FDA/GPhA Quarterly Meeting on GDUFA Implementation

December 16, 2014

Meeting Agenda

I.	Introductions	All
II.	Communications Transparency	FDA
III.	GDUFA Hiring Update	FDA
IV.	Inspection Parity Update	FDA
	Break	
V.	OSI (BE) Inspection Program	FDA
VI.	FY14 Update	FDA
VII.	Submission Quality Follow up	All
VIII.	Wrap-up and Next Steps	All

Communications Transparency

- Keith Flanagan
- Janet Woodcock
- Kathleen Uhl

CY14 - Deep, foundational restructuring to fulfill GDUFA commitments

A “perfect storm”

- Moved to White Oak.
- Reorganized and became a Super Office.
- New program and staffing infrastructure.
- New IT platform
- New OPQ
- Incoming submissions with goal dates for the first time.

Still need to tie up loose ends, but no additional restructuring is anticipated.

Thank you for your patience and understanding.

We appreciate you hanging in there with us.

CY15 – Attack pre-Year 3 workload

- Improve not only communications, but also performance
- Goals:
  - "Move the freight"
  - Focus on approvals, not actions
  - Don't let big first generics slip through the cracks

Next Steps:

- Assign Target Action Dates (TADs) to all pre-Year 3 submissions. (With caveats, and not all at once. See next slide.)
- Base TADs on workload management factors, with one exception: For big first generics, assign TADs roughly corresponding with expiry.
- In early CY15, start notifying applicants of TADs.
- "Launch planning updates" for big first generics 6 and 3 months before TAD.
- Certain other pre-launch "go/no go" communications.
- Iterative, "real-time communications" re deficiencies in current review cycle. Already started in CMC, scale this out to Bio next.
- Update Communications with Industry MAPP to formalize and clarify these changes.

GDUFA Hiring Update

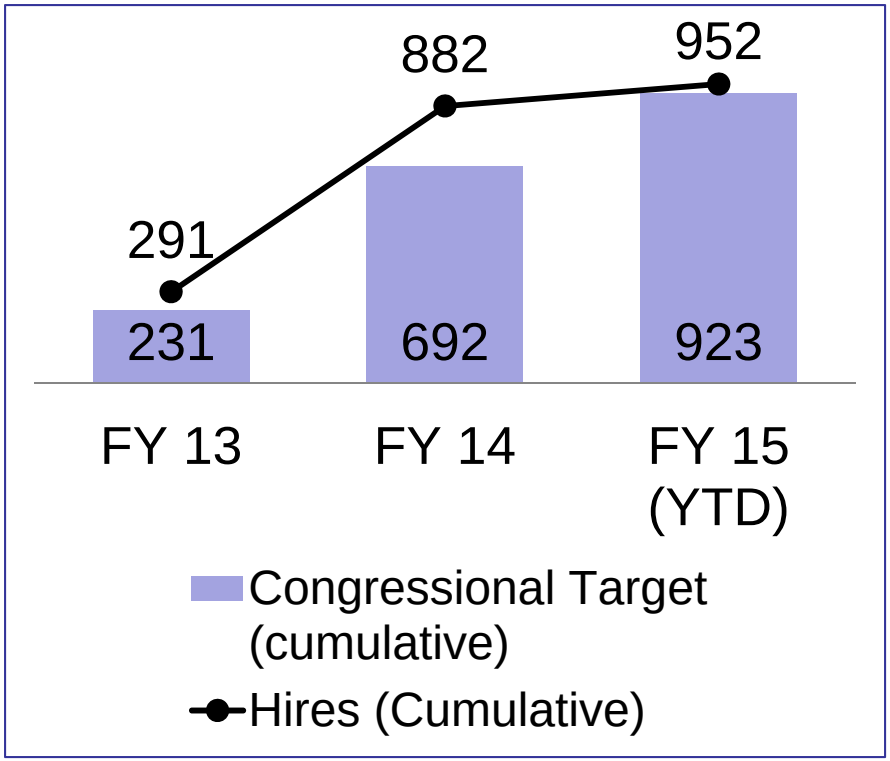
- CDER/OM – Sachin Shah
- ORA – Ann Marie Montemurro

