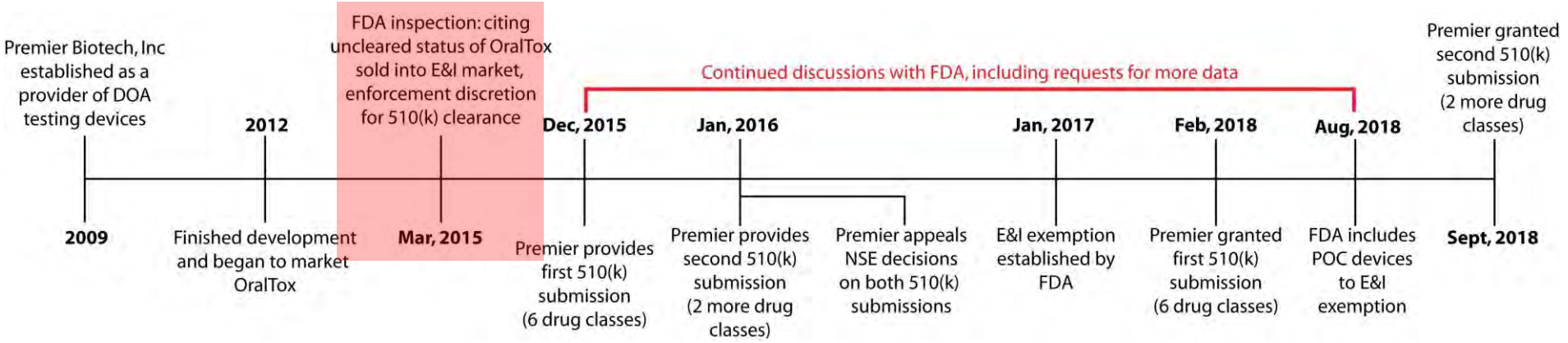
Timeline of events regarding OralTox



Company established based on owner's 15+ years experience in selling drugs of abuse testing products in industry

Developed concept, patented and marketed OralTox by 2012

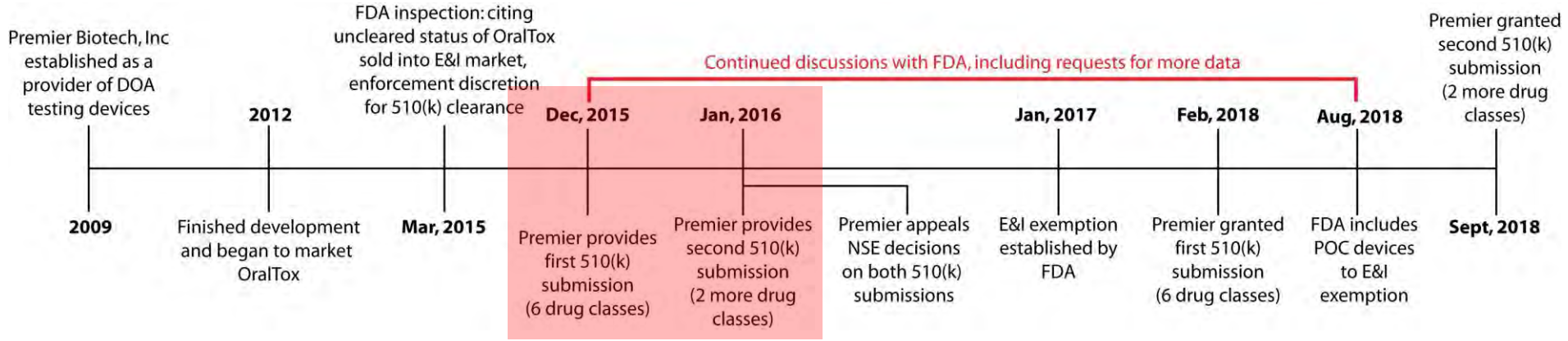
Focused on corrections and pre-employment industries, exempt from requiring pre-market clearance from FDA to market product



Visit by FDA, citing Premier of uncleared device sold into to employment

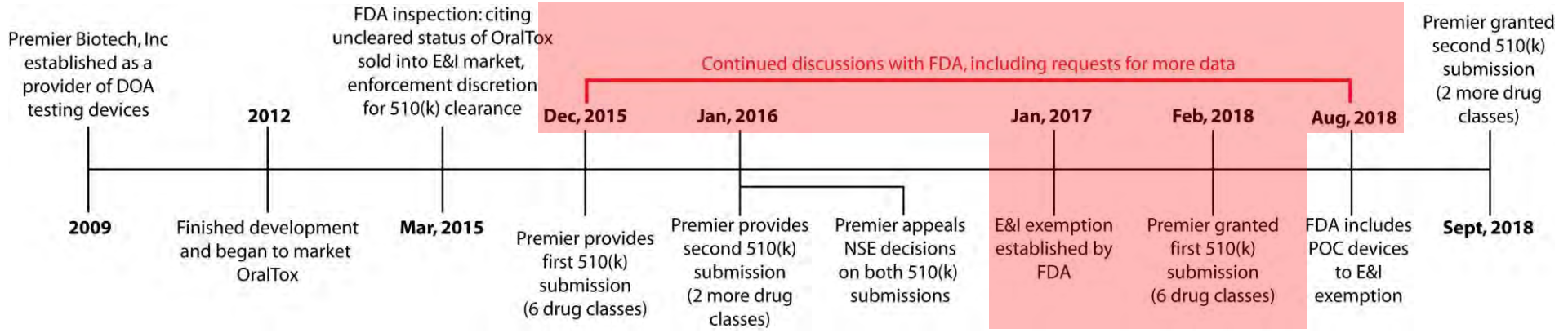
Premier/DuVal initially disagreed with FDA on intended use – similar to forensic purposes (non-treatment/diagnosis) and within FUO

Worked with FDA, agreed to submit 510(k); was able to continue marketing device as labeled during interim under negotiated enforcement discretion



Spent ~$2 million in obtaining data to provide two submissions to FDA in order to capture eight different classes of drugs intended for employment market

Due to Premier establishing a forensic/clinical drug testing laboratory, able to leverage variety of locations as testing sites

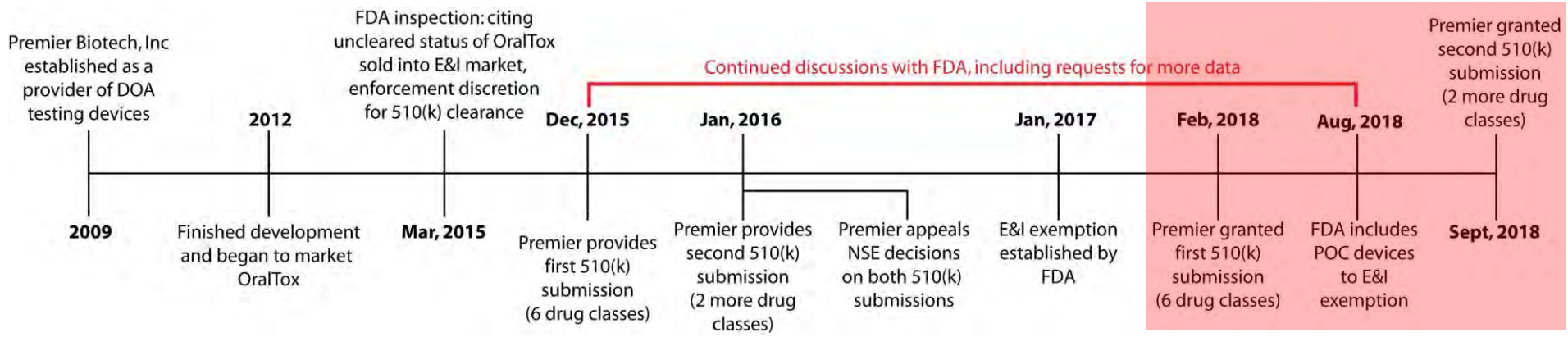


FDA required further testing and made a number of request to expand results

- **Premier able to leverage locations like needle exchange clinics to obtain fresh donor samples for PCP point of care testing.**

A few months prior to approval, FDA reached out to notify Premier about a new exemption status: "Employment and Insurance Use Only" (E&I)

- **Offered Premier to withdraw 510(k) submission; rejected this offer – too far into process**
- **FDA also initially claimed exemption would not cover point-of-care devices. Premier noted previous communications about this matter that contradicted that statement**



In 2018, Premier granted with two 510(k) clearances on OralTox for eight different drug classes

Remains the only 510(k) cleared oral fluid-based POC drugs of abuse testing device for eight drugs

Since 2018 510(k) clearance of OralTox:

- Premier considered adding barbiturates and benzodiazepines to 510(k), but instead used E&I exemption
  - Competitor devices were being added quickly under this new exemption with such clearances

- Labeled OralTox under E&I exemption as OralTox to help distinguish this version to end-users and make marketing material clear

- OralTox device has grown in popularity within employment and forensic sectors during and after pandemic

Thank you!

Update on VC Financings

Fox Rothschild LLP
ATTORNEYS AT LAW

Patrice H. Kloss, Partner, Fox Rothschild LLP

Tom Moran, Associate, Fox Rothschild LLP

Learn the pros and cons of structuring a strategic investment from experienced MedTech attorneys, along with guidance regarding governance, control, protection of intellectual property and additional rights often associated with strategic investments and acquisitions.

Benefits/Opportunities and Risks/Challenges

A. Benefits/Opportunities to Start-up Company

1. raise needed capital
2. broader marketing and distribution options
3. better access to, and credibility in capital markets with, other third parties (e.g., lenders) – also can be very important for future VC rounds
4. increased visibility and name recognition in marketplace
5. develop relationship with a potential acquirer
6. expertise at board meetings in the form of a Strategic Partner board observer or director
7. access to regulatory and other expertise
8. lower cost of capital, less dilution than often required with VC investors

Benefits/Opportunities and Risks/Challenges (con't.)

B. Risks/Challenges to Start-up Company

1. loss of control or independence – either through contract terms or as a result of issuing equity to Strategic Partner; possibility of "creeping acquisition"
2. loss of value or value of future opportunity, whether commercializing product or sale of Company; challenge of setting a value
3. loss of entrepreneurial and technological edge – Company may become R&D arm of Strategic Partner
4. accountability to Strategic Partner
5. Strategic Partner may back out – product or Company may be tainted
6. Turn-over of Strategic Partner's management team or loss of internal advocate

Key Terms

A. Governance

1. Board seat vs. observation rights
2. Limitation of participation when conflict of interest exists

B. Control

1. Voting thresholds
2. Special voting rights (consider Strategic Partners' ability to block a sale of the company)

C. Protection of Intellectual Property

1. Use of nondisclosure agreements
2. Limit what is disclosed when

Key Terms (con’t.)

D. Side Letters

1. Differs from VC management rights letter
2. Board observer rights
3. Information rights
4. Special confidentiality provisions
5. Restrictions on use of Strategic Partner’s name
6. Special rights (right of first negotiation or notice rights)

Key Terms (con't.)

E. **Additional Rights**

1. Types:
   - Option to purchase
     - Fixed price
     - Price based on some method of calculation
     - Exclusivity period.
   - Right of first negotiation
   - Right of first refusal
   - Distribution
   - Manufacturing
   - Licensing
   - R&D arrangements

2. Termination/Exercise Issues
   - Essential that arrangement END upon change of control – otherwise it will be very difficult to sell business to a third party.
   - Include appropriate performance measures/minimums in license/distribution agreement – need to be able to back out if it's not working out.
   - Consider when purchase options and rights of first refusal or negotiation are triggered

Conclusion / “Take-Aways”

A. **Go in with eyes wide open.**

B. **Develop well-defined and mutually beneficial goals for the alliance.**

C. **Make certain there is multi-level “buy-in” and support for the alliance by the Strategic Partner.**

D. **Provide for effective communications and management of the alliance.**

FDA Submissions: When to Appeal or How to Avoid It

Medtech Monitor Conference

September 21, 2022

Mark DuVal, President & CEO

DuVal & Associates, P.A.

DuVal & Associates
Drug, Device and Food Law

Our Panelists/Speakers

- **Dan Clark**
  - Founder, President & COO, Linear Health Sciences

Dan will tell the story of the tortuous path it took to obtain clearance of this device which also resulted in an appeal to Dr. Maisel, Director, Office of Product Evaluation and Quality (OPEQ), CDRH.

Our Panelists/Speakers

- **Sal Salamone**
  - President & CEO, Saladax Biomedical

Sal will tell the story of struggling with FDA review staff to obtain a clearance or a de novo for Saladax's TDM to monitor blood levels of the drug clozapine and how Saladax was finally able to obtain the de novo after an appeal to Dr. Maisel, Director, Office of Product Evaluation and Quality (OPEQ), on a Least Burdensome (LB) Flag.

LINEAR™
HEALTH SCIENCES

Connecting Patients to Treatment, Better

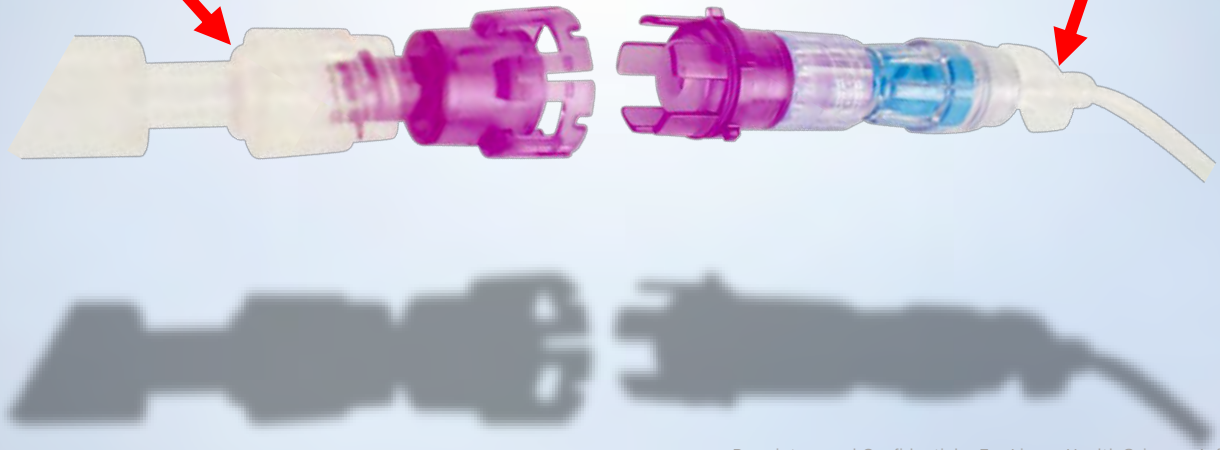
Daniel Clark
310.721.6222
Dan.Clark@linearsciences.com

Proprietary and Confidential – For Linear Health Sciences Information Only

ORCHID™
Safety Release Valve

IV Administration Set

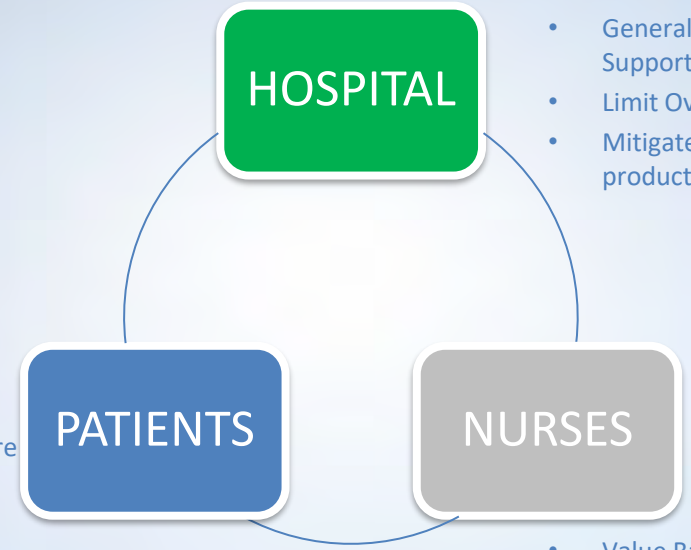
IV Extension Set



LINEAR™
HEALTH SCIENCES

Orchid SRV - Value Focused:

PILLAR TRIFECTA



- General Reimbursement Focused Support
- Limit Overtime re: redundant activity
- Mitigate wasted capital, redundant product use

- Retain IV Site Integrity, Continuity of Care
- Minimize Invasive Procedures
- Minimize Sharps Exposure
- Reduced Invasive Procedure Risk
- Patient Satisfaction

- Value Based Time
- Increased Value-Based Activity
- Minimize Sharps Exposure
- Minimize Fluids Exposure

