



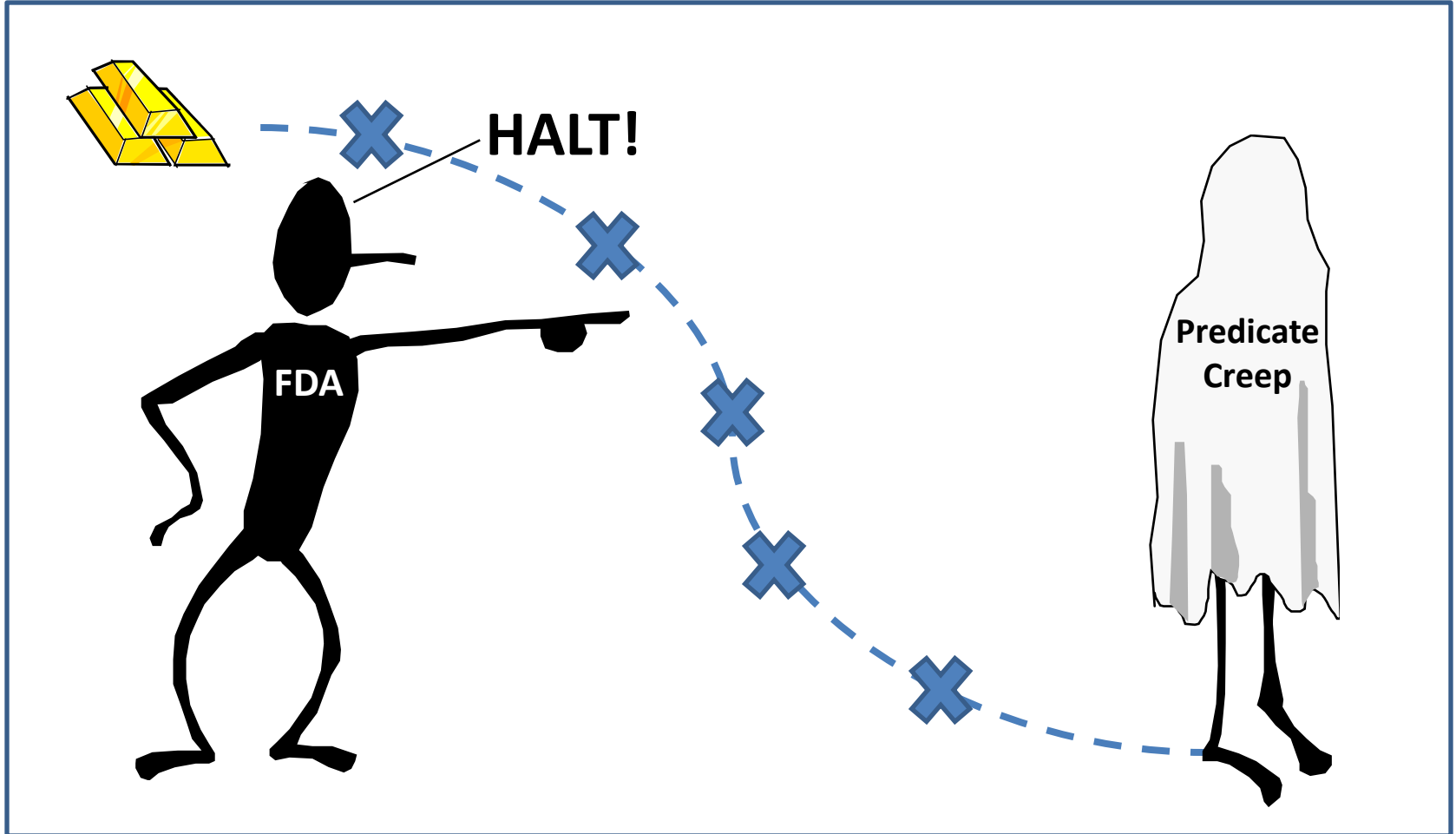
NEW WORLD REGULATORY SOLUTIONS INC.

*Strengthening the Center for Devices
and Radiological Health's 510(k) Review Process
February 18, 2010*

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**NWRS was founded in 2002 to help foreign
and domestic companies gain FDA approval
or clearance for innovative devices**