GDUFA Hiring Update

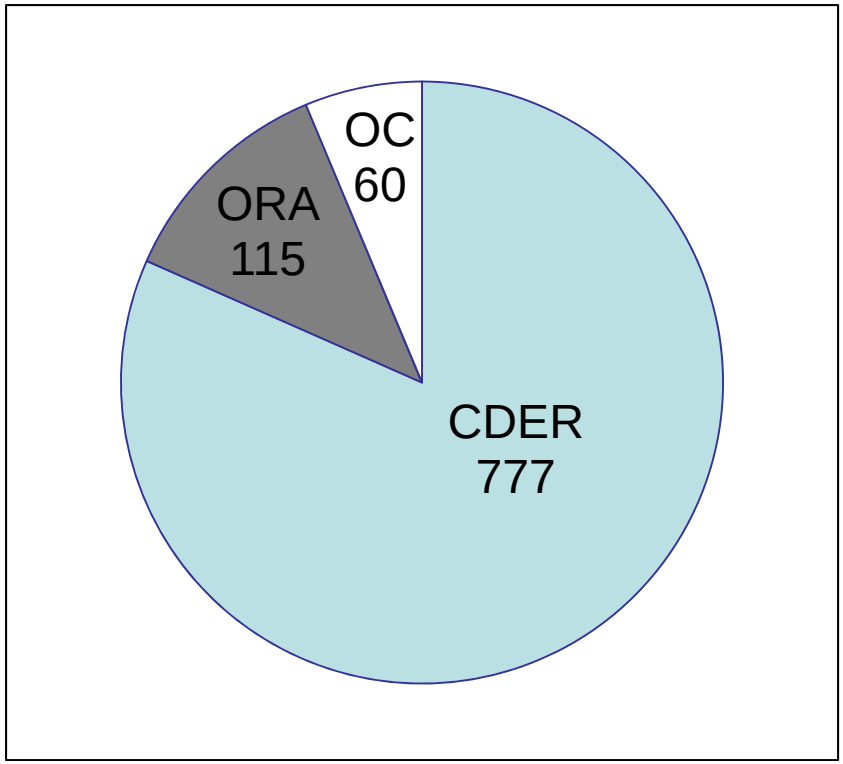
Melanie Keller
Associate Director for Management
Center for Drug Evaluation and Research
December 16, 2014

GDUFA Hiring: Goal Met

Hiring Progress by Fiscal Year



Hiring by Center/Office



All data through Nov. 19, 2014

Outreach For Talent

The July 18 GDUFA Hiring Event drew more than 3,000 people to the White Oak Campus

@FDA_Drug_Info

Fdacdergdufahiring

Social Media connected FDA to new sources of talent, increasing visibility and applicant quality.