LINEAR™ HEALTH SCIENCES

A Long Regulatory History

- **August 2019** – Linear Health Sciences initially submitted a 510(k) submission to Third Party Review Group (TPRG).
- **January 2020** – 510(k) submitted to Third Party Review Group (TPRG)
- **February 2020 –**TPRG recommended 510(k) submission for SE
- **March 2020 – 1st NSE issued**, no justification provided
- **March 2020 –** A clarification meeting was requested
- **March 2020 –** Reviewer requested that Linear provide context for the requested call; context provided; reviewer requested de novo path be followed
- **April 2020 – *Request for reconsideration of NSE filed to Dr. Maisel (beyond 30 days under 517A)***
- June 2020 – Receipt of substantive summary
- **June 2020 – *Reconsideration of NSE denied by Dr. Maisel***
- **July 2020 – *1st Pre-submission*** for De Novo ***clinical trial not needed***
- **August 2020 –** 2nd Pre-submission for De Novo acknowledgement
- **September 2020 –** PEUA Acknowledgement

LINEAR™ HEALTH SCIENCES

A Long Regulatory History

- **November 2020 –** revised meeting minutes for 1st Pre-submission (acknowledged 7/22/2020)
- **November 2020 –** ***cancelled 2nd Pre-submission*** for De Novo
- **November 24, 2020 –** ***Call with Capt. Stevens, no clinical trial required;*** instead justification provided, modified labeling
- **January 27, 2021 – 10.75 Appeal** (denied February 2, 2021)
- **March 3, 2021 – Informal appeal meeting with Dr. Maisel held**
- **May 27, 2021**—On the day of our second appeal meeting with the review staff and Dr. Maisel; review staff debated our data, but failed to tell us that de novo for SafeBreak Vascular was granted and new Special Controls created
- **July 16, 2021**—K212064 was accepted for substantive review
- **July 30, 2021**—***AINN issued; only deficiency related to Special Control 1***

LINEAR™ HEALTH SCIENCES

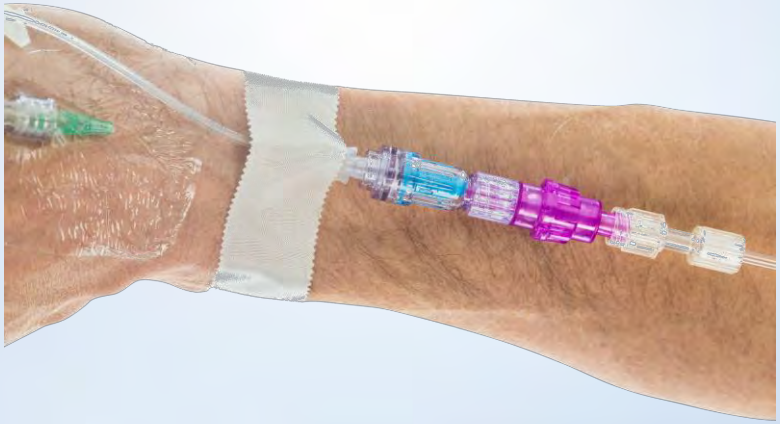
A Long Regulatory History

- **October 1, 2021—*AINN Letter issued (21 pages long)***
- **October 13, 2021—**A 10-Day Teleconference was held in which the review staff; ***reiterated that they were not asking for clinical testing, but simply wanted the missing justification***
- **October 26, 2021—**K212064/S002 was acknowledged under review
- **November 17, 2021—**Interactive deficiency letter received (10 pages long) with request for two-day turnaround
- **November 18-19, 2021—**Interactive deficiency responses to all deficiencies were sent to the review group
- **November 23, 2021—*2nd NSE Issued*; NSE stated separation force could only be answered with a clinical trial, *contrary to a) what the review staff had stated in the appeal meeting, b) calls and email with Capt. Stevens, and c) in the 10-Day teleconference with Payal Patel and Dr. Tina Kiang***

LINEAR™ HEALTH SCIENCES

A Long Regulatory History

- **January 18, 2022 – Appeal Hearing Held with Dr. Maisel**
- **March 3, 2022 –** Appeal findings returned, overwhelmingly in favor of Linear Health Sciences
- **April 4 –** Additional clarification call following Appeal Findings
- ***May 3, 2022 – FDA Clearance Provided***



LINEAR™ HEALTH SCIENCES

EXPERIENCES WITH THE FDA

FOX/DUVAL MEDTECH MONITOR CONFERENCE

September 21, 2022
Minneapolis, MN

Saladax BIOMEDICAL
DIAGNOSTICS THAT MAKE A DIFFERENCE

Sal Salamone, Ph.D.
Founder and CEO

SAL SALAMONE, FOUNDER AND CEO
SALADAX BIOMEDICAL, INC.

35+ years in leadership and R&D healthcare and medical devices

Roche Diagnostics As Vice President, R&D, his leadership resulted in the launch of 7 reagent product lines, 70+ FDA approvals and 200+ instrument applications that generated $1B+ in revenue

A global expert in therapeutic drug monitoring, with >100 publications. Inducted into the New Jersey Inventors Hall of Fame (2016) and recipient of C.E. Pippenger Award for outstanding work in the field of therapeutic drug monitoring (TDM)

INTRODUCTION TO SALADAX

A proven leader in developing high value, quality in vitro diagnostic assays

- Proprietary technology based on a flexible, instrument-agnostic, nanoparticle method
- Proprietary immunoassays
  - 60 granted US patents and 400+ international patents
- Saladax is ISO13485 certified and follows FDA cGMP guidelines
- Extensive experience in development, regulatory approval process and commercialization
- Expertise sought by leading global pharmaceutical companies
- Multiple international licensing agreements
- Located in Bethlehem, PA

Saladax BIOMEDICAL
DIAGNOSTICS THAT MAKE A DIFFERENCE

DISTRIBUTED WORLDWIDE

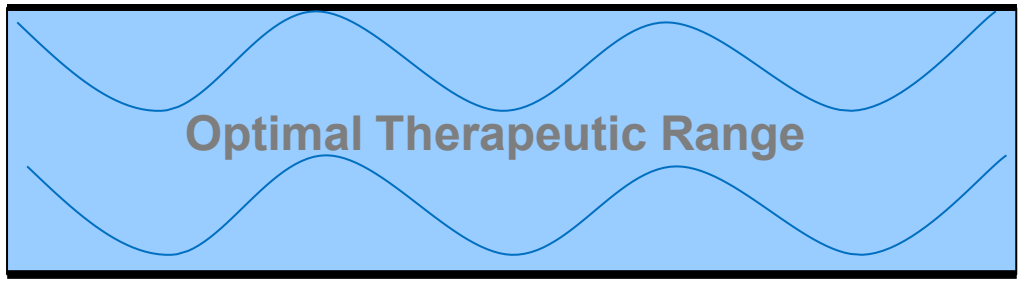
Addressed Markets

USA	Germany	Greece
Canada	France	Finland
United Kingdom	Italy	Denmark
Switzerland	Poland	Sweden
France	Spain	Croatia
Belgium	Israel	
Brazil	China	

- ISO 13485 certified for kits production
- GMP and GLP facility
- Multiple instrument and reagent placements
- Psychiatry and oncology products distributed worldwide

Therapeutic Drug Management

Too High → Toxicity; Treatment termination; Higher costs to healthcare system



Too Low → Lack of therapeutic response; Higher cost of recurrence

PSYCHIATRISTS CAN STOP GUESSING

Saladax has the first and only technology which provides doctors with rapid quantitative measurements of the active drug in a patient's blood.

At the Point of Care

In the Laboratory

MyCare™ Psychiatry

Saladax BIOMEDICAL
DIAGNOSTICS THAT MAKE A DIFFERENCE

Increasing Complexity Over Time

1980's

- 510(k) approvals averaged 3 months
- PMA's 1 to 2 years

1990's

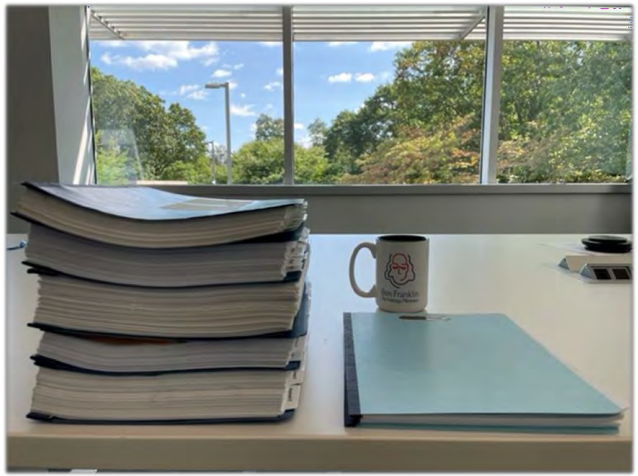
- Design Control implemented and created more complexity despite advertisements from the FDA that it would make the process easier.
  - Increased paperwork
  - Increased labor
  - Increased expenses
  - Typical 510(k) applications were 90 pages
  - De Novo process guidance documents developed

2000 and beyond

- Ever increasing requirements and very little negotiations
- Use of the de novo process to ask for additional studies
- Timelines have been extended
- Applications > 1000 pages

The Burdensome Approach to Approval

FDA submission 2021 versus pre-2000's



Design Control Files for one Assay (65 Folders)

Saladax BIOMEDICAL
DIAGNOSTICS THAT MAKE A DIFFERENCE

Concerns Moving Forward

- Changing requirement with additional work
- Cannot follow precedence of previous applications
- Advice from pre-subs often meaningless
- Inexperience reviewers
  - Requiring studies that are not relevant
  - Often impractical non-value added work
- Less flexibility and very little negotiations
- Request are becoming more burdensome and costly
- While the regulatory burden has increased the quality has not really improved

Saladax BIOMEDICAL
DIAGNOSTICS THAT MAKE A DIFFERENCE

DEVICE PRESENTATION

MyCare Psychiatry Clozapine Assay Kit

Intended Use (proposed in DEN190028):

Rx Only

The MyCare Psychiatry Clozapine Assay Kit is intended for the in vitro quantitative measurement of clozapine in adult human serum using automated clinical chemistry analyzers. Measurements obtained can be ***used to aid in the overall management*** of individuals prescribed clozapine ***by monitoring for therapeutic levels*** and ***assisting in the clinical evaluation of adherence***. This assay ***should be used in conjunction with other clinical and laboratory findings*** and ***results from this test alone should not be used to make treatment decisions***.

ASCP
American Society of Clinical Psychopharmacology

June 19, 2018

Dear Sirs:

The Board of The American Society of Clinical Psychopharmacology is offering an opinion in the context of the following:

It has come to our attention via a Board member who has small grant from Saladax to collect blood levels on patients receiving antipsychotic drugs that Saladax will be launching a line of rapid tests to measure levels of risperidone, paliperidone, clozapine, aripiprazole, quetiapine and olanzapine for use in monitoring adherence and determining appropriate therapy. These tests will be able to run on clinical analyzers found in most hospital laboratories. Saladax is formulating a request to the FDA for pre-market review of the assays. In discussions with the FDA during the Pre-Submission process, the FDA indicated:

1. *TDM for these drugs is not commonly used in US clinical practice, and questioned whether such measurements are clinically relevant.*

2. *There doesn't exist practice guidelines and consensus recommendations that are recognized and adopted by US physicians and clinical organizations for the management of US patients. Since the AGNP guidelines are European based, the FDA questions their applicability in the US. Saladax Biomedical has formulated a position for clinical utility based upon US literature citations and the internationally authored AGNP guidelines. The application would be significantly improved with supporting statements from US based organizations that physicians rely on for treatment guidance.*

ASCP

We firmly believe that therapeutic drug monitoring (TDM) is an important aspect of evidenced-based and personalized psychopharmacologic treatment.

The opportunity provided by TDM is greatly diminished, however, by the general lack of availability of rapid turnaround assays for many relevant medications. If such tests were readily available there would be many situations where clinicians would find them to be highly relevant in making day-to-day decisions.

…

It is also critical to recognize that therapeutic drug monitoring provides the opportunity to assess compliance/adherence, allowing for far more informed clinical decision making.

…

In summary, there is compelling evidence that TDM can be a very important source of critical clinical information. Making such data more readily available to clinicians is highly desirable. It will be very valuable to patients and families in improving outcomes.

are recognized and adopted by … organizations for the management of US patients. … delines are European based, the FDA questions their appli… e US. Saladax Biomedical has formulated a position for clinical …ility based upon US literature citations and the internationally authored AGNP guidelines. The application would be significantly improved with supporting statements from US based organizations that physicians rely on for treatment guidance.

Saladax BIOMEDICAL
…OSTICS THAT MAKE A DIFFERENCE

Clozapine Experience

August 2017 – Clozapine Pre-Sub

- Met with FDA October 2017 for feedback
- FDA was not aware of testing for this drug or antipsychotics in general

May 2019 – Clozapine De Novo

- AINN Letter received August 2019
- After multiple discussions it was apparent that the application would be rejected
- DuVal Submissions Issues Request / LB Flag December 2019
- Responses to deficiencies February 2020
- Granted April 2020

Final application > 1000 pages

Least Burdensome Flag Presentation

Point 1: The review staff has not followed precedent in the review of the MyCare Psychiatry Clozapine Assay Kit and is not being Least Burdensome

Point 2: The standard of “clinical validity” and a comparison to a standard of care has no application to the 510(k) or de novo programs for devices of the same device-type

Point 3: The review staff is inserting itself and intruding into the practice of medicine

Point 4: Even if the review staff could insist upon clinical validity, it exists in the literature today, which review staff refuses to recognize

Point 5: FDA cannot assume an unstated use for this device under review in violation of 513(i)(1)(e) of the Food, Drug & Cosmetic Act

CONCLUSION

- Appeal process can be an effective way to deal with the FDA
  - Time consuming
  - Increasing requirements
  - Higher expenses
- Appeal process with large diagnostic companies are not favored.
  - Major companies remain silent
  - Process is a disadvantage for smaller companies
- Home Brews by reference laboratories give an unfair competitive advantage
- Changes in the review and regulatory processes are needed

THANK YOU

Enhanced Access to RA/QA Intelligence

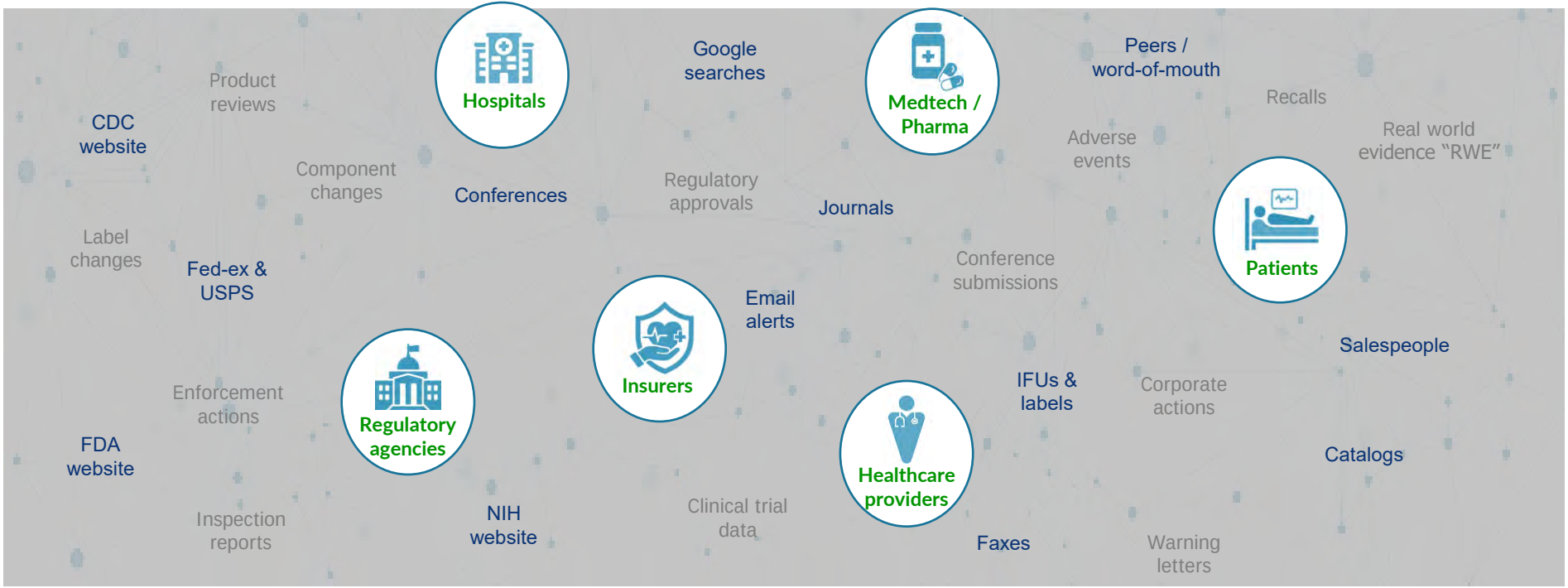
Leveraging Machine Learning to Expedite Regulatory Research and Enhance Quality