Current Status



Arresting the Predicate Creep

Strengthening the 510(k) Review Process, 18 February 2010



PERSPECTIVE is based upon EXPERIENCE



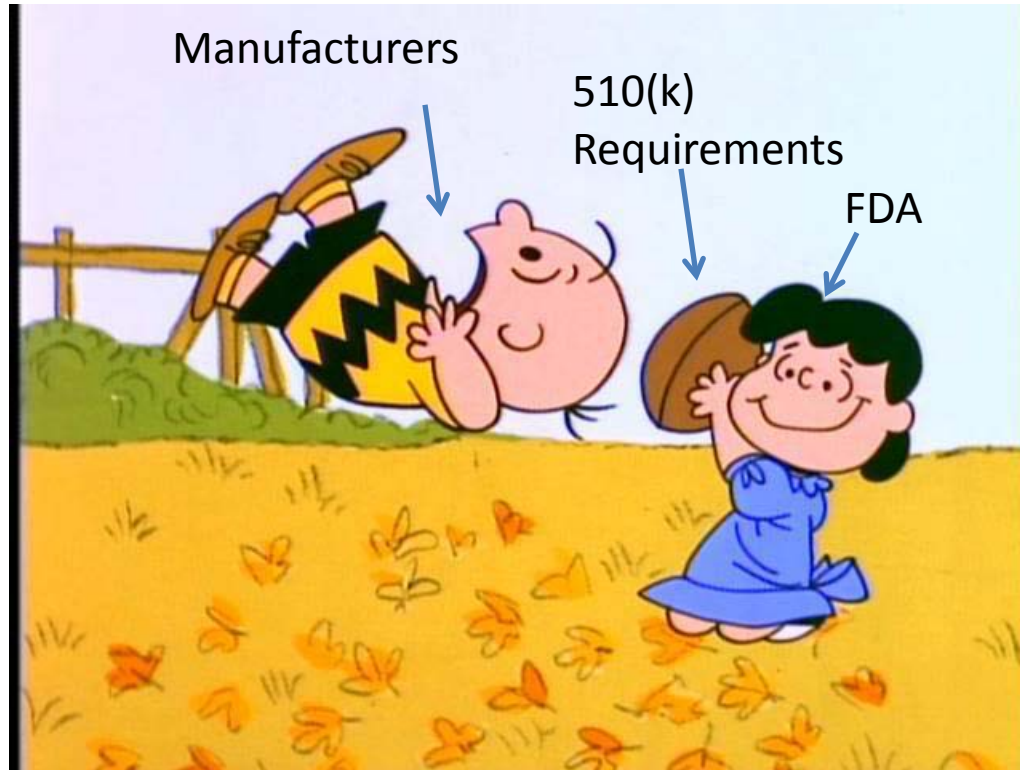
...and what we've heard from companies -- large and small, new and experienced, domestic and foreign

- Wouldn't it be nice if we could all exchange shoes?
 - We need to find a solution together



A Historical Review (we've always been here!)

- *New Medical Devices Challenge Scientists And Regulators Alike*, *The Scientist* 1990, 4(9):6
“... Congress and the public are increasingly concerned that FDA is not being tough enough and that technology is inflating health care costs.”
- *In Vitro Diagnostics Firms Frustrated By FDA Delays*, *The Scientist* 1997, 11(5):1
“When we were about to submit they changed the rules, and that set us back a significant period of time.”





III. A.1.a, 510(k) Searchable Database

How effective is the 510(k) database and search engine?

- Only as effective as the current review requirements! (i.e., not very effective!)
- More useful if you know the exact name of product, sponsor or product code

What aspects are useful?

- Searching by product code, K#, CLIA categorization, can find classification regs



III. A.1.a, continued

What could be improved?

- Better Filtering with key words
 - Seems harder to locate things than it used to be
 - Get too many irrelevant hits
- “Effective Dates” don’t always seem to make sense
- Multiple 510(k) summary types/formats are confusing



III. A.1.a, continued

What could be improved?

- Stock FDA response, “Check the database to see what was done for similar products” rarely helps, because the information seems to be obsolete



“FDA is a moving target these days”

- Policy appears to be made at the reviewer level:



“The rules are made up as they go along”



III. A.1.a, continued

What, if anything, should be added to: the 510(k) database and search engine?

- Enable searches through key words in *intended use* and *indications for use*
- Post comprehensive CLIA waiver submission summaries (posting “old rule” summaries generates frustration because submission of “old rule” studies will be denied)
- List all related 510(k)s numbers in one place, similar to PMA supplements
 - e.g., original and subsequent special 510(k) #s for one device on same page
 - can even annotate same 510(k) # with “SYY” for subsequent special 510(k)s.



III. A. 1.b., Effectiveness of public documents

cleared indications for use of each device?

- Provided under # 6 below

information that were used to determine substantial equivalence?

- 510(k) statements are no help in assessing predicates
- Lack information needed to plan SE studies for surgical, therapeutic or implantable devices
- The 510(k) Summary format (Device Advice) is not consistently followed.