Inspection Parity Update

- Russell Wesdyk

Meeting GDUFA Inspection Commitments

Surveillance Selection Rules

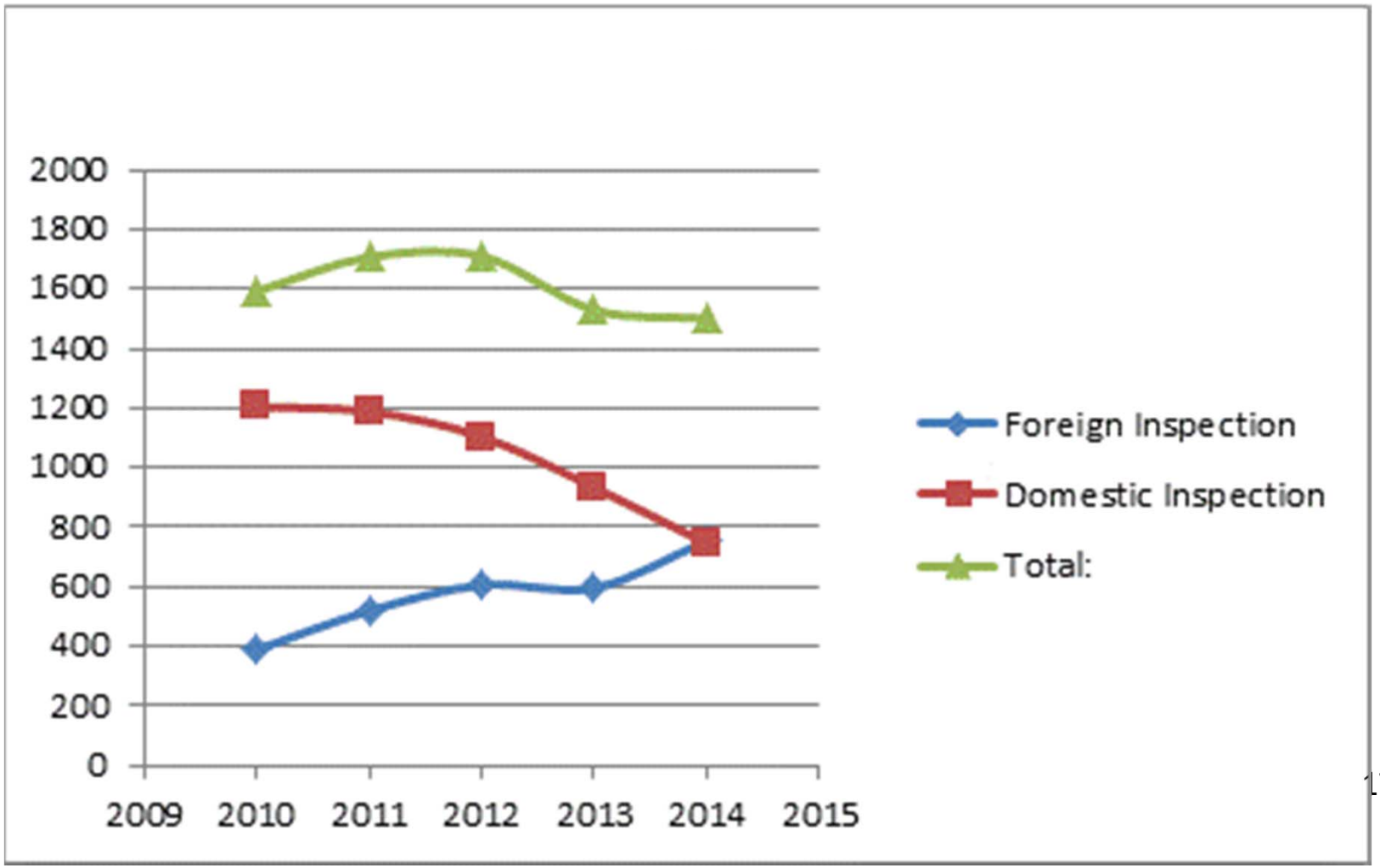
GDUFA Inspection Goals

- "FDA will conduct risk-adjusted biennial CGMP surveillance inspections of generic API and generic finished dosage form (FDF) manufacturers, with the goal of achieving parity of inspection frequency between foreign and domestic firms in FY 2017."

- "[…] with comparable depth and rigor of inspection."