Medtech Monitor 2022-09-21

Ross Meisner, Chief Commercial Officer

No Single Source of Healthcare Product-Centric Data

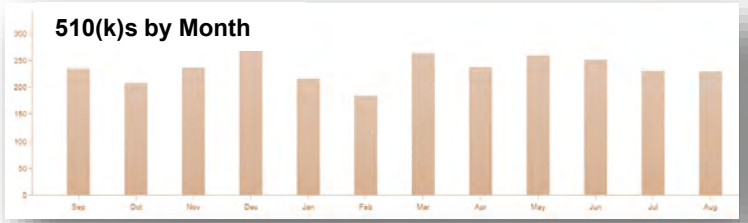
The healthcare industry struggles to stay informed on developments in medical devices, drugs and diagnostics – spending billions of dollars annually because of siloed data and fractured information flows

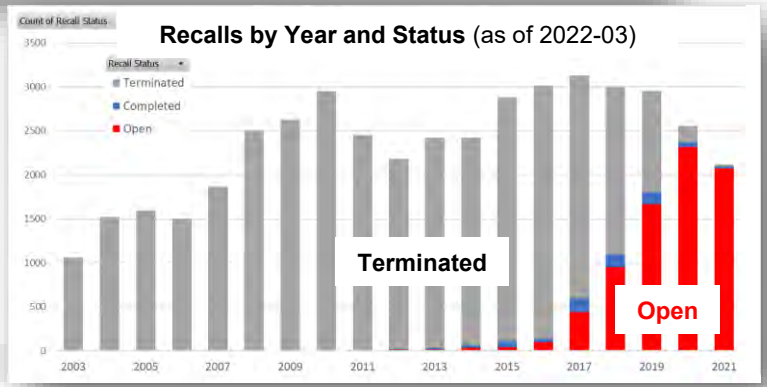


A Constant Deluge of New Healthcare Data

Nearly impossible to stay fully informed, even just within med-tech

- 164,276 510(k)s
  - >3,000 new 510(k)s annually
- 1,380 PMAs
  - >30 new PMAs annually
- 2,000-3,000 U.S. recalls per year
  - And >2.5M adverse events/year
- *What does this mean for patient safety and patient care?*
  - *How does it affect products in patients, products on the shelf, or products in development?*





* Charts by Basil of FDA data

Applying Tech to Save Time & Cost, & Improve Outcomes

State-of-the-art big data and machine learning technologies

- A web-based SaaS application – easy to set up and access
- Comprehensive datasets and trend analytics with **100M+ records** indexed and growing
- Intuitive, modern, customizable interface
- Customizable email alerts and notifications
- Data can also be delivered via an API to internal systems or BI tools

Tour of Basil's Two Analytical Modules

Simplifying research and increasing access to insights within the data

Regulatory Module

Regulatory Strategy

- Rapid mastery of tech landscapes
- Full-text search of every application, document, regulation, and product code

Includes Quality and PMS Data

- Insights, trends, and context for recalls and adverse events
- Powerful search, filter, and data export tools

Due Diligence & Product Marketing

- Product and competitive landscape intelligence
- Inform marketing strategies and M&A decisions

Post-Market Module

Immediate Insights Into Emerging Quality Issues

- Dashboard of all new recalls, adverse events, warning letters, and 483s – as they happen
- Scan across tech sectors, companies, and products
- Email alerts when new quality events occur

Rich Customizable Quality Research Tools

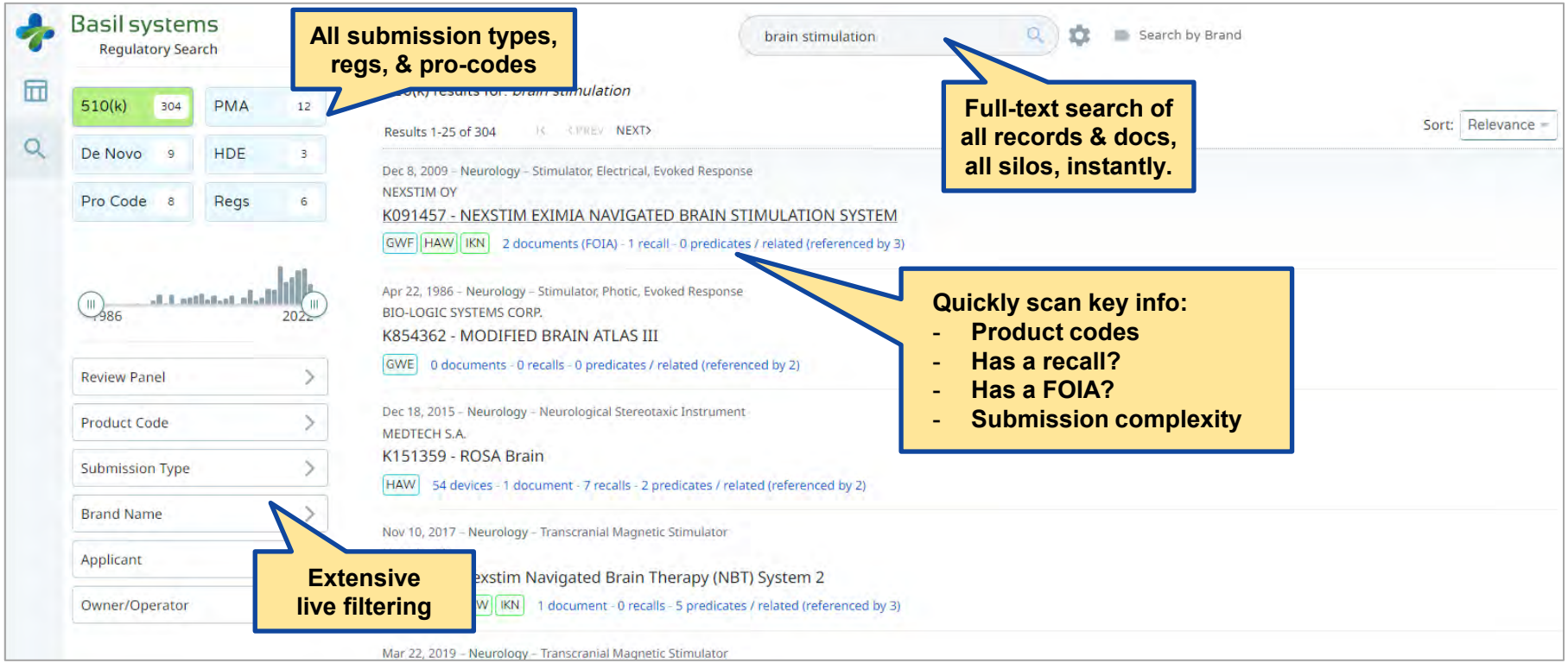
- Define custom datasets across any companies, products, or categories
- Monitor, analyze, update, & report at any time
- Export adverse events, recalls, UDI, and charts

