Using FDA Enforcement Data To Get FDA-Inspection Ready

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FDA Enforcement Data Enables You To:

- Allocate the right resources to the right areas
- Justify additional resources
- Identify key trends / insights

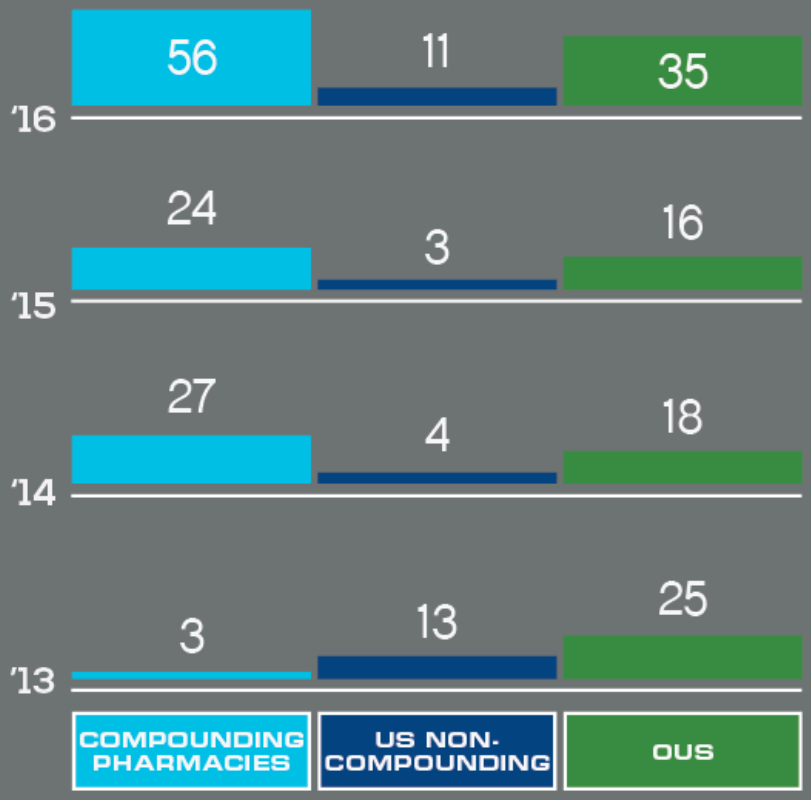
Today

- Big picture data
  (WL, Inspections, 483s, inspectors)
- Will Trump Impact FDA Enforcement?
- Case Studies – go deeper

DRUG GMP WARNING LETTERS SKYROCKETED IN 2016

TOTAL LETTERS
In the Past 4 Years

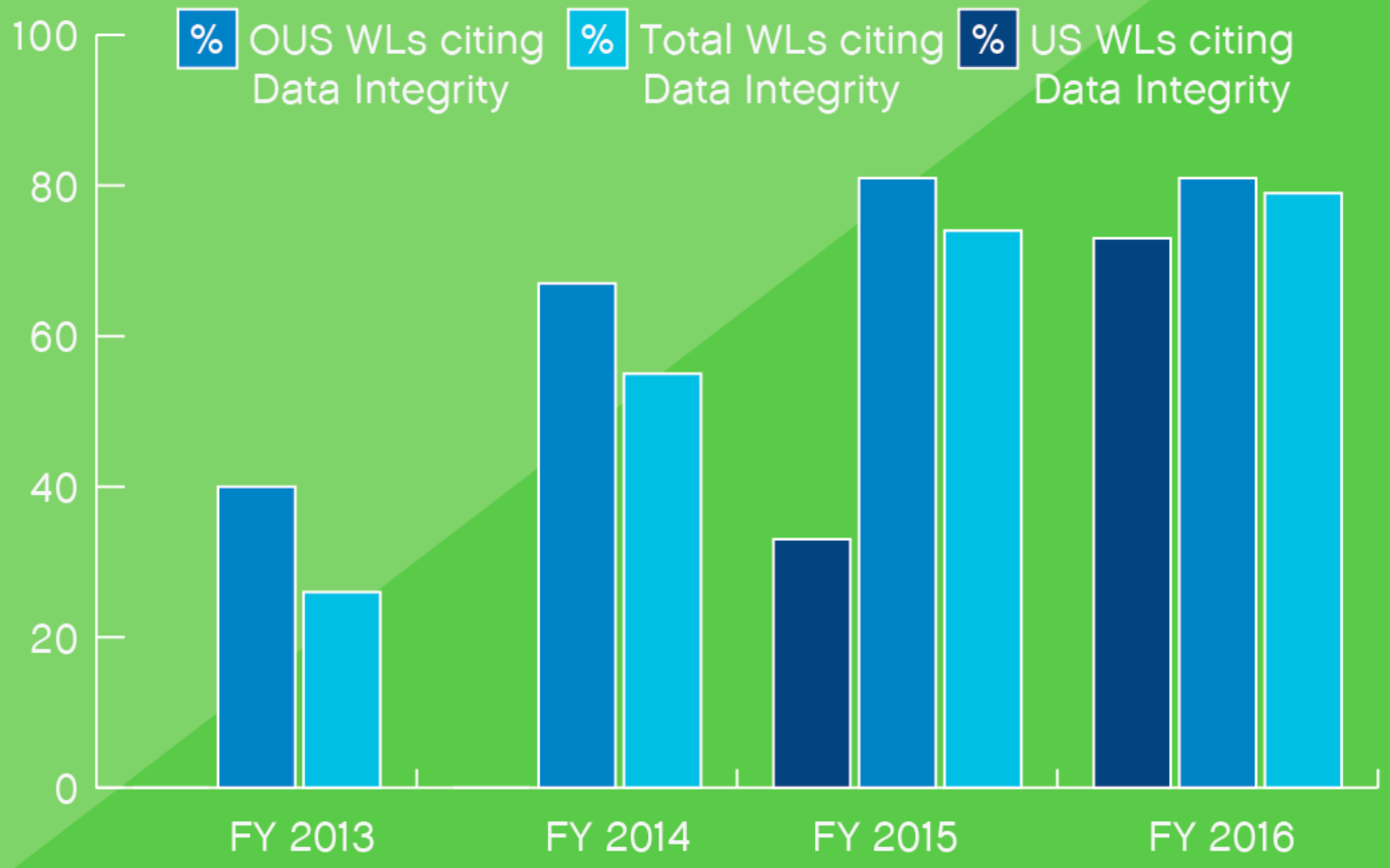
A CLOSER LOOK:
Drug GMP Warning Letters by Kind