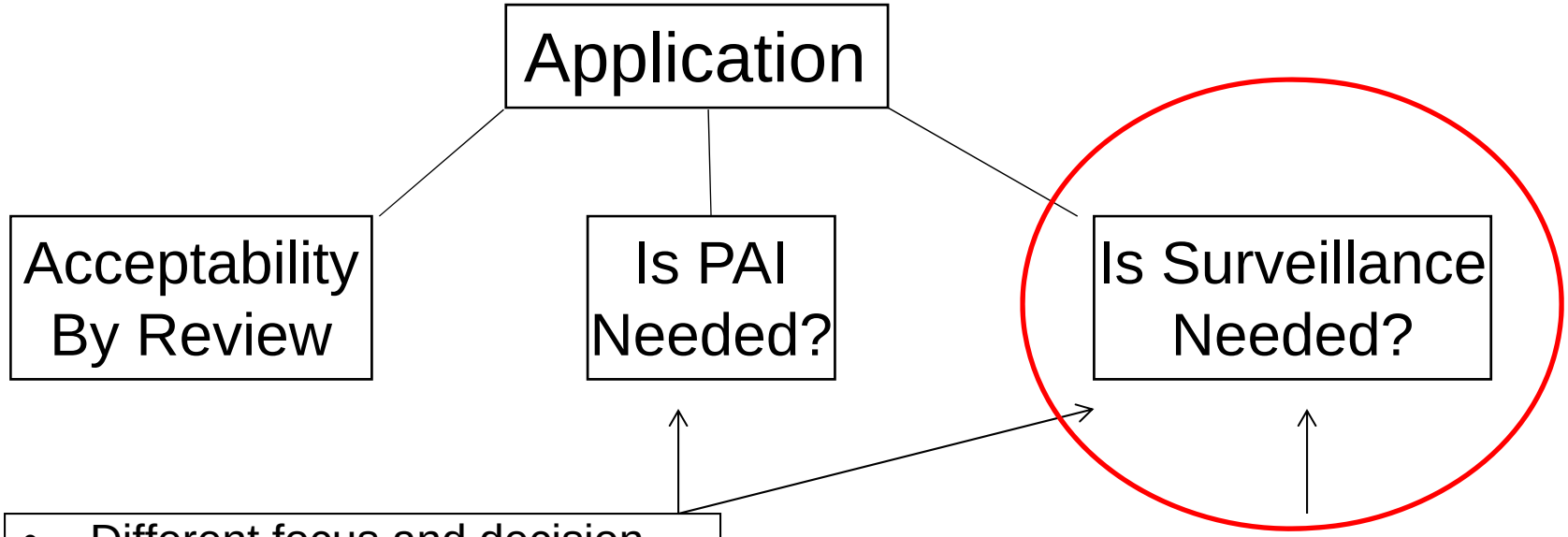
- Application timeline goals…

Surveillance Trends



INTRODUCTION

For Application Decisions



- Different focus and decision rules for PAI vs Surveillance inspections
  - PAI decision driven from molecule and technology; focus on data integrity
  - Surveillance decision driven from "2,3,4;" focus on systems

- Significant GDUFA implications and our focus
  - Not just for applications but for routine inspection

Biennial and 705

- Historic biennial requirement replaced with risk based approach detailed in FDASIA 705