CER/PSUR data tables for EU-MDR/IVDR

- Instantly create safety data tables for EU submissions

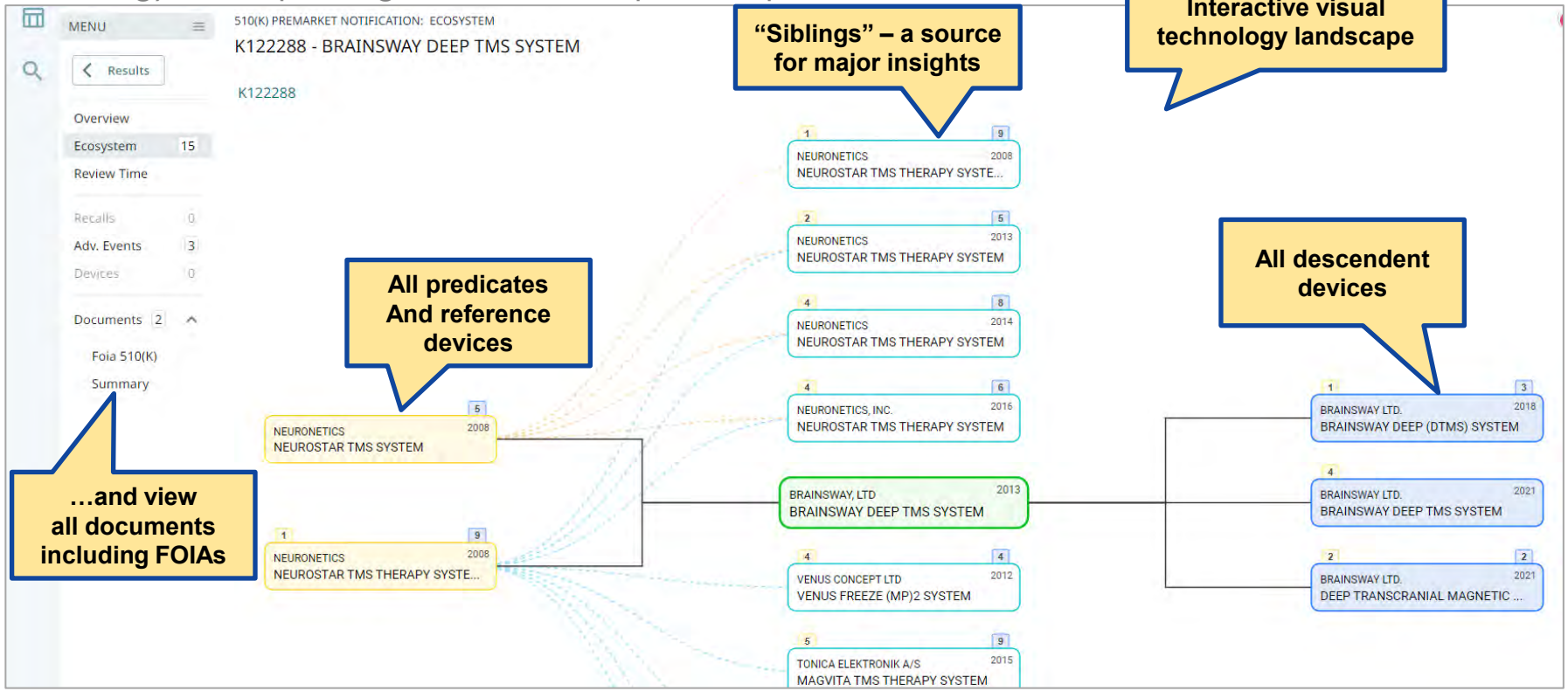
Regulatory: 510(k) Predicate Strategy

Global search for identifying potential predicate devices



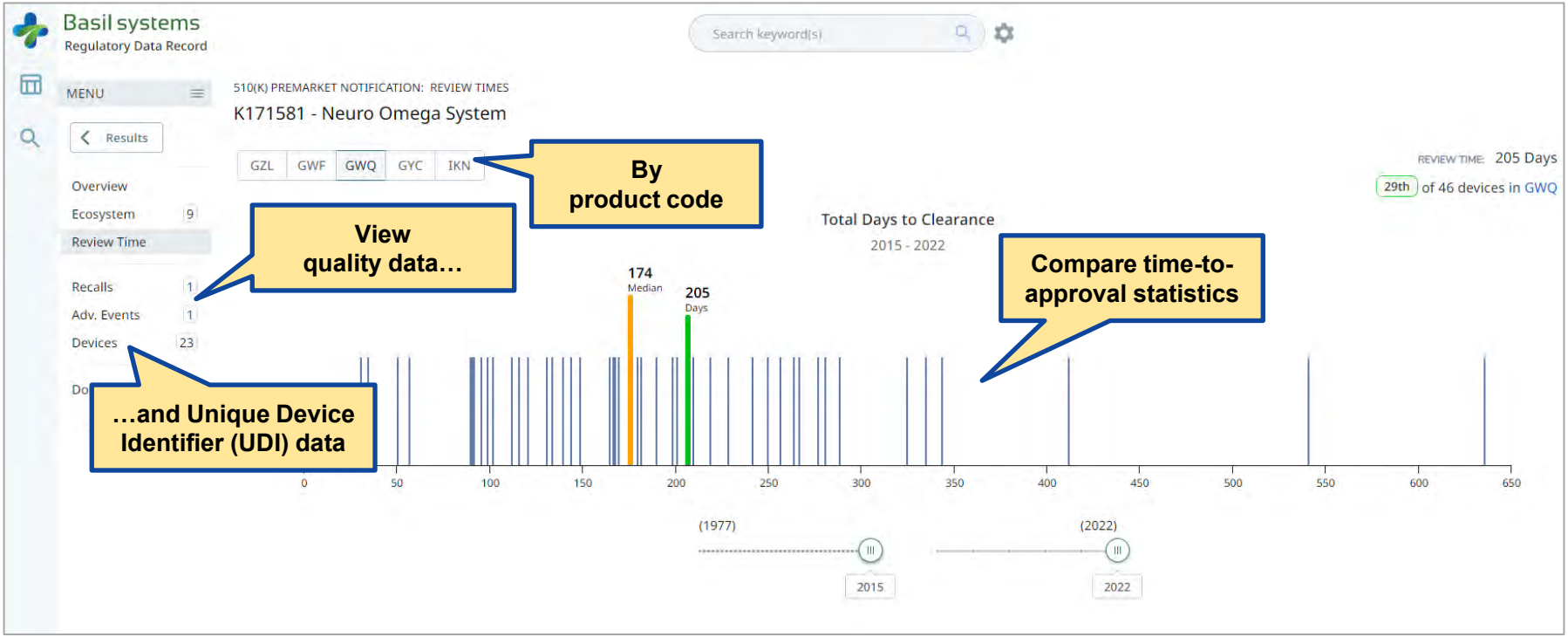
Regulatory: 510(k) Predicate Strategy

Technology landscape navigation to evaluate potential predicate devices



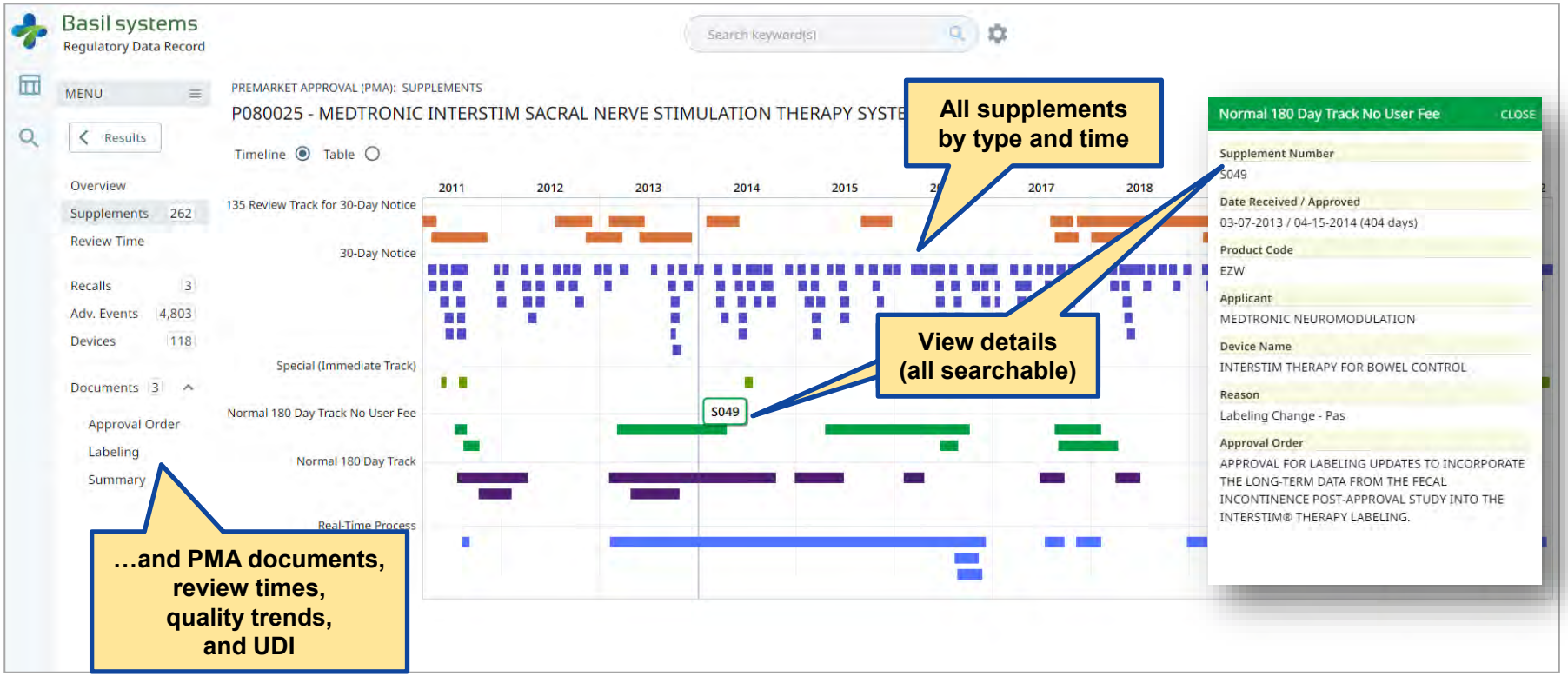
Regulatory: 510(k) Predicate Strategy

Evaluate time-to-approval statistics by product-code



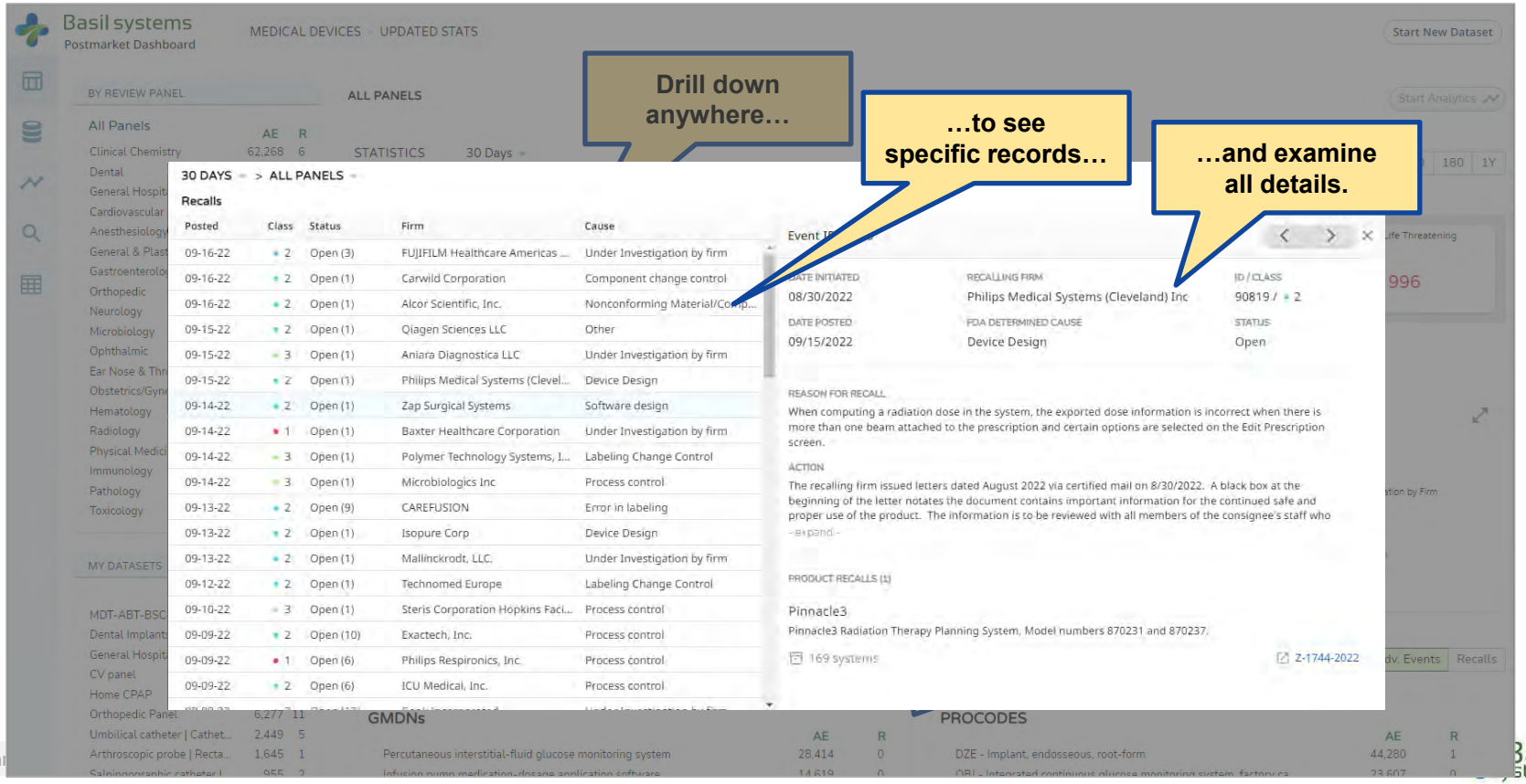
Regulatory: PMA Research

Simple efficient navigation of PMA supplements over time



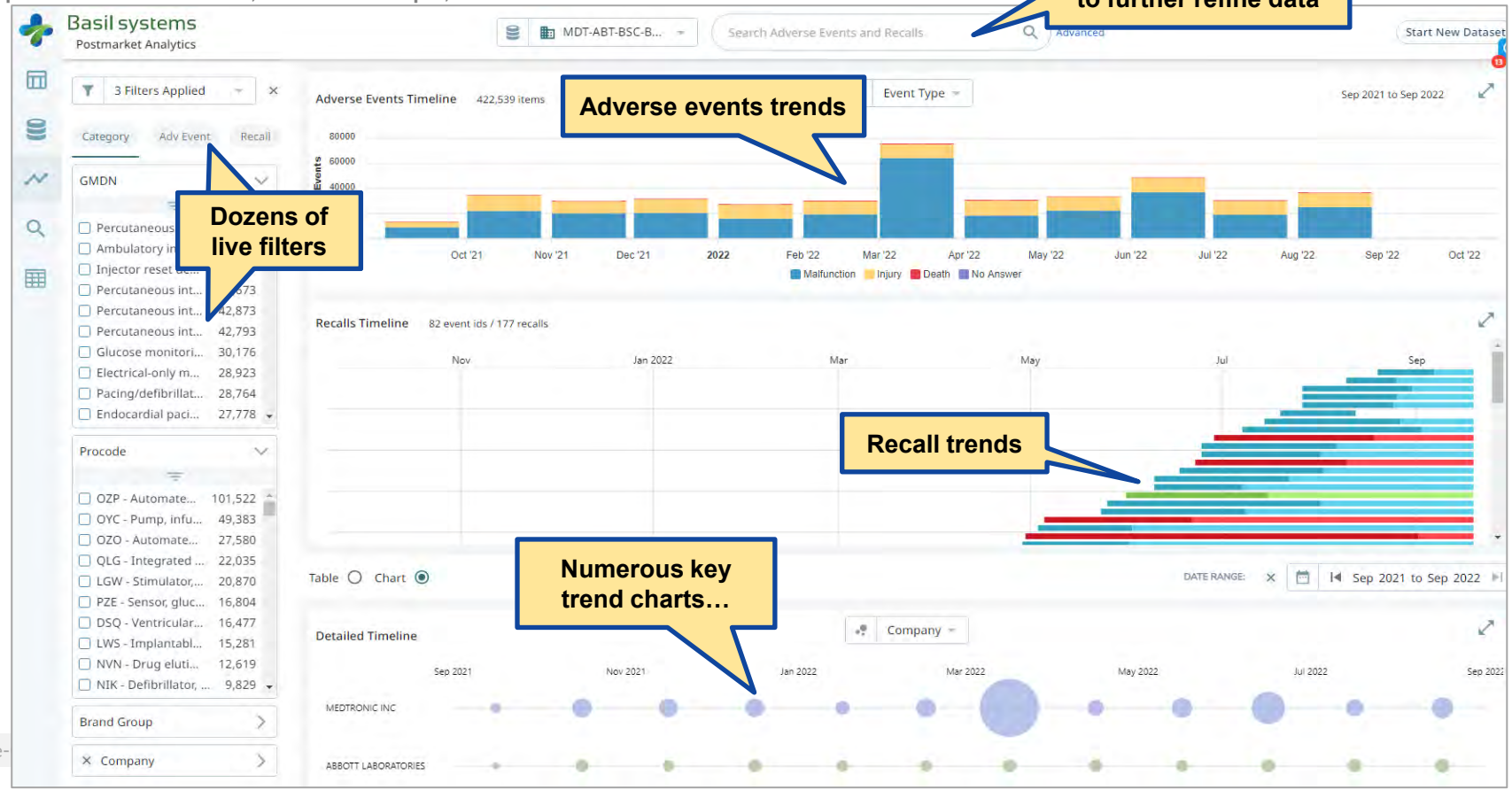
Post-Market: Dashboard

Everything new at the FDA that is quality-related



Post-Market: Quality and Safety Analytics

Deep dive into trends, relationships, and context



CER Tables for EU-MDR/IVDR: How Do We Do Them Now?

Basil systems

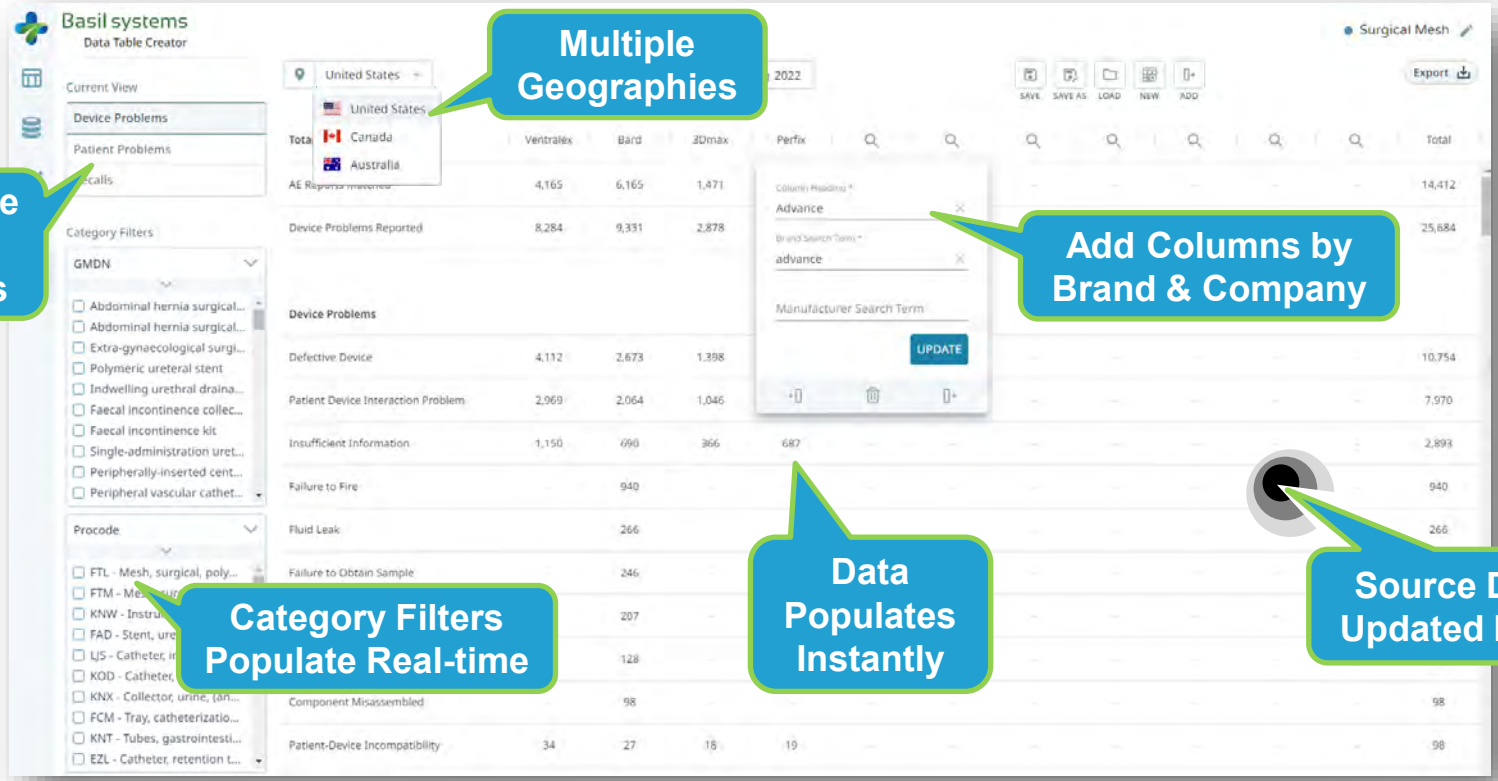
The New Approach

6. **In One Table, Instantly**
5. **Org. by Patient Problem, Device Problem, & Recalls**
4. **With Full-Text NLP Search**
3. **Connected to Brands, Apps, UDI, GMDN, & Pro-Codes**
2. **For Several Countries**
1. **You Have <u>All</u> the PMS Safety Data (AEs)**