All major categories of Warning Letters skyrocketed, more than 2X.

China experienced a dramatic explosion of warning letters. This is similar to what happened to India a few years back with the same FDA Investigator, Peter Baker, heavily involved.

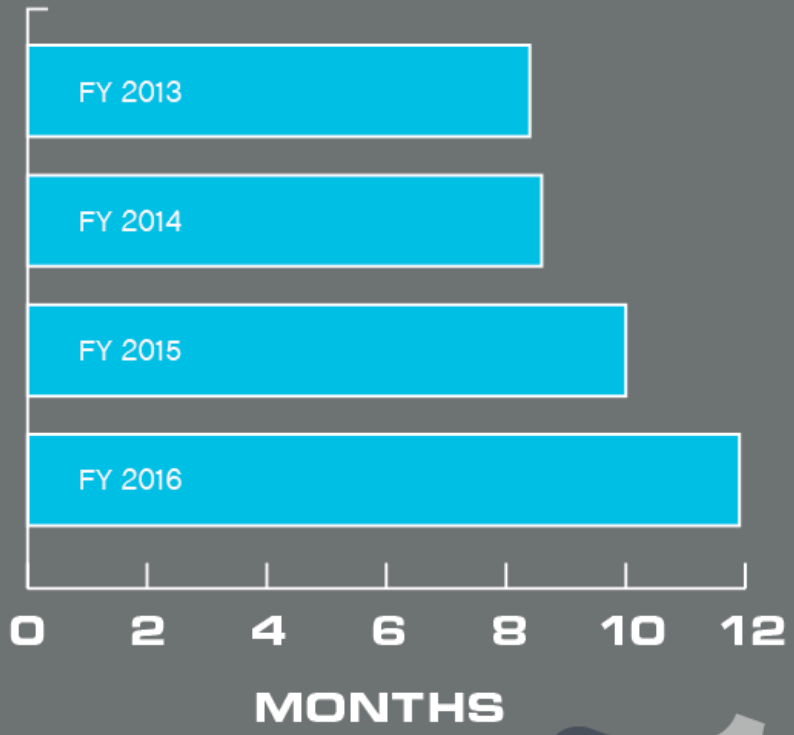
HOW DATA INTEGRITY PLAYS A HUGE ROLE:



Data Integrity is the BIG ISSUE for these warning letters - and not just for foreign sites anymore. The US has essentially "caught up" (in a bad way)

IT'S NOW TAKING THE FDA LONGER TO GET THESE WARNING LETTERS

Almost a year from the time they finish inspecting a facility.