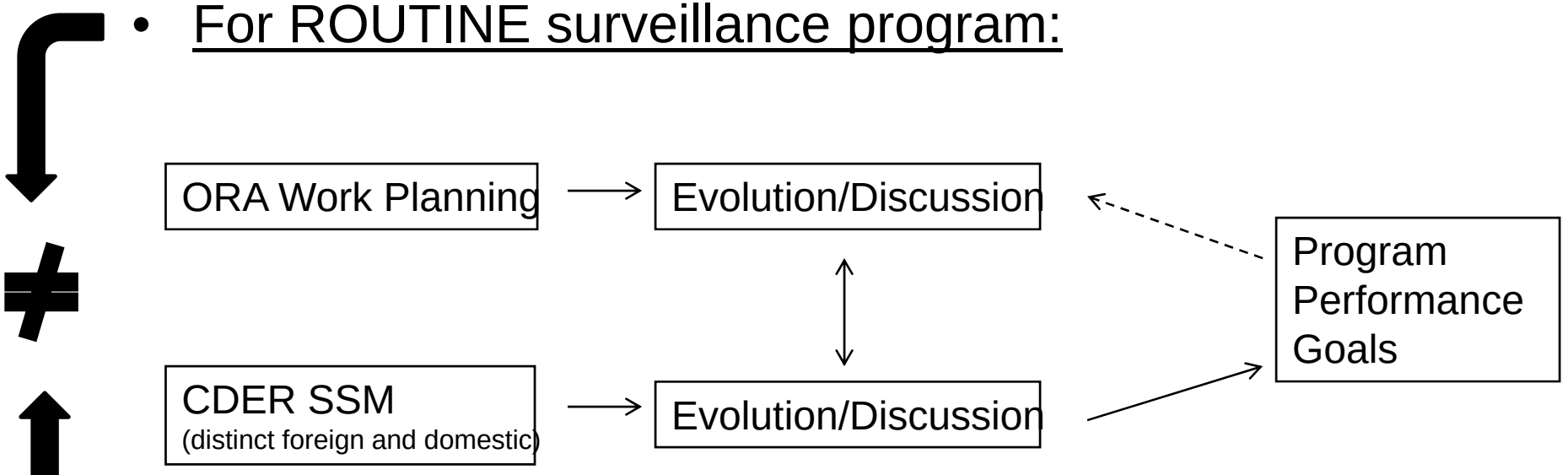
- FDASIA section 705 - In establishing the risk-based scheduled under paragraph (3), the Secretary shall inspect establishments according to the known safety risks of such establishments, which shall be based on the following factors:
  - ‘‘(A) The compliance history of the establishment.
  - ‘‘(B) The record, history, and nature of recalls linked to the establishment.
  - ‘‘(C) The inherent risk of the drug manufactured, prepared, propagated, compounded, or processed at the establishment.
  - ‘‘(D) The inspection frequency and history of the establishment, including whether the establishment has been inspected pursuant to section 704 within the last 4 years.
  - ‘‘(E) Whether the establishment has been inspected by a foreign government or an agency of a foreign government recognized under section 809.
  - ‘‘(F) Any other criteria deemed necessary and appropriate by the Secretary for purposes of allocating inspection resources

How Can We Align?

- Comply with new legislation
- Achieve GDUFA Goals
- Measure success

Historic Surveillance Rules

- For ROUTINE surveillance program:



- For APPLICATION decisions largely “2,3,4” plus individual refinement to 3,4,5
  - PAI rules distinct from that

Combined Foreign/Domestic
Inventory List
↓
Routine Surveillance
Inspection Decision Rules
↓
SSM
↓
Performance Goals

[redacted]