*** With full download of all records**

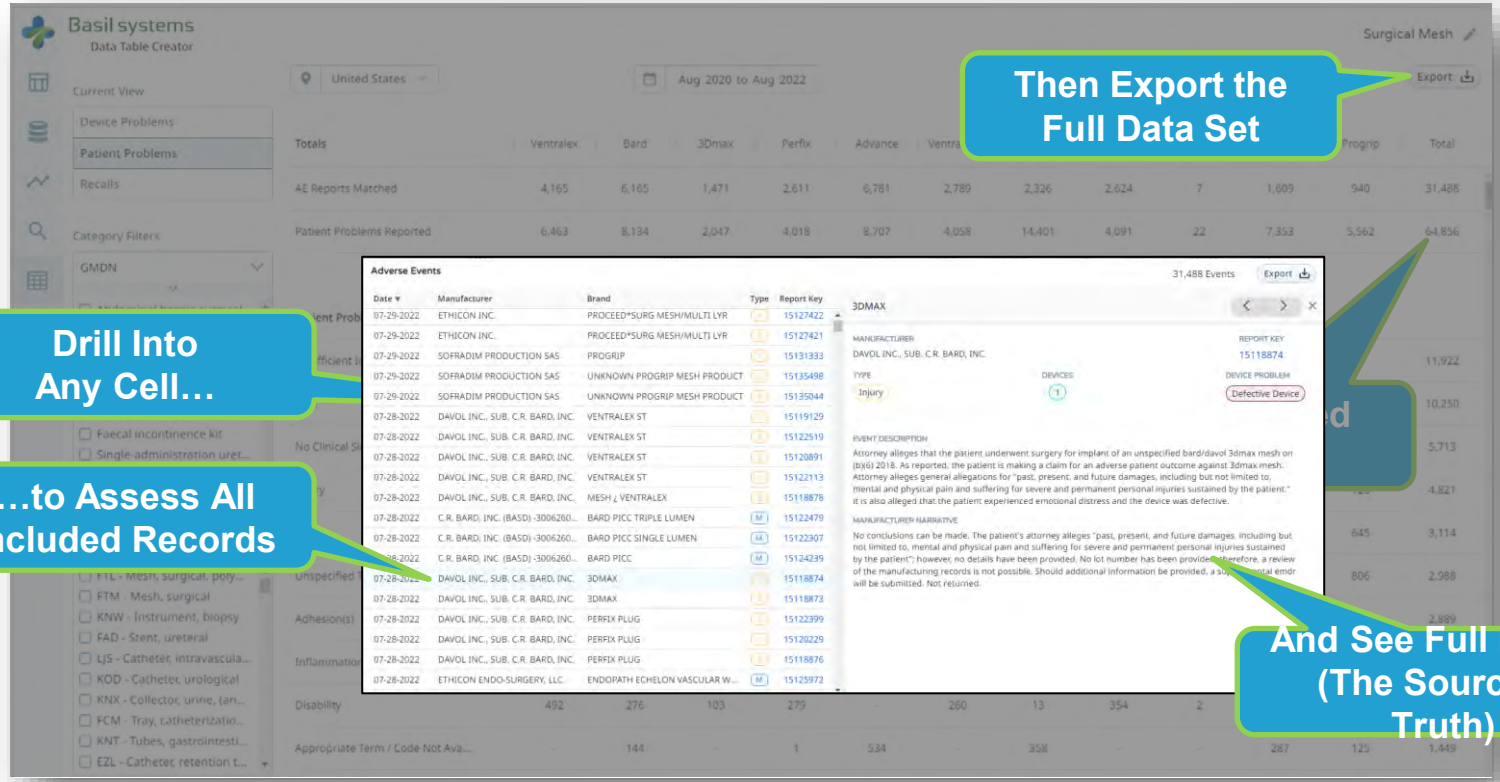
An Instant CER/PSUR Table Creator

Built upon a foundation of years of data science and software development



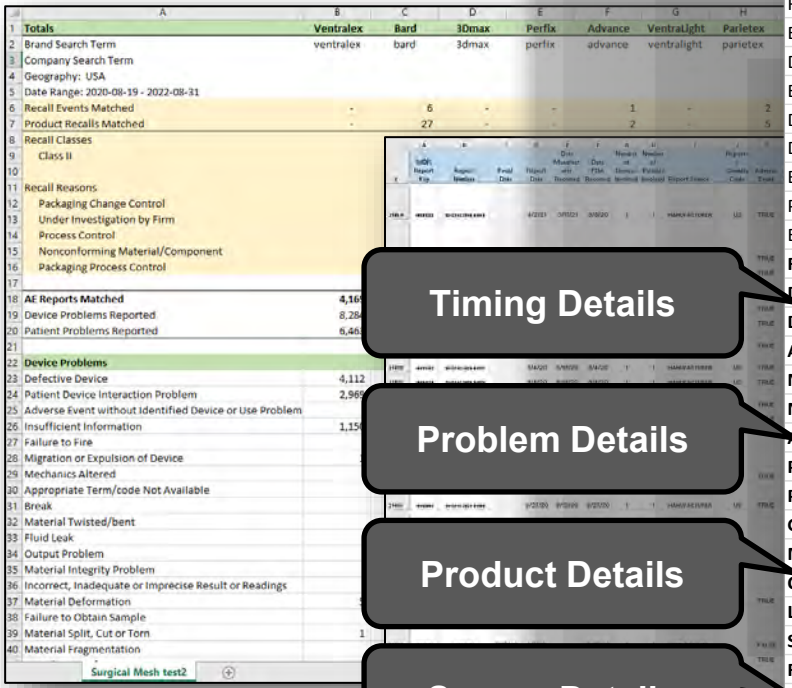
An Instant CER/PSUR Table Creator

Built upon a foundation of years of data science and software development



CER/PSUR Table Key Capability: Rich Offline Analysis

Unlimited Data Export, All Fields



Totals	Ventralex	Bard	3Dmax	Perfix	Advance	VentraLight	Parietex
Brand Search Term	ventralex	bard	3dmax	perfix	advance	ventralight	parietex
Company Search Term							
Geography: USA							
Date Range: 2020-08-19 - 2022-08-31							
Recall Events Matched	-	6	-	-	1	-	2
Product Recalls Matched	-	27	-	-	2	-	5
Recall Classes							
Class II							
Recall Reasons							
Packaging Change Control							
Under Investigation by Firm							
Process Control							
Nonconforming Material/Component							
Packaging Process Control							
AE Reports Matched	4,16						
Device Problems Reported	8,28						
Patient Problems Reported	6,46						
Device Problems							
Defective Device	4,112						
Patient Device Interaction Problem	2,965						
Adverse Event without Identified Device or Use Problem							
Insufficient Information	1,15						
Failure to Fire							
Migration or Expulsion of Device							
Mechanics Altered							
Appropriate Term/code Not Available							
Break							
Material Twisted/bent							
Fluid Leak							
Output Problem							
Material Integrity Problem							
Incorrect, Inadequate or Imprecise Result or Readings							
Material Deformation							
Failure to Obtain Sample							
Material Split, Cut or Torn	1						
Material Fragmentation							

Surgical Mesh test2

Surgical Mesh AE Details USA

Timing Details

Problem Details

Product Details

Source Details

BASIL SYSTEMS (29 fields)	**FDA MAUDE** (10 fields)
MDR Report Key	Web Link
Report Number	Report Number
Event Date	Event Date
Date FDA Received	Date FDA Received
Event Type	Event Type
Device Manufacturer	Device Manufacturer
Device Problem	Device Problem
Brand Name	Brand Name
Primary Reported Product Code	Product Code
Event Description(s)	Event Text (some Mfr narrative)
Report Date	--
Date Manufacturer Received	
Date of Manufacturer	
Application Number	
Number of Devices Involved	
Number of Patients Involved	
Adverse Event	
Patient Problem	
Product Problem (True/False)	
Generic Name	--
Model No.	
Catalog No.	
Lot No.	
Single Use Device	
Reprocessed Or Reused	
Other Product Codes	
Report Source	
Reporter Country Code	
Manufacturer Narrative(s)	--

All Fields, to Enable Rich Analysis

New Tools to Enhance Access to RA/QA Intelligence

Enabled by big data and AI/ML technologies

- **Simple, fast, effective access to essential data and insights**
  - Web-based online platform
  - Data updated daily
  - Opt-in email alerts on any topic(s) you define

- **Saving significant time and effort required to get products to market and keep them there safely**
  - In particular, addressing the large burden of EU-MDR/IVDR submissions

BAA Matrix and HIPAA Incident Tracker

Fox Rothschild LLP
ATTORNEYS AT LAW

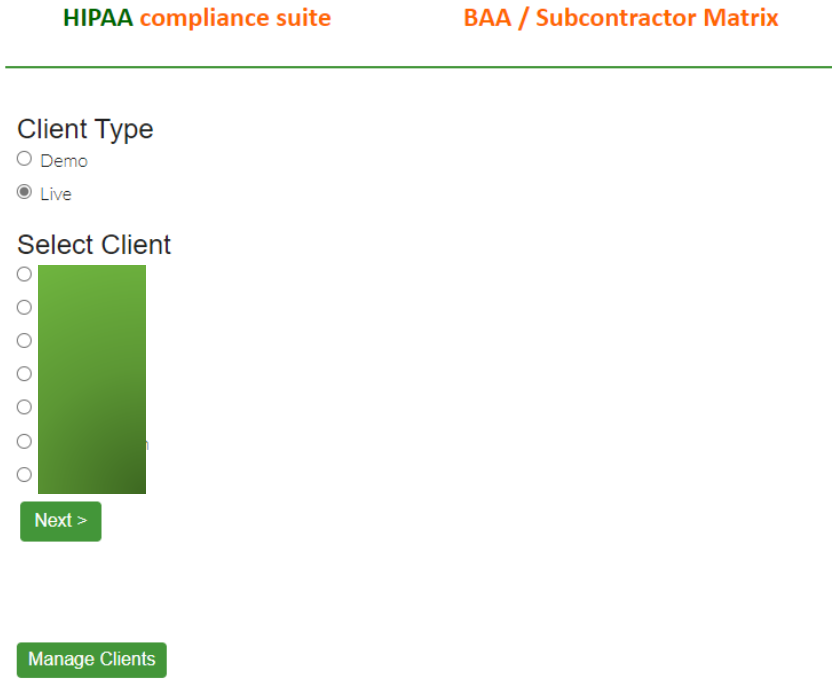
Elizabeth G. Litten

Partner

Fox Rothschild LLP

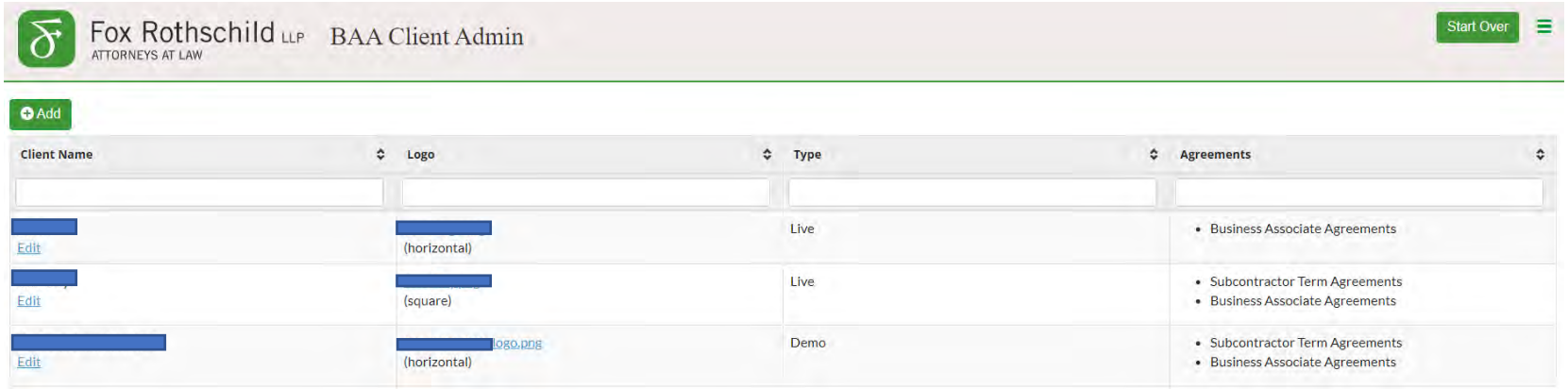
Landing Page and Edit Clients

- Landing Page for Admin Users
  - If an admin accesses the BAA Matrix this is the first page they will see. They are presented with the option to select from the list of live clients or to select a demo client (where admins and Fox Rothschild's Knowledge Management Department can test functions of the site without consequence to live client data).
  - A client will be taken directly to their BAA Matrix and only be able to view their data.



Landing Page and Edit Clients

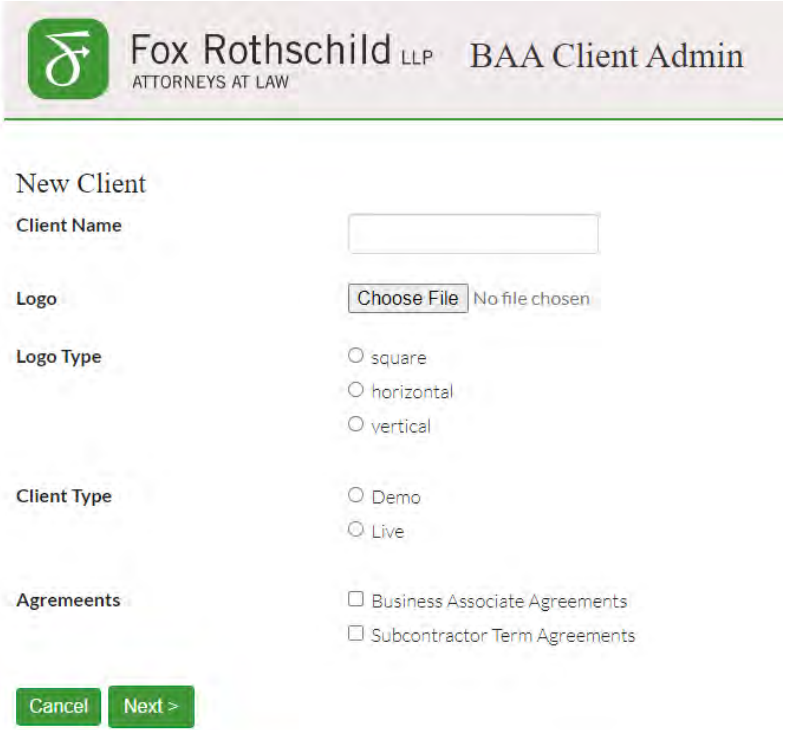
- Managing Clients
  - An admin will be able to see and click on the “Manage Clients” button. This will allow the admin to add/edit certain client information that will display on the BAA Matrix.
  - Client specific logos can be added to appear at the top of their matrices.



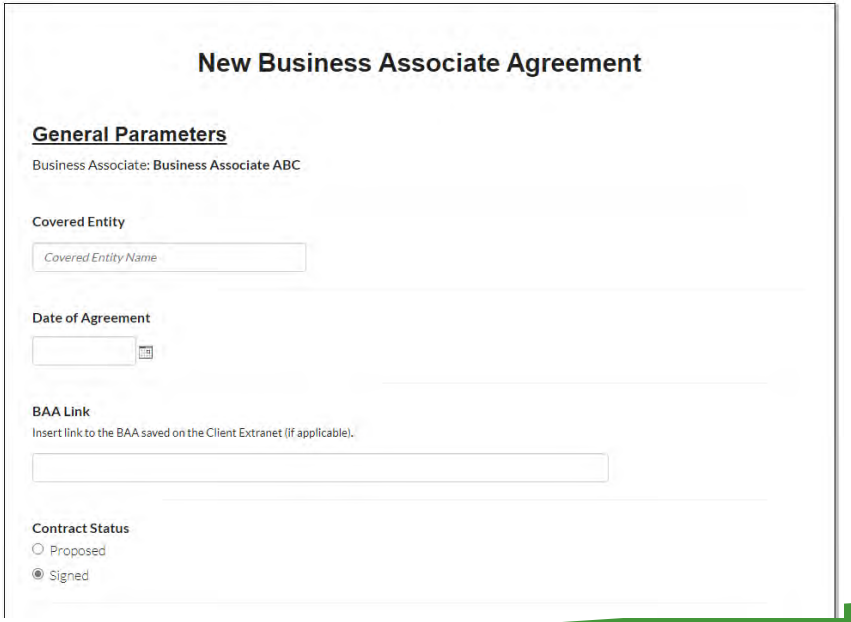
Landing Page and Edit Clients

- New/Edit Client
  - An admin* can simply click on the “Add” button or “Edit” link (for a specific client), and enter or edit information as needed.

**The admin is an individual approved (by client or Fox attorney) to have administrative privileges allowing the individual to upload agreements for the entry of key agreement terms, as described later. Only a Fox attorney may enter contract terms.*



Identify BAA Terms



Identify BAA Terms

Does BAA include requirements for Subcontractors?

- ○ BAA requires subcontractors agree to **same terms** as those that apply to BA.
- ○ BAA requires subcontractors agree to **substantially the same terms** as those that apply to BA.
- ○ SA requires subcontractors to **comply with HIPAA**
- ○ No

What is done to PHI upon termination of the BAA or the end of the underlying agreement?

- ☐ Return
- ☐ Destroy
- ☐ Other
- ○ N/A

Notice of Security Incidents

- ☐ Oral
- ☐ Written
- ☐ Not Specified
- ○ N/A

Notice of Breach/Potential Breach

- ☐ Oral
- ☐ Written
- ☐ Not Specified
- ○ N/A

Notice Recipient

- ☐ PO
- ☐ SO
- ☐ Other
- ○ Not Specified

Does the BAA prohibit the use or disclosure of PHI by the Business Associate outside of the United States?