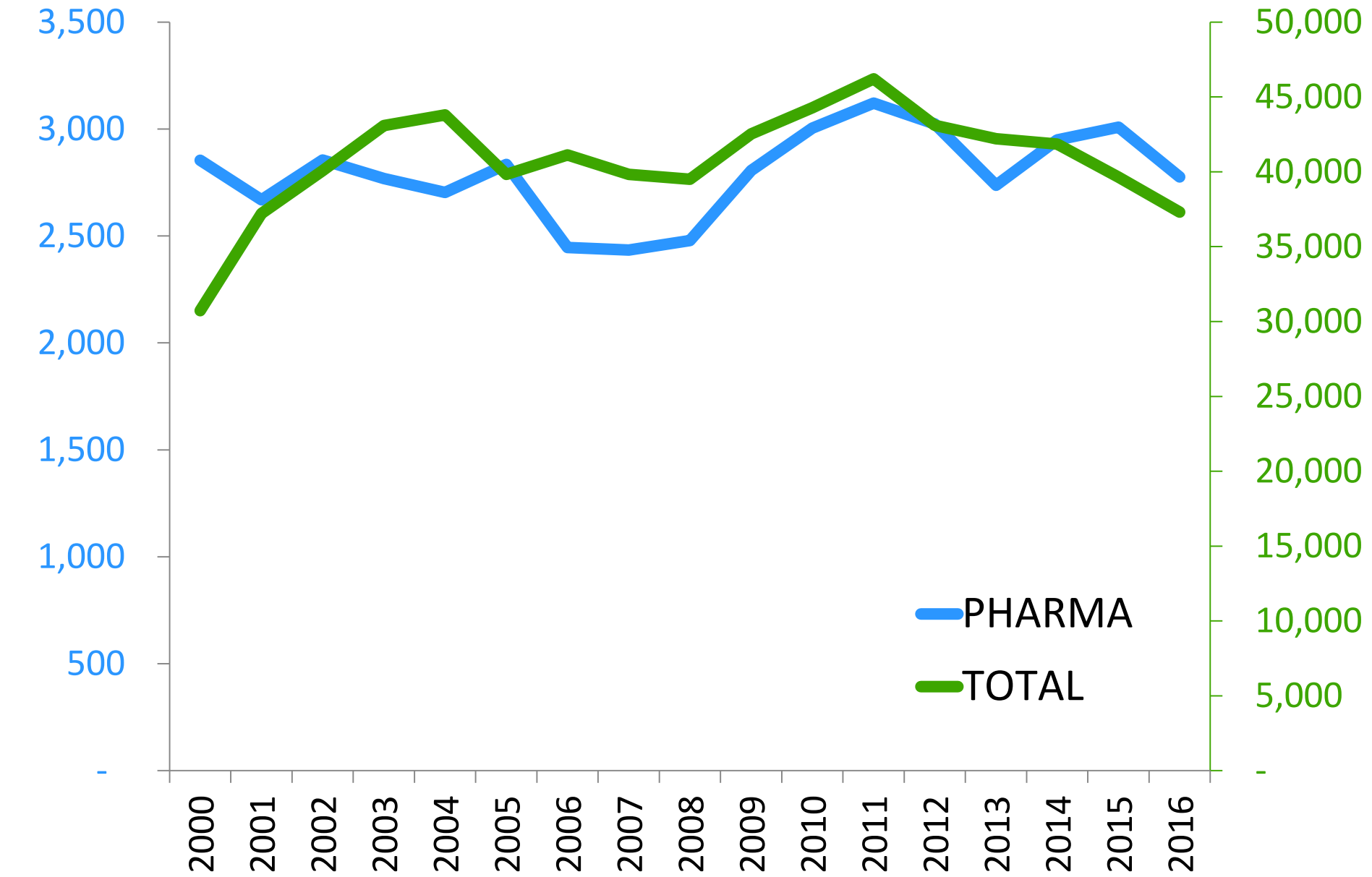


10.4 MONTHS

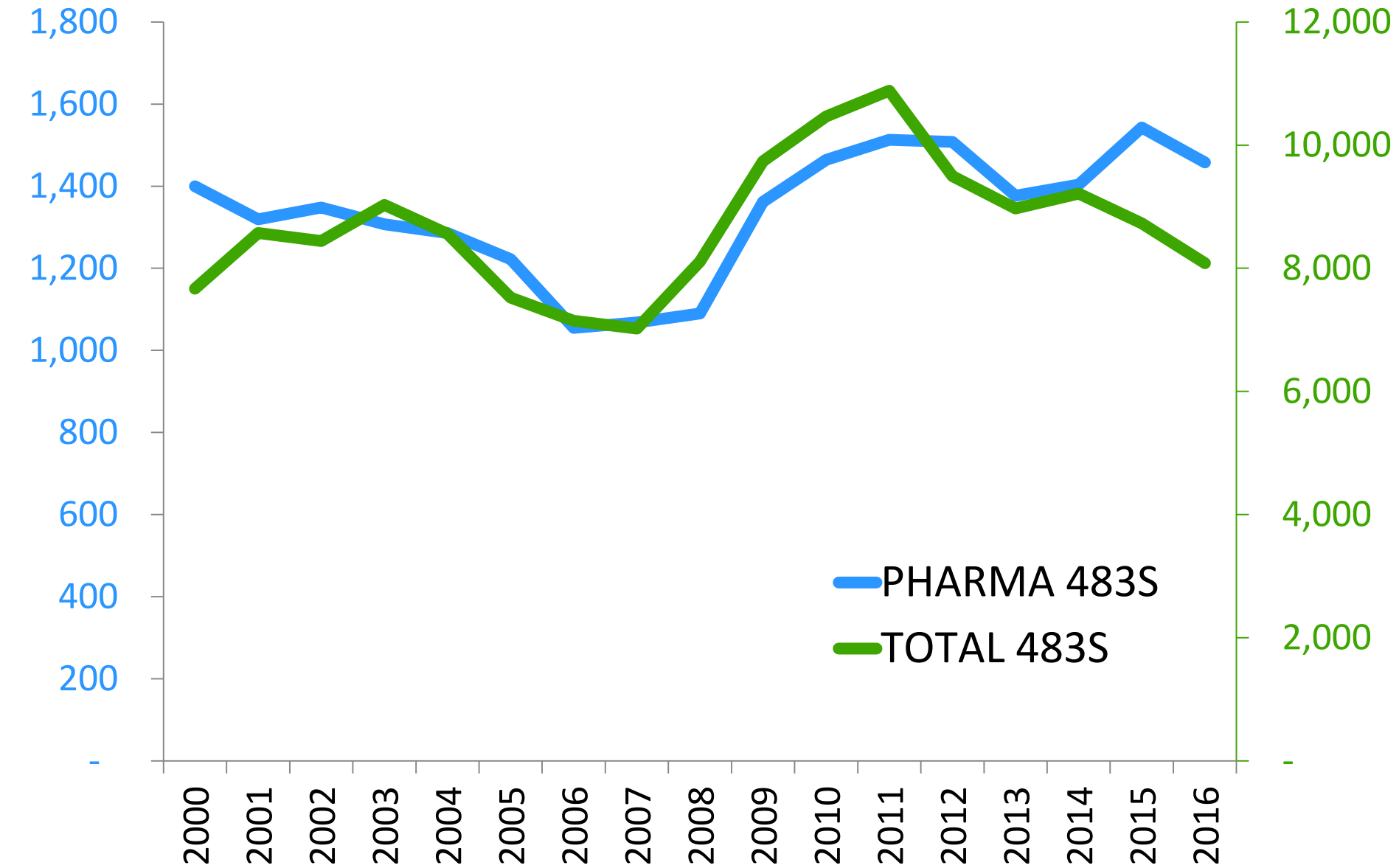
5.4 MONTHS

IT TAKES ABOUT HALF AS LONG FOR THE FDA TO ISSUE AN IMPORT ALERT VERSUS A WARNING LETTER