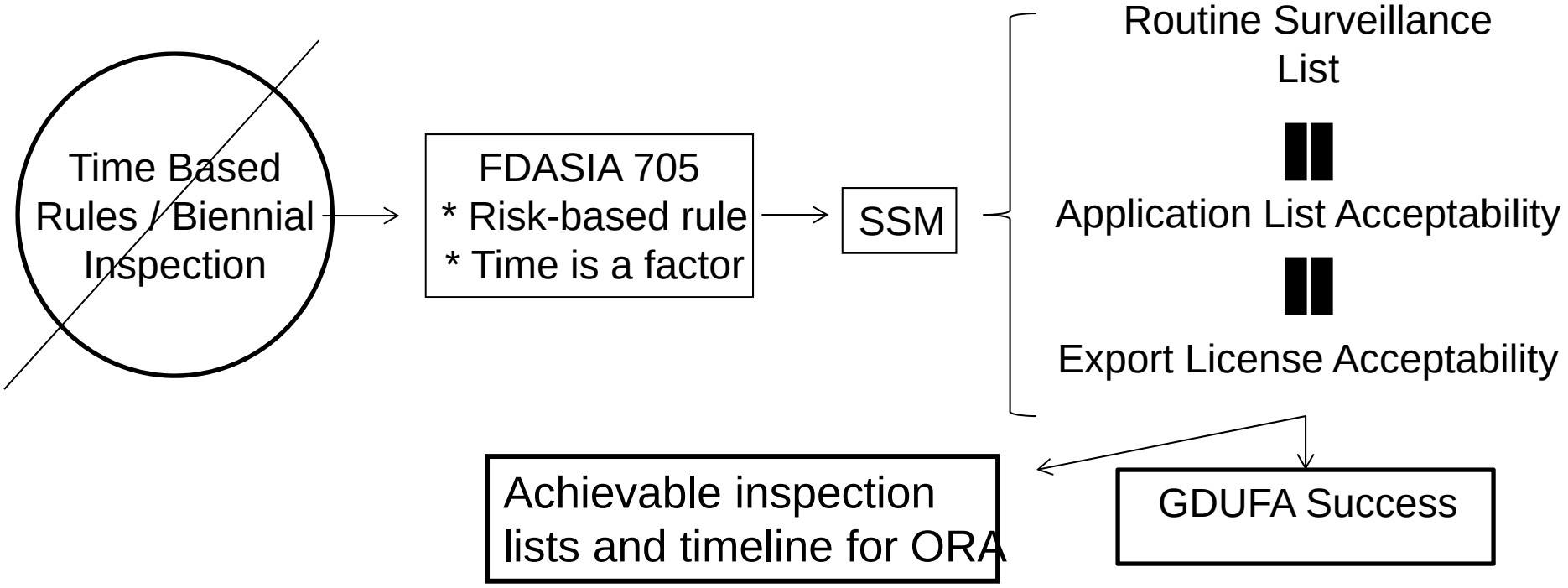
Application Surveillance
Inspection Decision Rules

GDUFA Inspection Goals: Measuring Success

- **Risk-based foreign and domestic frequency parity**
  - Propose to document success by following the output of the SSM
    - This addresses the “risk-adjusted” component
    - Is geography neutral ranking
  - Track progress against SSM list +/- 20%

- **Equal depth and rigor**
  - Document success by follow the NIPP protocol
  - This does not require measurement