- ○ Yes
- ○ No

BAA Terminated

- ○ Yes
- ○ No

Indemnification by Business Associate

- ○ Yes
- ○ No

Notes

Security Incident Parameters

Notice Required

- ○ Yes
- ○ No
- ○ N/A

Breach Parameters

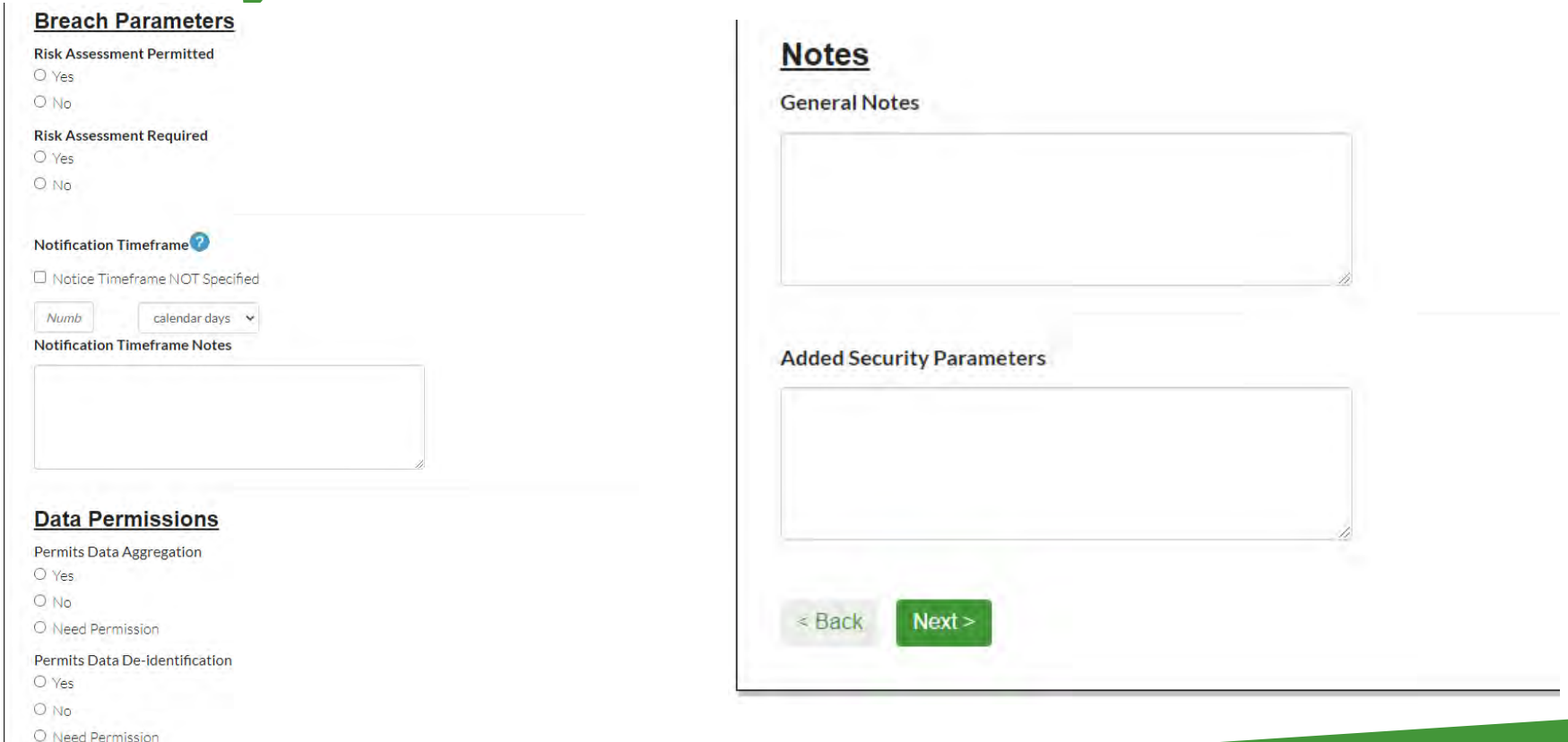
Risk Assessment Permitted

- ○ Yes
- ○ No

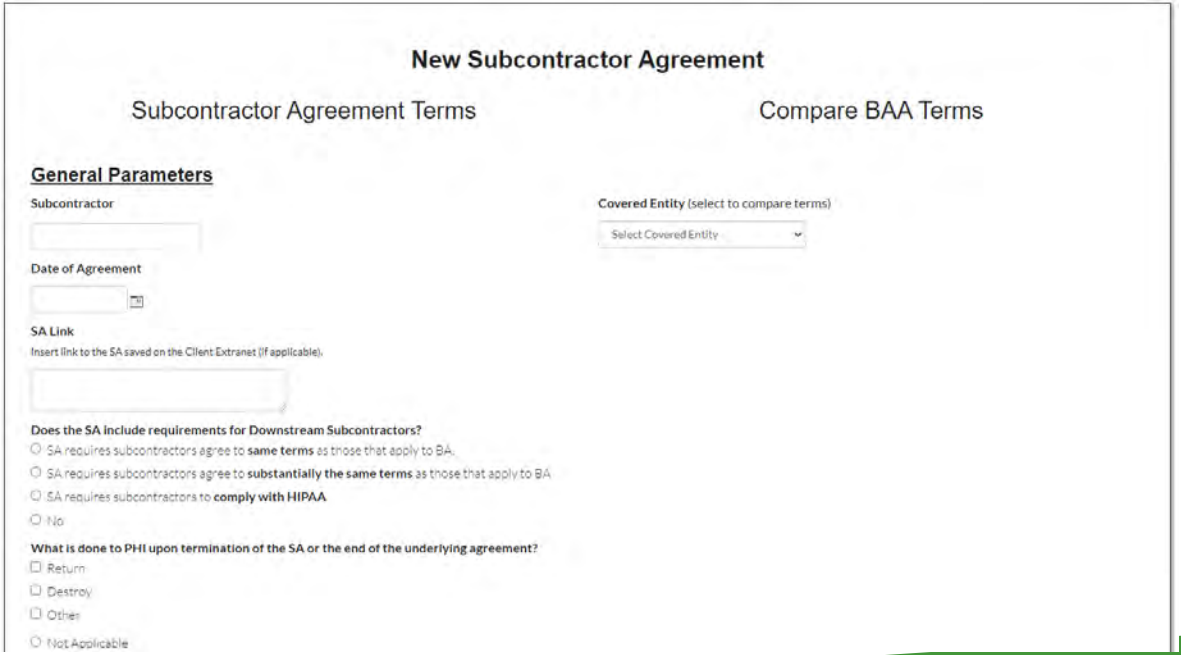
Risk Assessment Required

- ○ Yes
- ○ No

Identify BAA Terms



Identify SA Terms



Identify SA Terms

Does SA require written notice when return or destruction of PHI upon termination of BAA is not feasible?

- ○ Yes
- ○ No

Notes

For example, indicate if CE must approve infeasibility of return/destruction.

Does the SA prohibit the use or disclosure of PHI by the Subcontractor outside of the United States?

- ○ Yes
- ○ No

Indemnification by Subcontractor?

- ○ Yes
- ○ No

Notes

Security Incident Parameters

Notice Required

- ○ Yes
- ○ No

Notice Required for Successful Attempts?

- ○ Yes
- ○ No

Notice Required for Unsuccessful Attempts?

- ○ Yes
- ○ No

Security Incident Parameters

Notice Required

- ○ Yes
- ○ No

Notice Required for Successful Attempts?

- ○ Yes
- ○ No

Notice Required for Unsuccessful Attempts?

- ○ Yes
- ○ No

Notice Trigger

- ☐ All SIs
- ☐ Any PHI
- ☐ Client PHI
- ○ Not Applicable

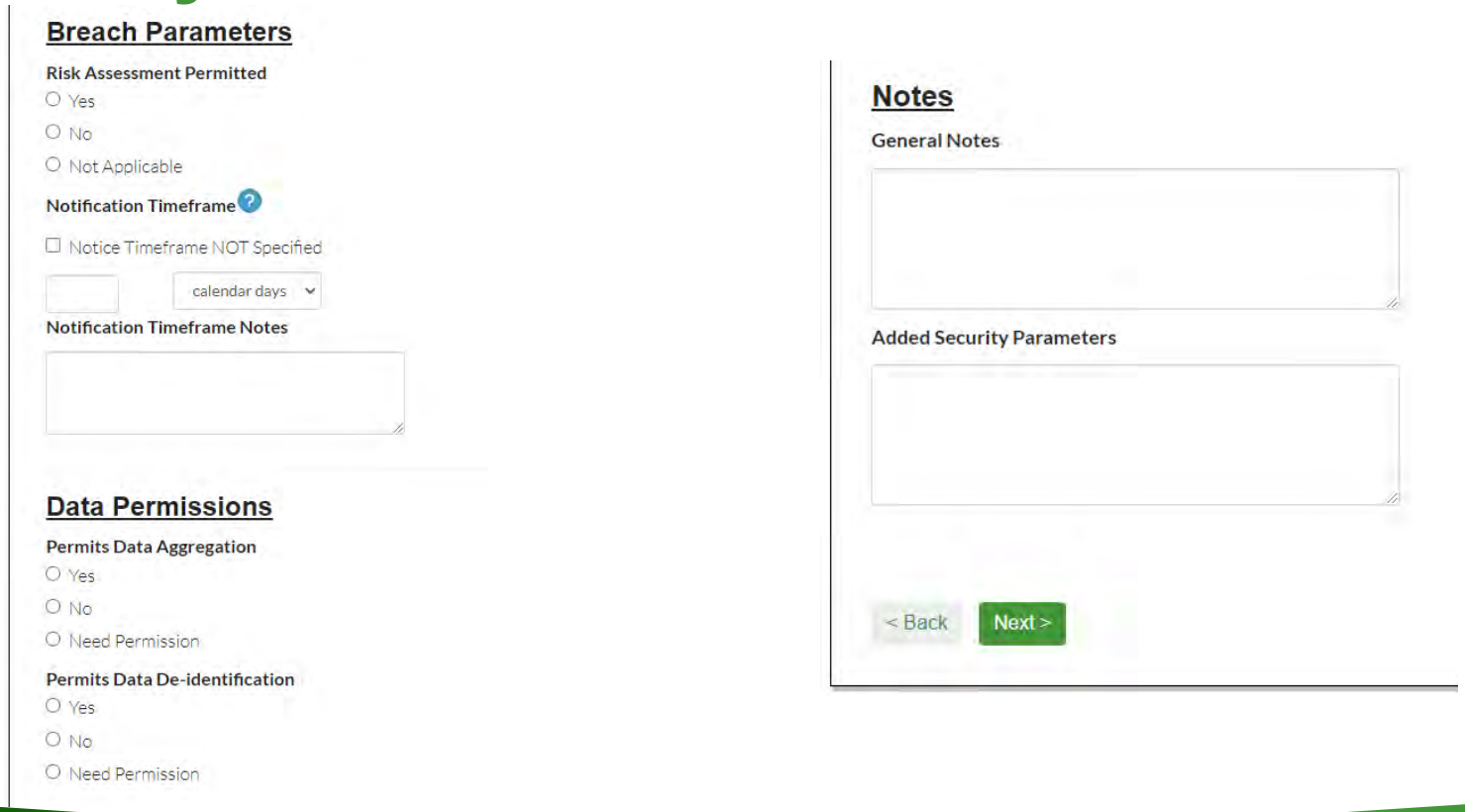
Notification Timeframe

- ☐ Notice Timeframe NOT Specified

calendar days

Notification Timeframe Notes

Identify SA Terms

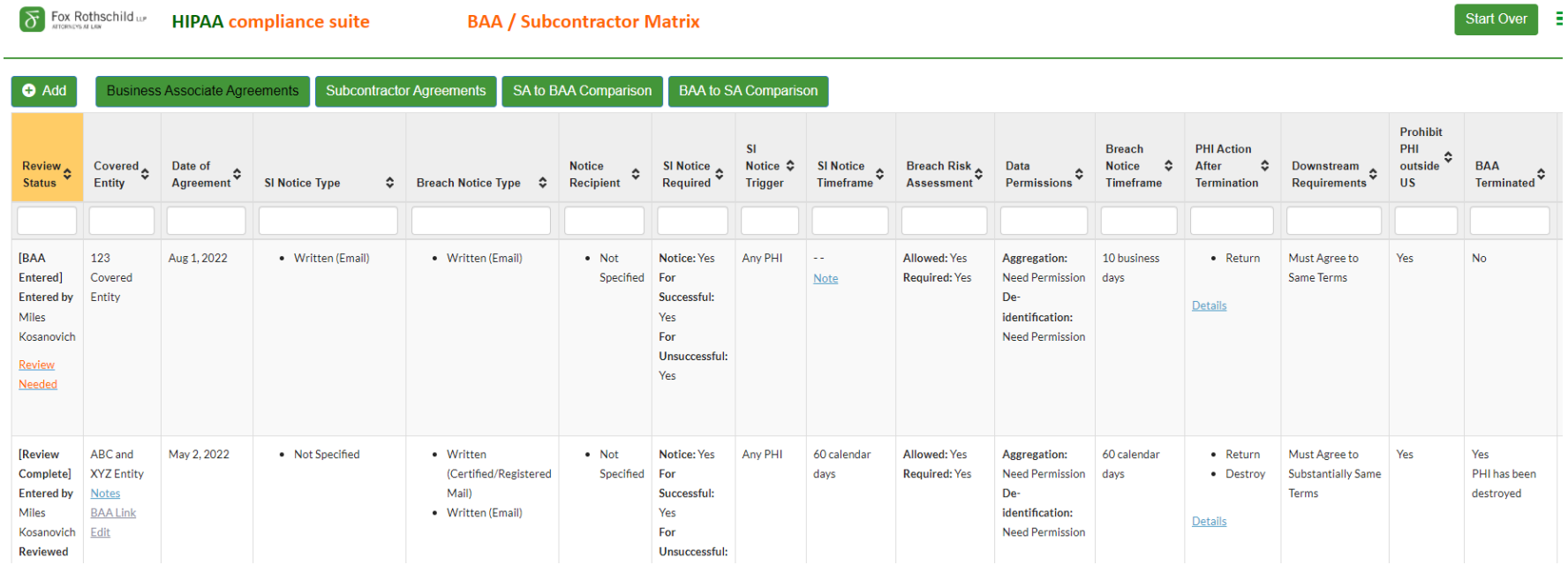


Business Associate Agreements

- BAA
  - This is the first page a client would see when using the app.
  - The BAA section displays all entered data associated with BAAs for a specific client along with a review status of that entered data. Once data is entered by one attorney it must then be reviewed again (by the same or another attorney) before the entered data will become viewable to a client. This is to ensure accuracy in the entered data before a client is able to see it.
  - Only admins can see the Review Status column, which indicates who has entered the data originally and who has reviewed the data, or whether review is still needed.
  - Each column header has a search box, allowing the ability to find specific text within that field/column

  Image on next slide

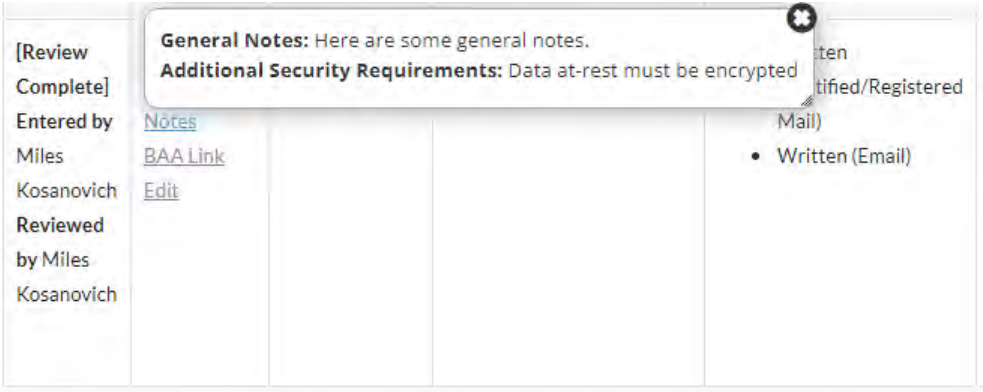
Business Associate Agreements



Review Status	Covered Entity	Date of Agreement	SI Notice Type	Breach Notice Type	Notice Recipient	SI Notice Required	SI Notice Trigger	SI Notice Timeframe	Breach Risk Assessment	Data Permissions	Breach Notice Timeframe	PHI Action After Termination	Downstream Requirements	Prohibit PHI outside US	BAA Terminated
[BAA Entered] Entered by Miles Kosanovich Review Needed	123 Covered Entity	Aug 1, 2022	• Written (Email)	• Written (Email)	• Not Specified	**Notice:** Yes **For Successful:** Yes **For Unsuccessful:** Yes	Any PHI	-- Note	**Allowed:** Yes **Required:** Yes	**Aggregation:** Need Permission **De-identification:** Need Permission	10 business days	• Return Details	Must Agree to Same Terms	Yes	No
[Review Complete] Entered by Miles Kosanovich Reviewed	ABC and XYZ Entity Notes BAA Link Edit	May 2, 2022	• Not Specified	• Written (Certified/Registered Mail) • Written (Email)	• Not Specified	**Notice:** Yes **For Successful:** Yes **For Unsuccessful:**	Any PHI	60 calendar days	**Allowed:** Yes **Required:** Yes	**Aggregation:** Need Permission **De-identification:** Need Permission	60 calendar days	• Return • Destroy Details	Must Agree to Substantially Same Terms	Yes	Yes PHI has been destroyed

Business Associate Agreements

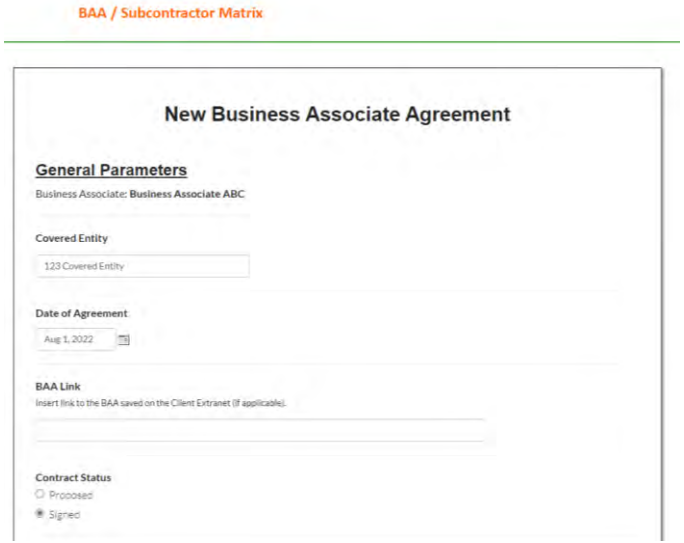
- Notes, BAA Link, Edit
  - Clicking “Notes” will display a pop-up of relevant information pertaining to the Covered Entity.
  - Clicking “BAA Link” will display the digital copy of the BAA that is saved on the associated client extranet (this requires that an extranet be created for the client).
  - Clicking “Edit” will return the user to the edit screen so that BAA term entries can be revised



Business Associate Agreements

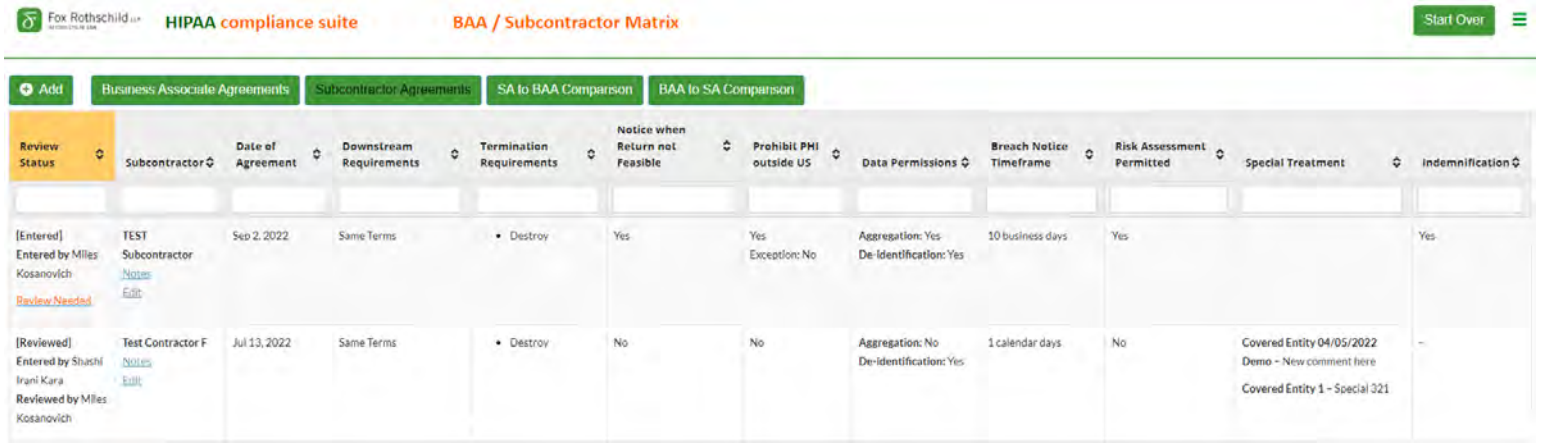
- New BAA Duplicate Page
  - Clicking the “Add” button will allow the user to add a new BAA to the matrix.
  - First, they will be asked if they wish to duplicate a previously entered BAA. Select “Yes” if a standard form of BAA is used for multiple Covered Entities. This will automatically populate terms into the “New Business Associate Agreement” terms template, and the attorney will simply enter the name of the Covered Entity and date of Agreement.