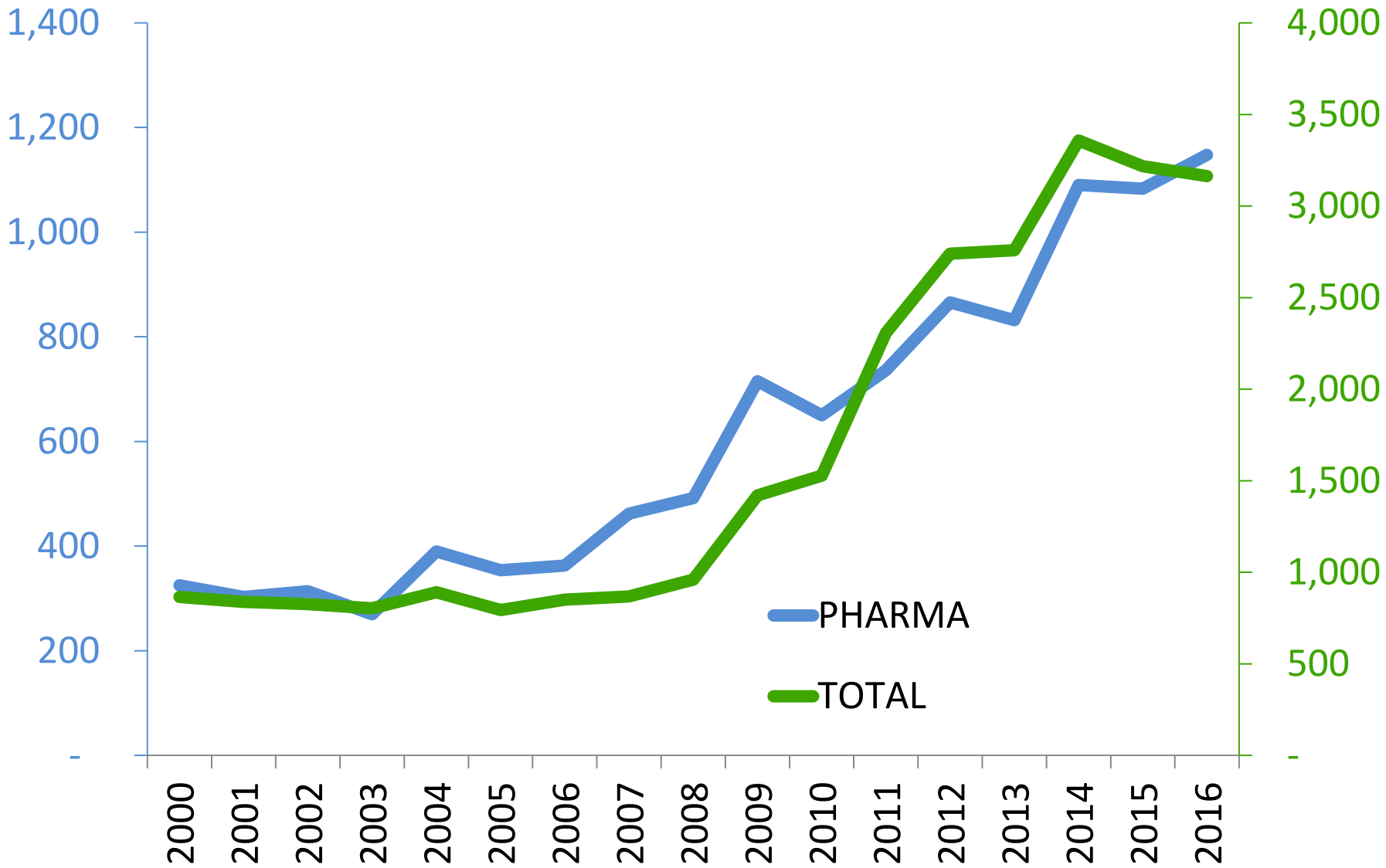
FDA INSPECTIONS



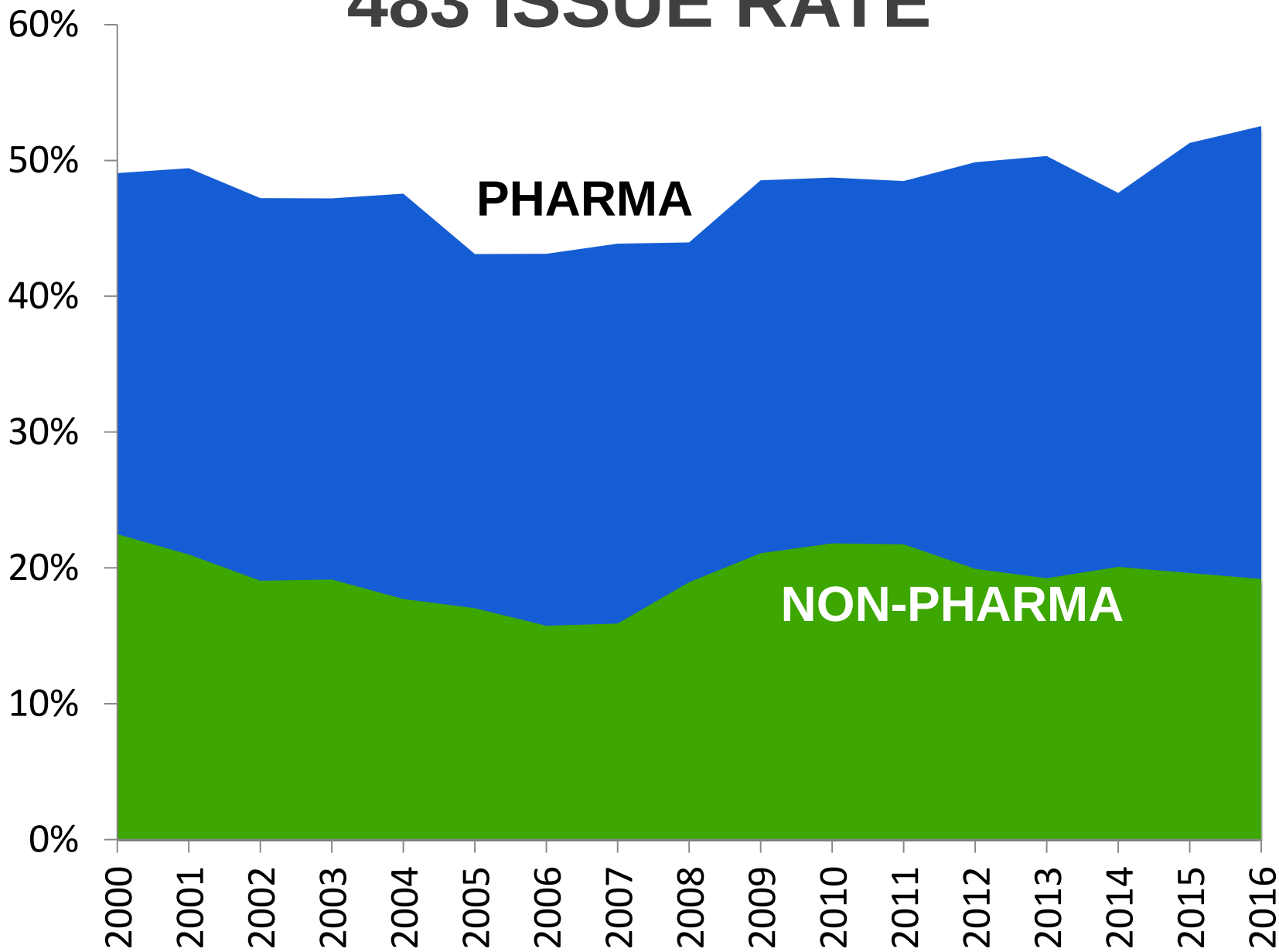
FDA 483s


1,800
1,600
1,400
1,200
1,000
800
600
400
200
-
12,000
10,000
8,000
6,000
4,000
2,000
-
PHARMA 483S
TOTAL 483S
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016

EX-US INSPECTIONS



PHARMA vs NON-PHARMA: 483 ISSUE RATE



TOP PHARMA INSPECTORS

InspectorRank for Human Drugs

CSV

Maximum achieved score is 177 by Baker, Peter E in 2013.