Summary

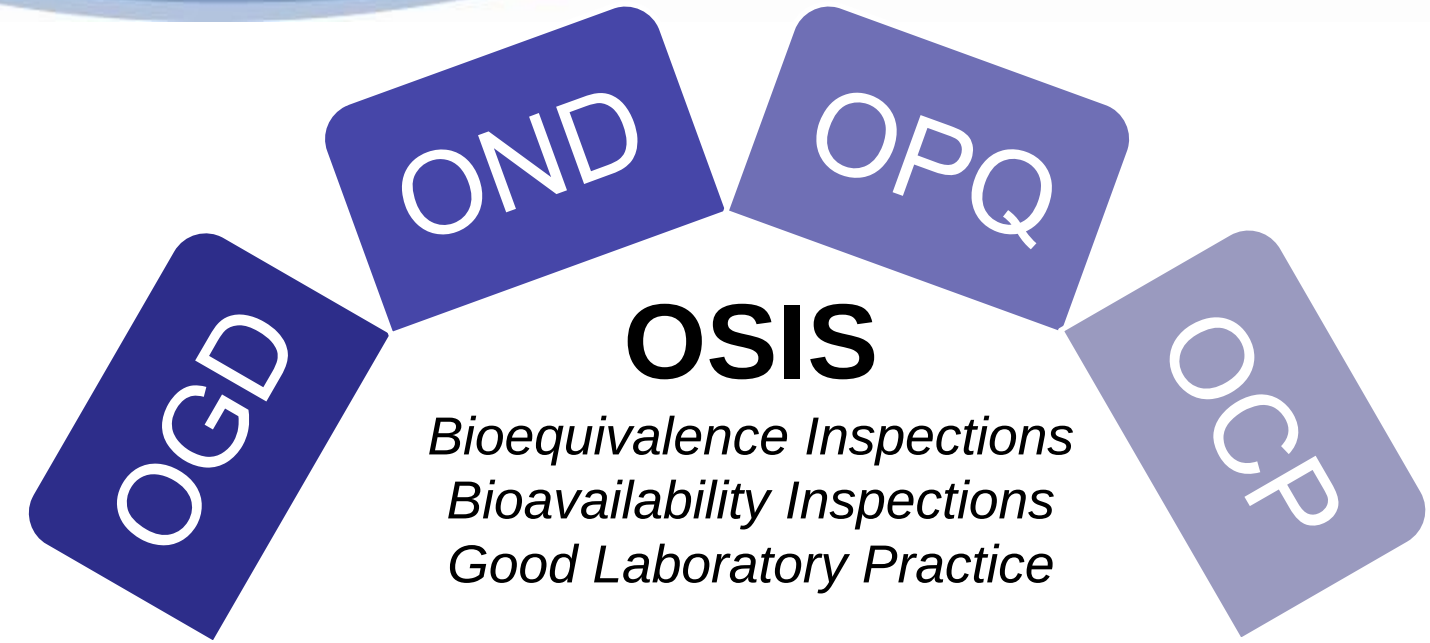

Time Based Rules / Biennial Inspection
FDASIA 705
* Risk-based rule
* Time is a factor
SSM
Routine Surveillance List
II
Application List Acceptability
II
Export License Acceptability
Achievable inspection lists and timeline for ORA
GDUFA Success

QUESTIONS?

Break Time

Office of Scientific Investigations

- Sean Kassim
- John Kadavil



OSI

Compliance Enforcement

OSIS = Office of Study Integrity & Surveillance

OSI = Office of Scientific Investigations

OSIS:
SITE INSPECTIONS for BIOEQUIVALENCE/BIOAVAILABILITY STUDIES

- **SURVEILLANCE INSPECTIONS**
  - **Clinical & analytical sites**
  - **More studies inspected at each site**

OSIS: *DETERMINATION for an INSPECTION*

- **Inspection history**
- **Date of last inspection**
- **New site**
- **Type of submission**
- **Study complexity**
- **For-Cause inspection requests**

OSIS: *EXPECTATIONS for COMPLIANCE*

- **Human subject protection, & clinical/analytical data integrity**
- **Documentation & record retention**
- **Protocols & SOPs**
- **Clinical sites: Inclusion/exclusion criteria, adverse events, sample collection (documented, consistent with protocol)**
- **Analytical sites (method validation & study sample analysis): Precision / accuracy / reproducibility of the method, stability**
- **Above expectations are not all-inclusive**

OSIS: *ISSUES to AVOID*

- **Following issues are not all-inclusive**
- **Inadequate documentation**
- **Clinical site issues include not maintaining or improperly storing/selecting reserve samples, not maintaining the blinding code**
- **Analytical site issues include unjustified repeats, not reporting failed runs**

OSIS: *REFERENCES to CONSIDER*

- **"Workshop/Conference Report — Quantitative Bioanalytical Methods Validation and Implementation: Best Practices for Chromatographic and Ligand Binding Assays",** *AAPS Journal, Vol. 9, No. 1, February 2007*

- **"2011 White Paper on Recent Issues in Bioanalysis and Regulatory Findings from Audits and Inspections",** *Bioanalysis, Vol. 3, No. 18, September 2011*