III. A. 1.b., SE information, continued

- **Consistency** between summaries for equivalent devices is lacking
 - e.g., performance within ranges not stratified consistently between drugs of abuse tests where range criteria exist
 - Positive, negative and total agreements not reported consistently as such
- It's not just the older ones... some newer summaries are worse than older ones
- USDA veterinary test guidelines are very prescriptive



III. A. 1.c.

Should FDA require... a redacted version of their 510(k) submission.. for public release? Please explain why or why not.

- No.
 - Already available through FOI
 - Redaction can render the document useless,
 - or companies will object to the transparency
- Should FDA make include the reviewers names in publicly released documents?
- A better approach might be to publish clear requirements (to the extent possible) and hold everyone's feet to the fire



III. A. 1.c., continued

- Standardized and continually updating requirements will best protect the public health and will provide a level playing field
 - Require “grandfathered” devices to meet new standards
 - Use ISO as an example for implementation time frame (e.g. 3 years)



III. A. 2.

510(k) submitters' poor portrayal of similarities and differences

- Due to:
 - lack of complete information, for reasons mentioned above, and lack of publicly available predicate labeling
 - inexperience
 - pushing the envelope on substantial equivalence



III. A. 2., continued

Steps FDA should take to address it:

- CONTROVERSIAL:
 - Provide cleared labeling for every device.
- RATIONALE
 - It's done for drugs
 - These devices are used to ensure public health
 - The public has the right to know
- ENFORCEMENT
 - Require updated labeling to be filed with FDA (as a part of Document Control)
- REALITY
 - Competitors will have easier ride, sponsors will object



III. A. 3.

Generally, a device that has a clearance under the 510(k) process may be used as a predicate, regardless of whether or not the device is still in use, remains relevant to current standards of care, or has been replaced by new technology.

- A predicate should represent the accepted standard of practice and clinical utility.
- If new devices cannot be compared to old devices, then should those old devices be allowed to remain on the market?



III. A. 3., continued

stricter criteria for eligible predicate devices?

- Criteria lack definition for recognized predicates -- what statistical agreements are required? How many samples?
- Need standardized criteria for what constitutes agreement with predicates (January 2008 CLIA Waiver Guidance)
- FDA is beginning to “strongly recommend” predicates now – we need set criteria for eligible predicates to avoid the impression of FDA



“favoritism” or “moving target”



III. A. 3., continued

specific examples that favor use of “outdated” predicate

- Not even outdated, but less familiar...
- FDA “strongly recommended” a specific predicate (comparative method) for a CLIA Waiver, based on their familiarity with it, even though technology differences were a disadvantage for some analytes.
- In this case, different predicates for different analytes would have been advantageous, but a two-predicate approach was not allowed.



III. A. 4.

*Incremental device changes... “predicate creep”...
“non-inferiority creep”*

- FDA should consider a more thorough review of cumulative incremental changes if there is evidence that device safety and effectiveness have become compromised (post marketing surveillance may be required)
- Review of post marketing data may be conditional for clearance, e.g.,
 - $\geq 3^{\text{rd}}$ degree from predicate devices
 - all new devices for a predetermined period of time (or number of uses)
- Creep can also be in a positive direction



III. A. 4., continued

- An incremental approach is needed to implement changes to the 510(k) review process.
- A sudden and significant increase in clearance requirements (and cost) can discourage manufacturers of new, improved devices from seeking clearance
 - Look at OIVD's declining CLIA Waiver applications (and approvals) since the new guidance
- As a result, older, “inferior” (lower confidence limits) devices, which are not challenged to meet new standards, will dominate the market
 - How can this policy ***protect the public health?***



III. A. 5.

Do “Split predicates” serve the public health goals of the 510(k) program?

- Double-edged sword
- Clinical validation needed
- de Novo route may be better



III. A. 6.

“intended use” versus “indications for use”

- In general
 - *Intended Use*, Used for what
 - 21CFR 801.4, “the objective intent”
 - *Indications for Use* -- Used where, by whom, on whom, on what
 - 21 CFR 814.20(b)(3)(i) cites “general description” but requires specific indications
 - Often identical/interchangeable
 - Major source of confusion
 - Combining into a single term with a concise description could alleviate confusion



III. A. 6.

“criteria for differences”

- Not Intended Use Population (Indication for Use)
 - e.g., some Home Use (lay user) criteria are less stringent than CLIA Waiver (intended user) criteria
 - hCG
 - Glucose Meters
 - Drugs of Abuse
 - Cholesterol
 - OTC Route less burdensome for CLIA Waiver
 - Blurs OTC/Professional Use differences for 510(k)
 - Rather than submitting a new Traditional 510(k), gain intended user clearance through User/Flex Studies commensurate with Risk in Special 510(k)



What We All Can Do:

FDA

- Help Reduce Whiplash
 - Signal before changing lanes
 - Avoid Sudden Starts
- Follow Quality System tenets for FDA Outputs
 - Lot-to-Lot consistency for 510(k) Decision Summaries
 - Clean up the water that passed under the bridge
 - Rationale: Companies without Quality Systems as of June 1, 1997 still had to comply; thus their marketed devices should also comply with newly implemented regulations to help protect the public health.
- Improve “precision” in communications
 - Between reviewers, between divisions





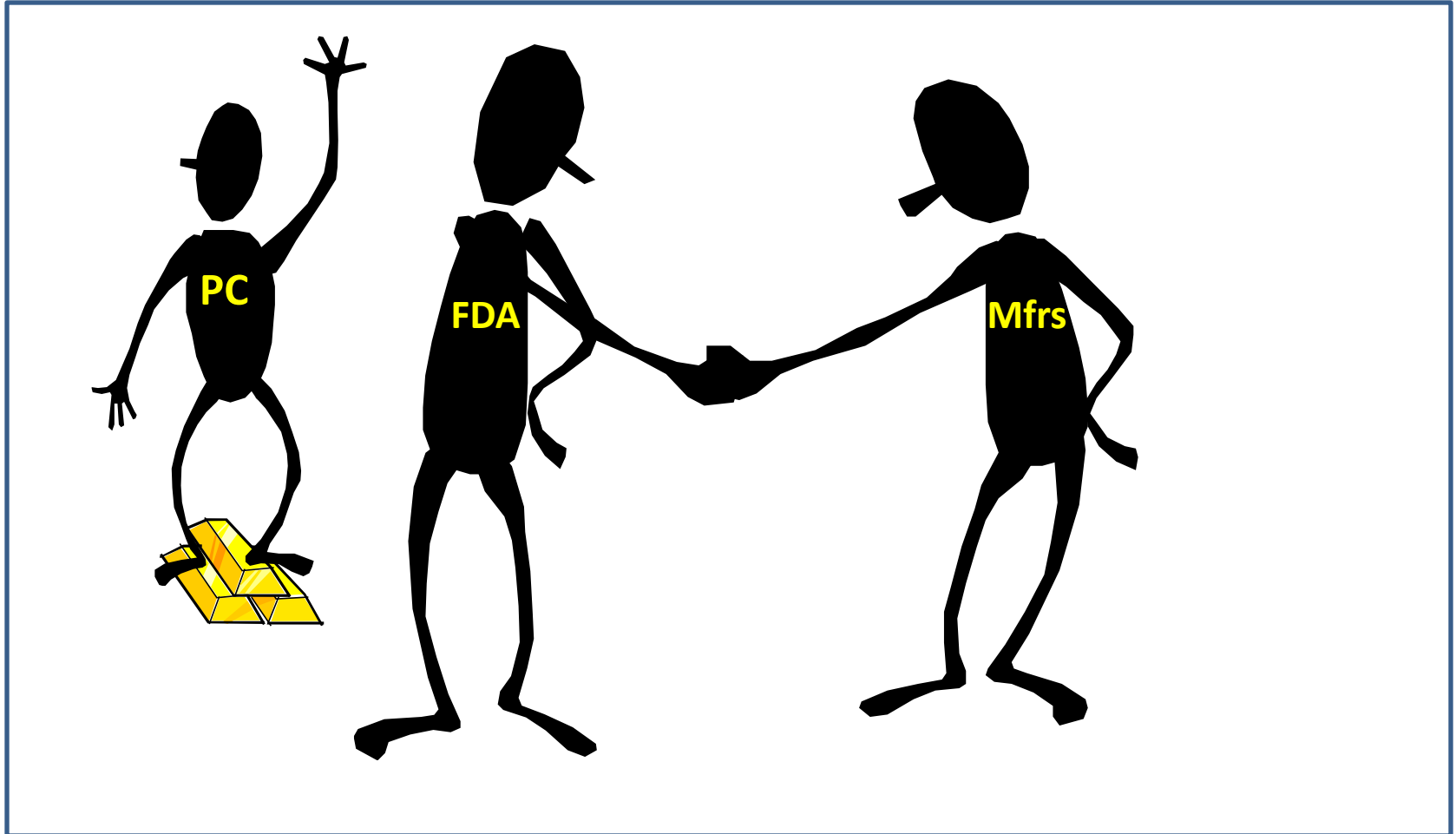
What We All Can Do:

Industry

- Plan studies to support claims
 - Protocols, statistics
 - Communicate with FDA
 - “I don’t ask if I think I won’t like the answer”
 - Recognize the FDA staff workload – their shoes are very tight!
 - Thorough, complete submissions
 - Account for every data point



Future Status



Establishing what is “Predicately Correct”



NEW WORLD REGULATORY SOLUTIONS INC.

THANK YOU!

***slides will be posted on our website under
“Industry News”***

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