2016

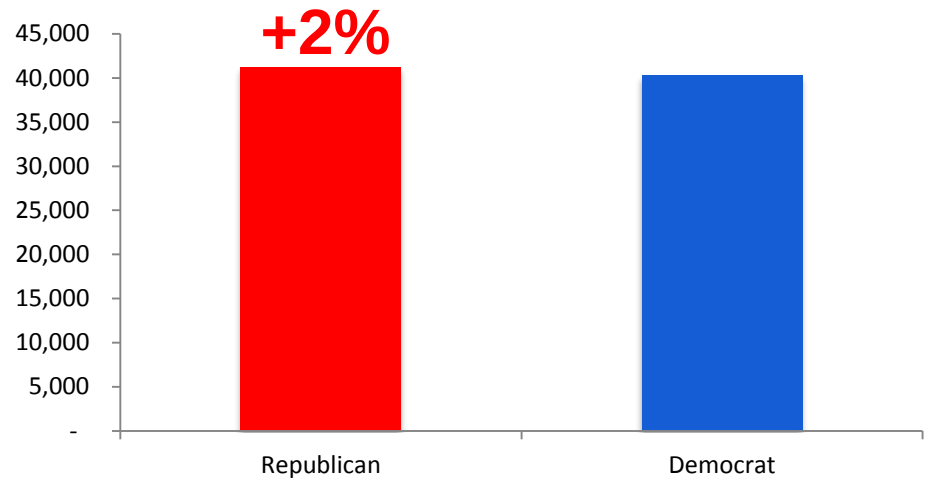
1	Boyd, Justin A	117
2	Motamed, Massoud	84
3	Morgan, Jason K	72
4	Baker, Peter E	72
5	Hicks, Kellia N	72
6	Hughes, Sandra A	66
7	Limchumroon, Uttaniti	60
8	Harouaka, Djamila	57
9	Upadhyay, Pratik S	57
10	Jassal, Charanjeet	57

2015

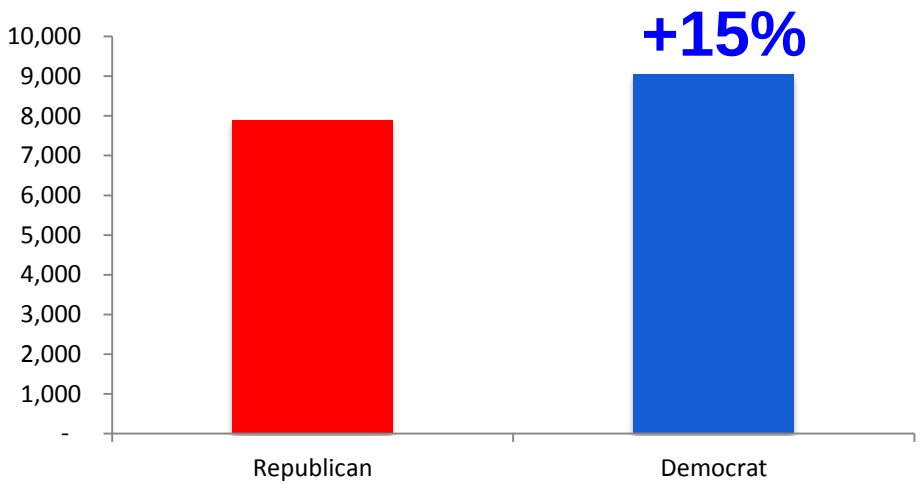
1	Baker, Peter E	114
2	Boyd, Justin A	108
3	Limchumroon, Uttaniti	84
4	Zabinski, Roger F	84
5	Daramola, Ademola O	81
6	Roberts, Daniel J	81
7	Menachem, Arie	75
8	Barreto-Pettit, Ileana	75
9	Clausen, Cheryl A	72
10	Kurtzberg, Alan P	72

INSPECTIONS & POLITICS?