- New BAA Edit Page
  - Otherwise, the user can select “No” and enter all new data.



Subcontractor Agreements

- The Subcontractor Agreements section functions exactly like the Business Associate Agreements section, except SAs are displayed instead of BAAs.

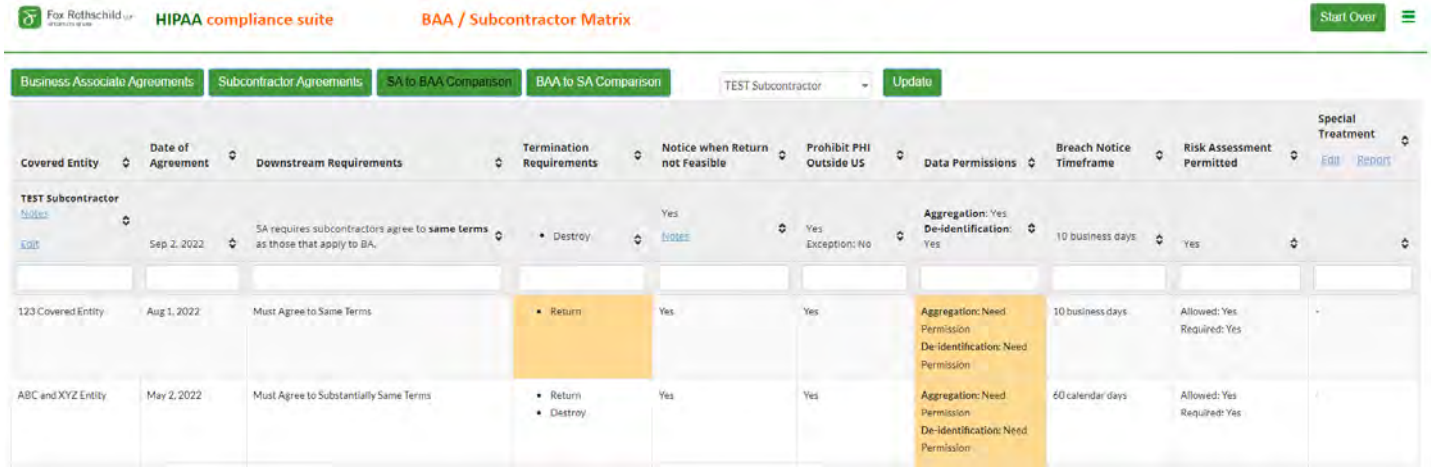


SA to BAA Comparison

- SA to BAA Comparison – Select a Subcontractor
  - When a user clicks “SA to BAA Comparison” they must select a subcontractor and click “Update”

SA to BAA Comparison

- The data for that subcontractor will display immediately below the column headers. Below the data for the subcontractor will be data for each covered entity. BAA terms that potentially conflict with SA terms will appear highlighted in yellow.
- The “Notes” and “Edit” links here function exactly like they do in the Business Associate Agreements section.
- The Special Treatment field/column is editable from the data grid. Click on “Edit” to add or edit a client’s special treatment. A list of clients with special treatments can be generated and downloaded by clicking on “Report”.

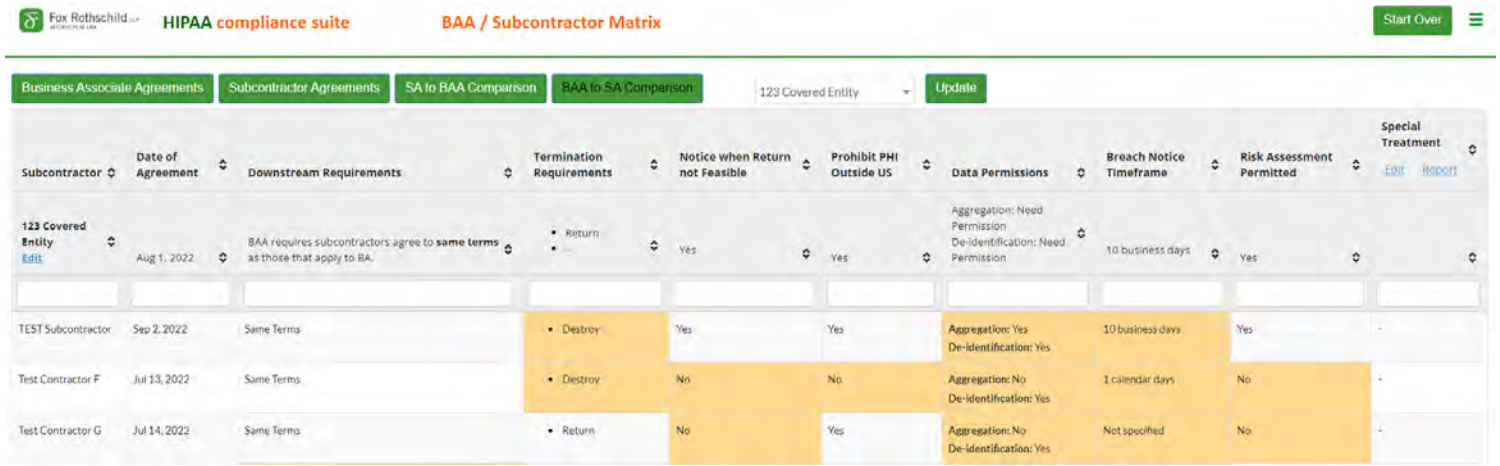


BAA to SA Comparison

- Select a Covered Entity
  - The BAA to SA Comparison section functions exactly like the SA to BAA Comparison section, except a user must select a covered entity (instead of a subcontractor) before clicking “Update.”

BAA to SA Comparison

- BAA to SA Comparison
  - The data for that covered entity will display immediately below the column headers, and below the data for the covered entity will be data for each subcontractor.



Subcontractor	Date of Agreement	Downstream Requirements	Termination Requirements	Notice when Return not Feasible	Prohibit PHI Outside US	Data Permissions	Breach Notice Timeframe	Risk Assessment Permitted	Special Treatment Edit Report
123 Covered Entity Edit	Aug 1, 2022	BAA requires subcontractors agree to **same terms** as those that apply to BA.	• Return • ...	Yes	Yes	Aggregation: Need Permission De-identification: Need Permission	10 business days	Yes	
TEST Subcontractor	Sep 2, 2022	Same Terms	• Destroy	Yes	Yes	Aggregation: Yes De-identification: Yes	10 business days	Yes	-
Test Contractor F	Jul 13, 2022	Same Terms	• Destroy	No	No	Aggregation: No De-identification: Yes	1 calendar days	No	-
Test Contractor G	Jul 14, 2022	Same Terms	• Return	No	Yes	Aggregation: No De-identification: Yes	Not specified	No	-

Highlighting in the SA to BAA and BAA to SA Comparison Sections

- Generally
  - When a term in an agreement under review (whether a BAA or SA) is not compatible with a term in signed agreement, the term in the signed agreement will highlight to indicate a potential incompatibility
- Downstream Requirements
  - If the SA (the downstream agreement) includes terms that allow uses or disclosures not permitted by the BAA, the term in the SA will highlight; if the SA also does not permit this use or disclosure, the term will not highlight
  - If the BAA requires an action with respect to return/destruction of PHI upon termination and the SA does not (or requires a different action), the term in the SA will highlight

Highlighting in the SA to BAA and BAA to SA Comparison Sections

- “Same Terms” Requirement
  - If the BAA requires that Subcontractors agree to the “same terms” as those included in the BAA, any incompatible terms (including Breach Notice Timeframe) will be highlighted

Thank You

Elizabeth Litten

Partner and Chief Privacy & HIPAA Compliance Officer

609.895.3320

ELitten@foxrothschild.com

Fox Rothschild LLP
ATTORNEYS AT LAW

Big Data and AI

Fox Rothschild LLP
ATTORNEYS AT LAW

Gunjan Agarwal

Partner

Fox Rothschild LLP

Polling Question:

1. I use AI tools in my practice
2. My company uses AI
3. My company offers AI as a product or service
4. AI is not relevant to my practice

Why should you care about protecting AI and Data?

- Exclusive rights give you a competitive advantage
- Third party IP or Data rights can stop you from selling your products/services
- Build market value: investors and lenders want it
- Defensive strategy: your competitors are doing it

Talking Points

- What is Artificial Intelligence (AI)?
- What is Big Data?
- Protections available
- Comprehensive IP Strategy

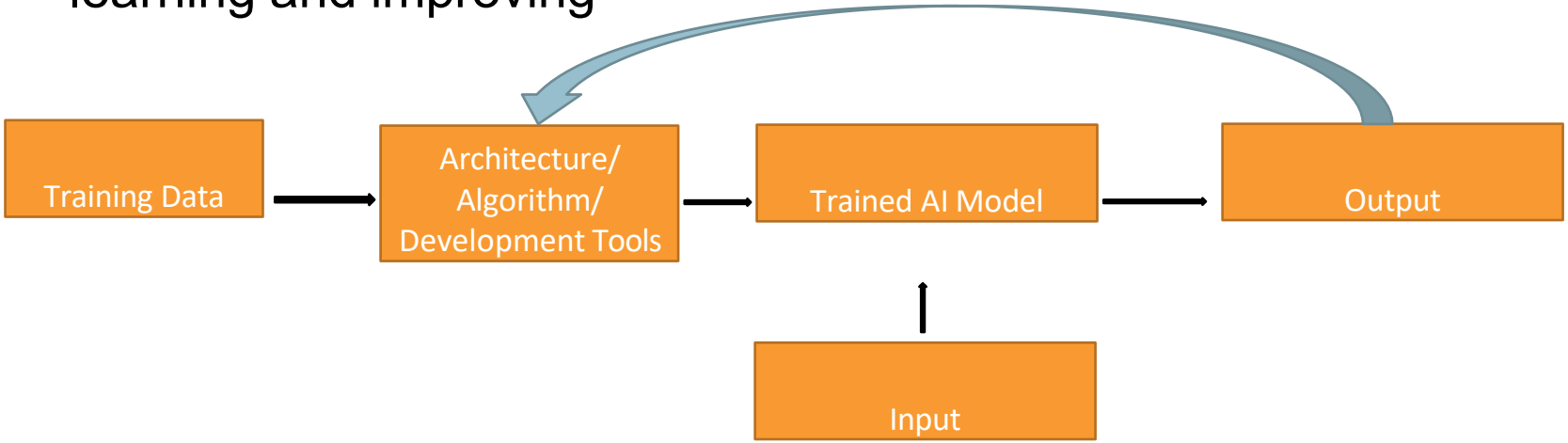
What is Artificial Intelligence?

- A machine that can learn with limited or no human intervention!
- It is more than machine learning.

--WIPO Technology Trends 2019: Artificial Intelligence. Geneva: World Intellectual Property Organization

Artificial Intelligence Pipeline

- An iterative process where an algorithm/model is constantly learning and improving



What is Big Data? Should it be protected?

- AI algorithms learn best given a very, very large amount of data.
- More Data ➔ Better performance!
- Types of Data
  - Training Data: Raw Data and/or Labeled Data
  - Input: Production data entered into trained AI model to produce output (collection and formatting of production data, creation of a suitable query, etc.)
  - Output (e.g., pictures, text data, classification labels, sounds, disease diagnosis, etc.)
- Expensive collection, storage, and processing (e.g., selection, arrangement or compilation, labeling, analysis, etc.)

What Else Needs to be Protected?

- Architecture/Algorithm/Development Tools
- AI methods (e.g., training, prediction, etc.)
- Trained AI Model: Continuously evolving iterations
- Application of the output (e.g., robotic control, disease treatment, predictive maintenance, etc.)
- Overall System and Hardware Elements

Example Transactions

- Hiring of AI engineers or scientists for developing a model
- Training Data supplier
- Software-as-a-Service – generate AI outputs
- AI platform/tools provider
- AI products
- Mergers/acquisitions

Types of Protections Available

Patents	• Inventions
Copyrights	• Original Expression of ideas
Trade Secrets	• Secret information with commercial value
Contracts	• Parties' Agreement
Trademarks	• Source of a product or service

Trade Secret

- Trade Secret protection is available for most aspects of protecting AI and Data.
  - No registration/government approval requirements
  - Useful because of the iterative nature of AI and Data
- However:
  - Requires reasonable measures to maintain secrecy (that can get expensive and/or onerous):
    - Physical security, Access control, Proprietary markings, Company Policy, Agreements, etc.
  - Reverse Engineering: When product deployed
  - May prevent collaboration
  - Competitor could patent it

Data Protection: Training Data & Production Data

- Copyright / Database Rights
  - Original (?): Distinguish between content (i.e., data) vs. a database
  - Authorship: Reinforce human involvement
  - Database Rights: Cannot be machine-generated (except in UK)
- Patent
  - Likely not available for data itself
  - Processing, novel data structure schemas, feature vectors, encoding/encryption techniques, etc. may be patentable.
- Contract
  - Data Licenses: Define ownership and permitted use; exclusivity; modification
  - Ownership of resultant data (e.g., output data) and model
  - Employment contracts: Express assignment
  - NDAs

Data: Risks?

Training Data and Production Data:

- May include data from numerous sources, including third-party data, open-source data, text and mining data, licensed data, and/or company-owned data
  - Copyright Infringement:
    - Fair Use?
    - License?
  - Privacy issues (e.g., HIPAA, GDPR, PII)
  - Violating terms of use?
  - Data Quality
- Practice Tips:
  - Be mindful of copyrights in collected data
  - If licensed: Review Data as well as Software Licenses

Data Protection: Output Data/Inferences

- Copyright
  - Original (?)
  - Authorship: AI, AI Model developer, or End-user
- Patent
  - Inventorship
  - Subject Matter Eligibility
    - Output Data itself not patentable but its generation, particular properties, and/or use tied to a practical application maybe
- Contract
  - Who owns it?
  - Scope of use
  - Residual rights
  - Confidentiality
  - Reverse engineering restrictions

Output Data: Risks?