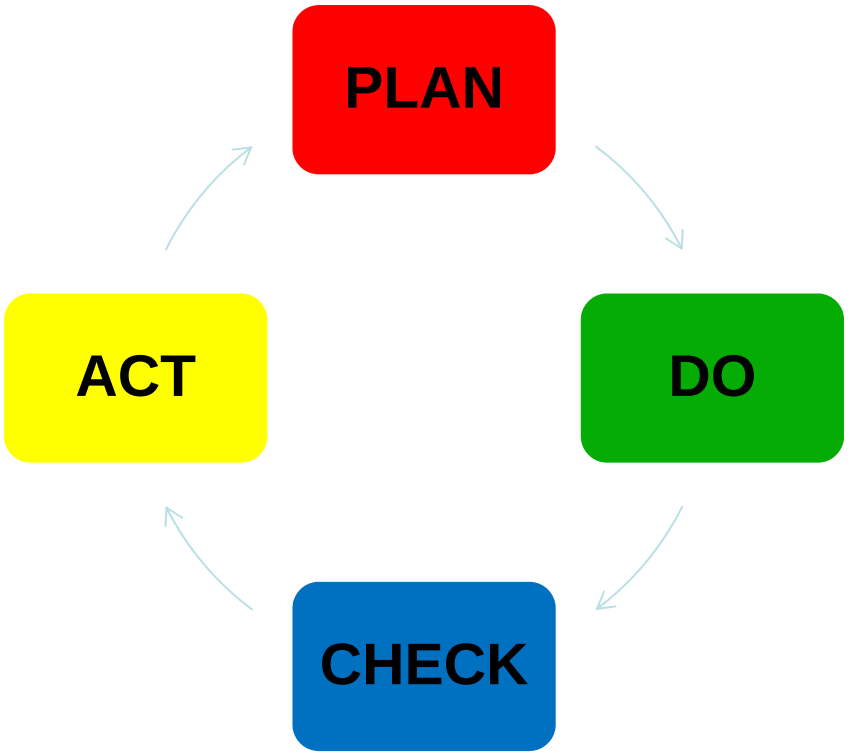
- **"2012 White Paper on Recent Issues in Bioanalysis and Alignment of Multiple Guidelines"**, *Bioanalysis, Vol. 4, No. 18, September 2012*

FY14 Highlights & Update

- Kathleen Uhl

SUCCESSFULLY IMPLEMENTING GDUFA …BUILDING A QUALITY SYSTEM

- Hire & Train
- Process & Policy
- Inspectorate
- Informatics ("Platform")
- Regulatory Excellence
- Agency Alignment



GDUFA BACKLOG

- 2866 original ANDAs
- 1873 PAS supplements

90% get first ACTION by end of GDUFA YR 5 (9/30/2017)

First Actions 10/1/2012 to 9/26/2014:

	Original	PAS	Total
Number with First Action**	1707	1362	3069
% Complete	60%	73%	**65%**
AP	447	779	1226
TA	105	3	108
CR with inspection	953	408	1361
RTR	70	2	72
WD	132	170	302

** Numbers are tentative and do not reflect actual numbers for Congressional reporting purposes

APPROVALS & ACTIONS

	PRE-GDUFA FY2012	GDUFA FY2013	GDUFA FY2014*
ANDA approvals	517	440	409
PAS approvals	275	535	659
Tentative Approval (TA)	102	95	91
Complete Response (CR)	84	1251	1254
TOTAL **	978	2226	2413
DMF Completeness Assessment (CA)	0	1699	1706

* Numbers are rounded and do not reflect actual numbers for Congressional reporting purposes

** FDA will aspire to the extent possible to maintain levels of productivity at least similar to pre-GDUFA levels, while hiring and training incremental staff necessary to achieve the program performance goals, building necessary systems and implementing outlined program changes in years 1 and 2 of the program (GDUFA Commitment Letter, page 3)

Actions 10/1/14 to 12/9/2014

ANDA Approvals	**80**
ANDA Tentative Approval (TA)	**18**
ANDA Complete Response (CR)	**148**
ANDA Refuse to Receive (RTR)	**14**
Supplement Approvals	**901**
CBE 0/30 Status Denied	**21**

Submission Quality Follow-up

- GPhA

Wrap-Up and Next Steps