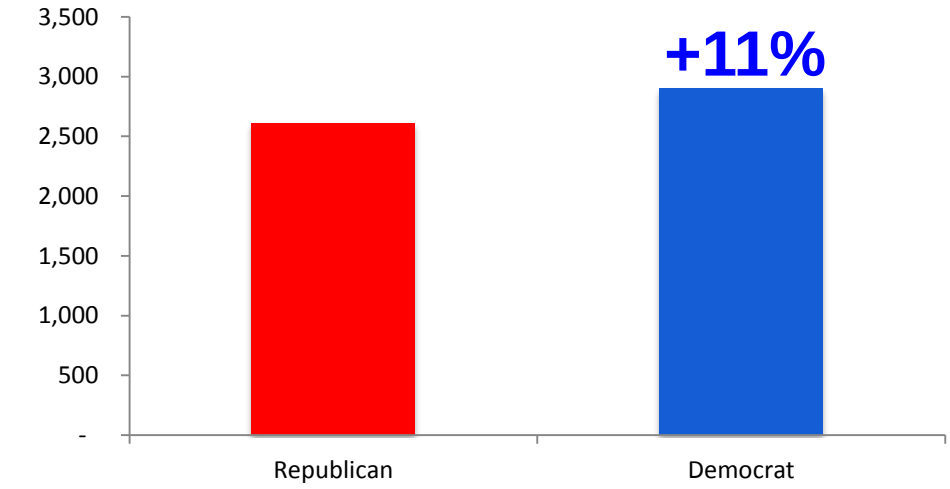
Average Inspections/Year



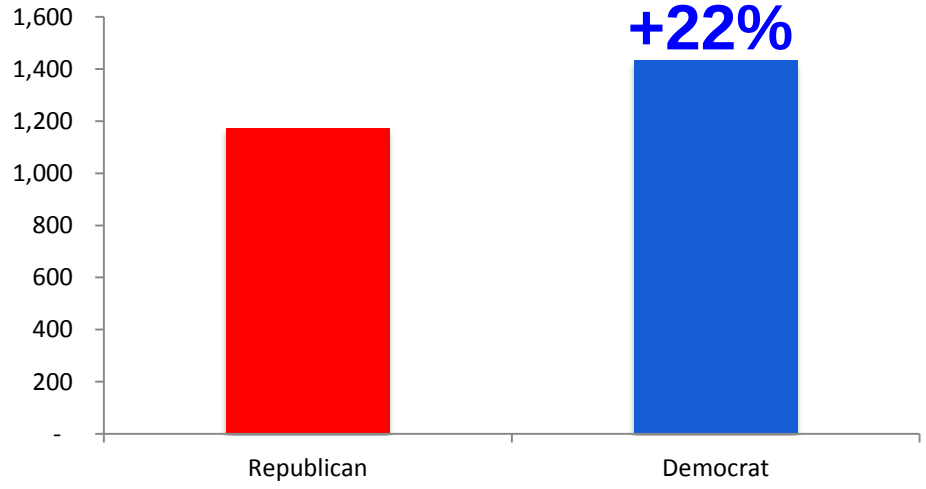
Average 483s/Year



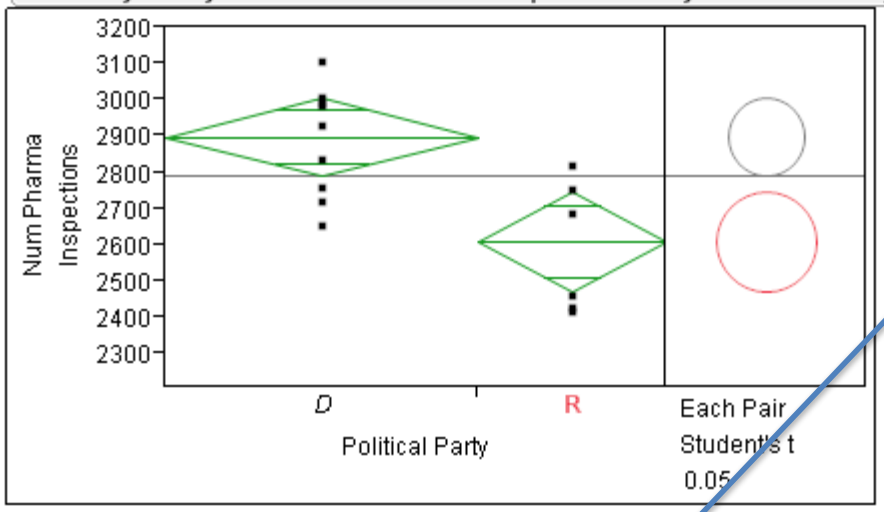
Average Pharma Inspections/Year



Average Pharma 483s/Year



Oneway Analysis of Num Pharma Inspections By Political Party



Excluded Rows 1

Oneway Anova

Summary of Fit

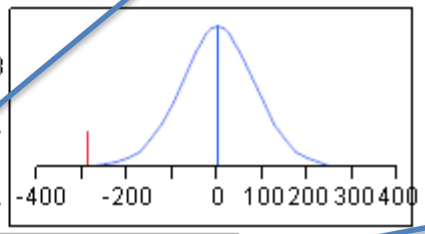
Rsquare	0.472676
Adj Rsquare	0.43501
Root Mean Square Error	157.7811
Mean of Response	2791.563
Observations (or Sum Wgts)	16

t Test

R-D

Assuming equal variances

Difference	-288.63	t Ratio	-3.54248
Std Err Dif	81.48	DF	14
Upper CL Dif	-113.88	Prob > |t|	0.0032*
Lower CL Dif	-463.39	Prob > t	0.9984
Confidence	0.95	Prob < t	0.0016*