- Copyright Infringement
  - Unfair competition laws
- Privacy issues (e.g., HIPAA, GDPR, PII)
- Ethical concerns

Architecture/Algorithm and AI Methods

- Copyright
  - Can protect software (not functionality)
  - “Open software” issues
- Patent
  - Non-obvious and new architectures, training methods, and algorithms
  - Subject matter eligibility: as long as technical effect/practical use identified
  - Adequate written description
  - Draft claims to detect infringement
- Contract

Application of the Output

- Patents
  - Computer implemented with a technical effect/tied to a particular field.
  - Broaden the scope beyond a particular application (?)
- Contracts

Overall System and Hardware

- Patents

Trained Model

Essentially a mathematical model or method that includes parameters and values! Constantly Evolving…

- Copyright
  - NA
- Patent
  - NA
- Trade Secret!
- Contract: Careful Deployment and Licensing terms
- BEWARE of model security attacks…

Comprehensive Strategy

- Identify the valuable assets: Data, algorithms, models, outputs, hardware, etc.
- Identify elements that have human involvement
- Identify available (or best) IP protections and take appropriate steps to avail the protections
  - Copyright
  - Patents
  - Trade Secrets
- Fill in the gaps with contracts

Trade Secret Protection: Critical

- Monitor the use of open source software and applicable licenses.
- Control marketing and product deployment in a strategic manner
- Host and protect the training data and/or trained model internally
- Legally binding agreements
  - Prohibit reverse engineering
  - Maintain confidentiality: NDAs and restrictive licensing
  - Cybersecurity policies
  - Clearly defined ownership interests

Copyrights

- Connect functionality of software (not protected as a copyright) to the specific original expression in software.
  - Specific assignment of “work for hire”
  - Be mindful of third-party licenses and open-source licenses
- Authorship
- Registration
  - Version control
- Redaction of trade secrets

Patents

- Filing date is important
- Inventorship
- Patent drafting: Dig Deep
  - Describe problem and technical solution/improvements
  - Describe training data/data collection/data processing
  - Describe system inputs
  - Network Architecture
  - Training process
  - Prediction process: Describe “how” rather than the “end result”
  - Specific hardware
  - Claims should be directed to a practical application
- Draft claims in a manner that allows detection of infringement

Contracts: Close the Loopholes

- AI and data IP protection and ownership laws are in a flux
- Consider the following:
  - Who is providing the component?
  - Who will use the component?
  - How will the component be used?
  - Who owns the component?
- Carefully draft contract terms:
  - Is the data clean? Who assumes risk?
  - Secure Ownership: Data, IP, and Derived data
  - Scope of Use; Residual rights
  - License: Data license and IP license
  - Manage Risk
  - Ethical Use terms (?)

Due Diligence Considerations

- User Company
- Model developer
- AI platform provider
- Infrastructure provider
- Training Data provider

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Digital Health

MedTech Monitor

September 21, 2022

Presented by:
Aaron Hage, Senior Director Legal-Regulatory & Compliance,
DuVal & Associates, P.A.

Agenda

1. Introduction
2. What is a medical device?
3. What is Digital Health?
4. Legal basis under 21st Century Cures
5. FDA's regulatory position and policies
6. FDA enforcement trends
7. What's in store for the future
8. Questions

Topics to Learn

- What makes a product a medical device
- What allows certain digital health products to be excluded from being a medical device
- How FDA regulates and enforces digital health devices
- What is on tap for the legal/regulatory future of digital health

Do you have a medical device?

A "device" is:

- "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—

  – recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

  – ***intended for use*** in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

  – ***intended to affect*** the structure or any function of the body of man or other animals,

  AND which does ***not achieve its primary intended purposes through chemical action*** within or on the body of man or other animals AND which is ***not dependent upon being metabolized*** for the achievement of its primary intended purposes."

  Section 201(h) of the Food, Drug & Cosmetic Act [Emphasis added]

So, is it a medical device?

Perfect size for everyday use

Non-toxic, BPA free ice packs

Perfectly sized to fit in all types of lunch bags and boxes.

“So go ahead and send them off to school with cheese, milk, fruit or veggies knowing that what you pack will stay cool and fresh.”

Soft touch fabric conforms to the body and remains flexible after freezing

Convenient and ready to apply to skin without a cover or wrap

Helps relieve pain and swelling fast

Ideal for relieving inflammation and joint pain, and increasing circulation

Medical devices are…intended for use in the diagnosis … or in the **cure, mitigation, treatment, or prevention** of disease…

Is this a medical device?

Intended for the general public

Intended for use in construction and industrial applications

Not intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease (prevents dust and debris, rather than microbial or viral particles)

Intended for a medical purpose

Provides antimicrobial or antiviral protection

Provides liquid barrier protection to prevent infection transmission

Medical devices are…intended for use in the diagnosis … or in the cure, mitigation, treatment, **or prevention** of disease…

In short…

	Class I Low Risk Devices e.g., toothbrush	Class II Moderate Risk Devices e.g., catheter	Class III High Risk Devices e.g., heart valve
Regulatory Requirements	General Controls	General Controls Special Controls	General Controls Special Controls Premarket Approval (PMA)
Marketing Application	Most - exempt* Some – Premarket Notification (510(k))	Most - Premarket Notification (510(k)) Some – exempt*	Premarket Approval (PMA)

*Devices classified as exempt from 510(k) are subject to limitations.

Digital Health

- Digital Health includes:
  - Mobile health devices
  - Health information
  - Sensors/wearable technology
  - Telehealth/telemedicine
  - Personalized medicine
- Focus today: When is digital health a medical device and when is it just unregulated information?

Exclusions: 21st Century Cures Act (2016)

Section 201(h) of the Food, Drug & Cosmetic Act:

The term “device” does not include software functions excluded pursuant to section 520(o) of the Food, Drug, & Cosmetic Act.

Exclusions: 21st Century Cures Act

Under Section 520(o) of the FDCA the definition of a medical device shall not include ***software function*** intended to:

- ***Provide administrative support***
- ***Maintain or encourage a healthy lifestyle*** that is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition
- ***Serve as electronic patient records***
- ***Transfer, store, convert formats, or display*** clinical laboratory tests or other data
- ***Provide decision support*** where the health care professional can independently review the basis for the recommendation

Multiple Function Devices Under 21st Century Cures Act

Under Section 520(o)(2):

- When a product combines:
  - a software function that does not meet the definition of a medical device, and
  - a function that meets the definition of a medical device:

  The non-device software function is not regulated as a medical device

- Caveat:
  - The impact of the non-device software function on the device function may be assessed

Multiple Function Devices

Other Caveats Under Cures Act

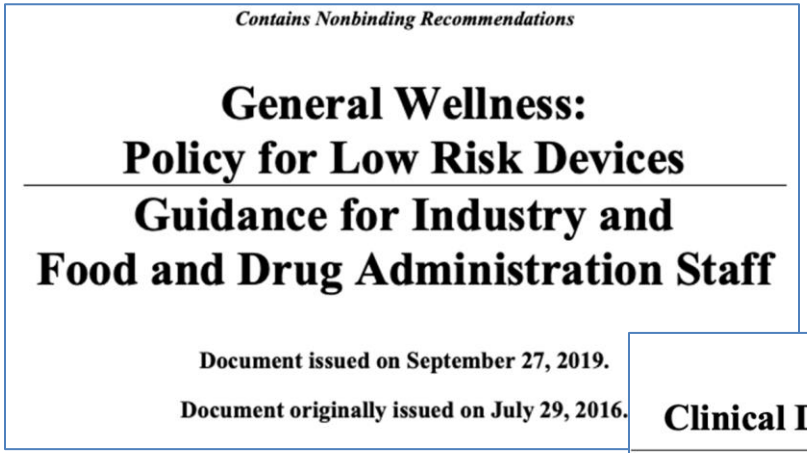
FDA may still regulate software that:

- Is reasonably likely to have serious adverse health consequences (upon notice and comment)
- Is used in the manufacture and transfusion of blood/blood components to assist in the prevention of disease in humans
- Is life supporting or sustaining or presents a potential unreasonable risk of illness or injury (i.e., Class III device)

Enforcement Discretion

- ***Medical device definition carve-out only applies to software function***
- ***FDA has authority to exercise enforcement discretion***
  - The product would still meet the definition of a medical device
  - FDA still has jurisdiction over the product as a medical device
  - Based on factors, such as intended use and risk, FDA will not enforce violations of FDCA or applicable regulations
- ***Enforcement discretion based on FDA rulemaking and guidance documents:***
  - Often chills and/or directs industry behavior, but:
    - Guidance documents are non-binding recommendations
    - Not final agency action; only represents FDA's "current thinking"

Three overlapping/interrelated guidance documents



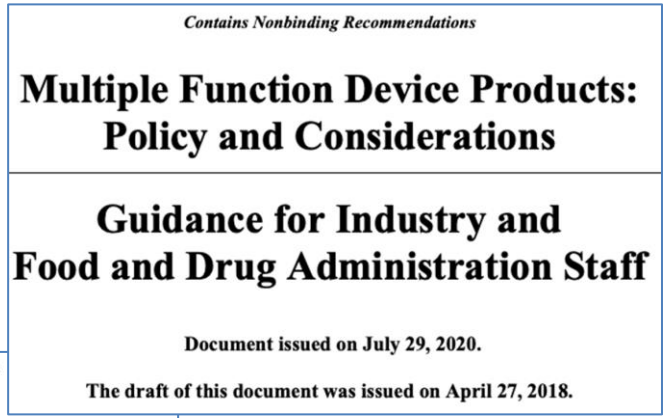
Contains Nonbinding Recommendations

General Wellness:
Policy for Low Risk Devices

Guidance for Industry and
Food and Drug Administration Staff

Document issued on September 27, 2019.

Document originally issued on July 29, 2016.



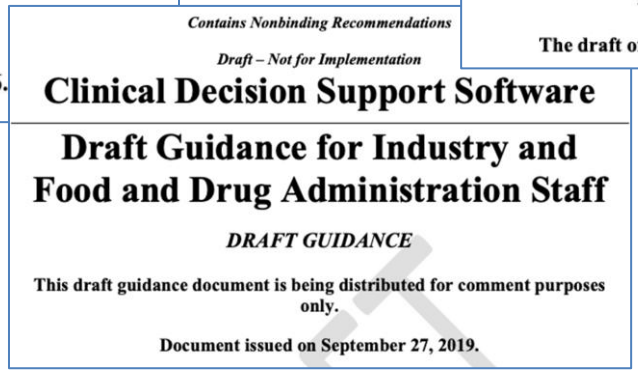
Contains Nonbinding Recommendations

Multiple Function Device Products:
Policy and Considerations

Guidance for Industry and
Food and Drug Administration Staff

Document issued on July 29, 2020.

The draft of this document was issued on April 27, 2018.



Contains Nonbinding Recommendations

Draft – Not for Implementation

Clinical Decision Support Software

Draft Guidance for Industry and
Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on September 27, 2019.

General Wellness Guidance

Contains Nonbinding Recommendations

General Wellness: Policy for Low Risk Devices

Guidance for Industry and Food and Drug Administration Staff

Document issued on September 27, 2019.

Document originally issued on July 29, 2016.

General Wellness Guidance

- ***Claims about sustaining or offering general improvement to functions associated with a general state of health that do not make any reference to diseases or conditions*** (applies to both software and hardware).
  - Weight management, physical fitness, relaxation
  - But not treat obesity or anxiety disorder
- ***Intended uses to promote, track, and/or encourage choice(s), which, as part of a healthy lifestyle, may help to reduce the risk of, or may help to live well with, certain chronic diseases or conditions***
  - Promote healthy lifestyle choices, such as sleep and diet, which may help to reduce the risk of type 2 diabetes
  - Must have a generally accepted role based on scientific publications

General Wellness Guidance

- **Must be low risk:**
  - ***Noninvasive*** (cannot penetrate or pierce skin or mucous membranes)
  - ***Not implanted***
  - ***Not of a technology that may pose a risk if regulatory controls are not applied***
    - Currently regulated by FDA?
    - Are special controls in place to reduce risk?
    - Examples that may pose a risk: UV radiation, lasers, electrical stimulation

Clinical Decision Support Guidance

Contains Nonbinding Recommendations

Draft – Not for Implementation

Clinical Decision Support Software

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

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Document issued on September 27, 2019.

Clinical Decision Support Guidance

- ***FDA expands upon the statutory device definition exclusion***
- ***Under the law, the exclusion only applies to:***
  - Products not intended to acquire, process, analyze a signal or pattern from a medical image, IVD, or signal acquisition system
  - Use by health care professionals to display, analyze, or print
  - Where the HCP can independently review the basis of the recommendation
  - Applicable to providing HCP information on clinical management even in critical situations

Clinical Decision Support Guidance (cont.)

FDA enforcement discretion provides:

- Ability for a user or patient or caregiver to use recommendation to make decision
  - Informing clinical management
    - Provide options and information, rather than aid, triage, or treat/prevent/diagnose
  - Only in non-serious situations
    - Timely treatment important but not critical
    - Will not result in irreversible consequences, permanent impairment, or death
  - Only where recommendation can be independently reviewed
    - Not primarily rely
    - Be able to review the basis of the recommendation being provided

Clinical Decision Support Guidance (cont.)

- ***Ability for an HCP user to obtain recommendation even when the basis of the recommendation cannot be independently reviewed***
  - Example: Algorithm where logic not explained
  - Again, only for informing clinical management and non-serious situations
- ***Expanding concepts outside of software***
  - IVDs and Laboratory Developed Tests that gather information, but do not treat or diagnose a disease or condition
  - Decision making left to HCP based on independent medical judgment

Multiple Function Guidance

Contains Nonbinding Recommendations

Multiple Function Device Products: Policy and Considerations

Guidance for Industry and Food and Drug Administration Staff

Document issued on July 29, 2020.

The draft of this document was issued on April 27, 2018.

Multiple Function Guidance

- ***21st Century Cures Act provides that non-device software function ("other function") of a product would not be regulated with the device function of the product***
- ***FDA Policy outlined in guidance document:***
  - *Although section 520(o)(2) of the FD&C Act applies to the regulation of products containing at least one device function and at least one non-device software function, FDA believes the same principles should apply to the assessment of all multiple function device products, whether those functions are software-based, hardware-based, or both.*

Multiple Function

- ***FDA's Multiple Function Policy expands on this "other function": Function that does not meet the device definition (including hardware)***
  - 510(k) exempt function (Class I and some Class II)
  - Device function that FDA is exercising its enforcement discretion
- ***FDA will review impact of "other function" on device function***
  - Negative impact or positive impacts that will go on labeling

Other Digital Health FDA Policies

- ***Device Software and Mobile Medical Applications***
  - FDA enforcement discretion for low-risk functions
  - Allow patients to self-manage and automate simple tasks for HCPs
- ***Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices***
  - **Not a device:** solely intended to transfer, store, convert formats, and display
    - Including software that interfaces with active patient monitoring (multiple function)
  - **Device:** software functions that analyze or interpret medical device data in addition to transferring, storing, converting formats, or displaying
- ***Off-The-Shelf Software Use in Medical Devices***
  - Risk based approach dependent on Level of Concern (to what extent the software may affect the patient)
- ***COVID-19 Digital Health Policies***
  - Remote monitoring, treating psychiatric disorders

Warning Ahead

- The products under FDA enforcement discretion (non-software) remain a medical device
- FDA policies are non-binding
- FDA may still enforce regulations

FDA Enforcement Trends

- ***Little if any public FDA enforcement***
  - Warning Letters are not common (if any at all)
- ***FDA is getting more active behind the scenes***
  - Untitled Letters are common
  - Competitors complaining to FDA
- ***Preparing for policy changes***
  - Digital Center of Excellence
  - Pre-Certification Pilot Program
  - Cures 2.0

Best Practices

- ***Consider compliance to Quality System Regulations***
  - Easier transition if product becomes an FDA enforcement priority
  - If FDA seeks a marketing submission, Quality System compliance may allow your device to remain on the market during the submission review
- ***Design considerations (multiple function)***
  - Design-in independence where risks or changes to one function will not impact the other function
  - Risk-based assessment to understand and mitigate adverse impacts

Best Practices

- **Review labeling and promotional claims**
  - ***Ensure claims do not creep into the realm of a medical device***
    - Does not claim to cure, mitigate, treat, or prevent
    - Intended to provide information to make independent decisions
  - ***Ensure claims are truthful and non-misleading***
    - Help avoid competitor complaints and FDA scrutiny
    - Differentiating permissible, First Amendment-protected, scientific dissemination from promotion
    - Help remain on the market during potential FDA submission review

Future of Digital Health

- **Current statutory/regulatory paradigm not well suited**
  - ***Artificial Intelligence / Machine Learning***
    - Algorithm that allow for active changes in response to new data
    - Device will be obsolete and on to the next version by end of FDA review
    - Currently only locked algorithm have been cleared by FDA
  - ***Cybersecurity***
    - New and evolving issues that may impact device safety
    - Devices increasingly connected to networks and other devices

FDA's Digital Health Center of Excellence

- ***Goals and Objectives:***
  - Coordinate digital health across FDA
  - Share knowledge
  - Support regulatory review of digital health devices
- ***Software Precertification Pilot Program***
  - Fast track digital health products
  - Evaluate company's culture of quality
  - Quality based evaluation does not fit under current statutory framework
- ***Cures 2.0: FDA report to Congress on collaboration/alignment***

Questions?

Contact

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