Means for Oneway Anova

Level	Number	Mean	Std Error	Lower 95%	Upper 95%
D	10	2899.80	49.895	2792.8	3006.8
R	6	2611.17	64.414	2473.0	2749.3

Std Error uses a pooled estimate of error variance

43% of variability in Number of Pharma Inspections can be explained by the Political party that appoints the FDA commissioner

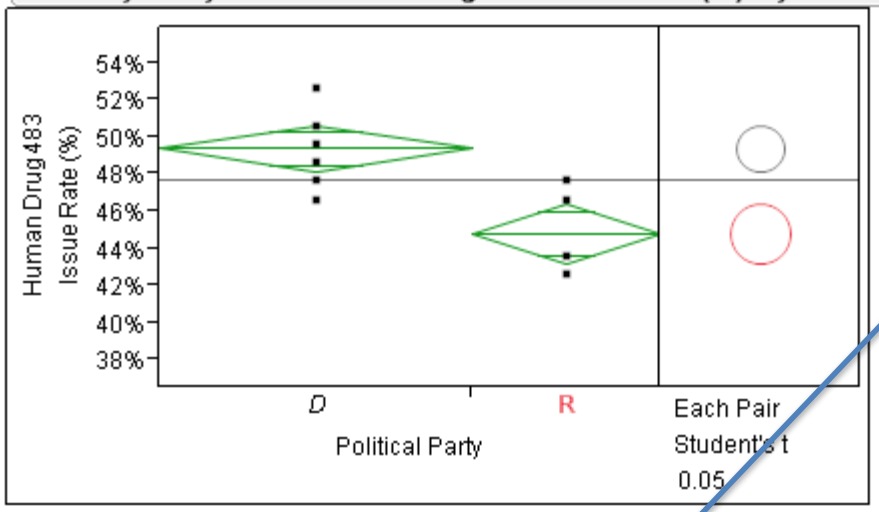
This 43% is <u>statistically significant</u>.

The probability of finding this result by random chance alone is **less than 3 in 1000**

The magnitude of difference is 2,600 vs 2,900.

Bottom Line: **10% reduction in inspections**

Oneway Analysis of Human Drug 483 Issue Rate (%) By Political Party



Excluded Rows 1

Oneway Anova

Summary of Fit

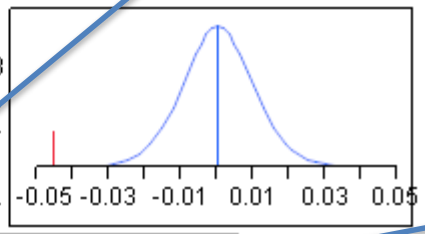
Rsquare	0.613667
Adj Rsquare	0.586072
Root Mean Square Error	0.018753
Mean of Response	0.476875
Observations (or Sum Wgts)	16

t Test

R-D

Assuming equal variances

Difference	-0.04567	t Ratio	-4.71573
Std Err Dif	0.00968	DF	14
Upper CL Dif	-0.02490	Prob > |t|	0.0003*
Lower CL Dif	-0.06644	Prob > t	0.9998
Confidence	0.95	Prob < t	0.0002*



Means for Oneway Anova

Level	Number	Mean	Std Error	Lower 95%	Upper 95%
D	10	0.494000	0.00593	0.48128	0.50672
R	6	0.448333	0.00766	0.43191	0.46475

Std Error uses a pooled estimate of error variance

59% of variability in Issue Rate of 483s to Drug companies can be explained by the political party that appoints the FDA commissioner

This 59% is <u>statistically significant</u>.

The probability of finding this result by random chance alone is **less than 3 in 10,000**

The magnitude of difference is 49% vs 45%

Bottom Line: **10% rate of 483 issuance to drug companies**

WHAT TO EXPECT FOR 2017

Continued focus OUS where most generic drugs are made.

The continued balancing act between enforcement actions and drug shortages.

Continued increase, both US and OUS, of failures in the area of data integrity.

We'll see more of the same, but the political climate may suggest a diminished enforcement environment (ala the GWBush era).

Intervals between inspections and WL continue to increase, import alerts are on average issued in the ½ the time of a WL.

WHAT TO EXPECT FOR 2017

Compounding pharmacies and outsourcing facilities do not appear to be turning the corner on compliance here….almost like they are clueless and not paying any attention.

Case Studies

FDA

WWW.FDAZILLA.com

"In my decades of experience in the industry, I've never seen anything like this - having a centralized source for inspector and inspection data is extremely valuable."

- Director, Regulatory Affairs and Quality Assurance

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- Tony Chen, CEO FDAzilla
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