IPA Meeting with the FDA

Quality Forum

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IPA Quality Forum

Outline of Presentation

- About IPA
- IPA Quality Forum
  - Context and Focus
  - Vision and Mission Statement
  - Near Term Objectives and Initiatives
  - Impact Assessment
  - Subgroup 1: Data Integrity and Reliability
  - Subgroup 2: Best Practices and Metrics
  - Subgroup 3: Culture and Capacity Building
- 1st IPA Annual Conference: Focus on *Quality*

About IPA

Current Members (20)

- Alembic
- Alkem
- Cadila Healthcare
- Cadila Pharmaceuticals
- Cipla
- Dr Reddy's
- Glenmark
- INTAS
- IPCA
- J B Chemicals
- Lupin
- Mylan
- Micro
- Natco
- Panacea Biotech
- Sun
- Torrent
- Unichem
- USV
- Wockhardt

About IPA

Contribution

- 85% of Private Sector Spend in R&D
- 60% of Exports of Pharmaceuticals
- 43% of Domestic Sales*
- **75% of Exports to USA**
- 43 % of Total NLEM Sales*

* AIOCD Pharmasoftech AWACS Pvt Ltd, MAR MAT 2014

"Pharmacy of the World"

IPA Quality Forum

Established to Jointly Develop Solutions and Address Quality Challenges

Context

- **Challenges about quality of products from India**
- Quality - a bottleneck for access to affordable healthcare
- In this context a **few questions** stood out:
  - How can we help the industry learn and implement best practices?
  - How can we help the industry engage various stakeholders to help shape initiatives for Quality improvement?
- Hence, **the Quality Forum** to **address cross cutting challenges** in quality

Focus

- Near term focus on a pragmatic set of Quality related interventions
- Post that, scale up portfolio of initiatives and broaden participation

IPA Quality Forum
Developed a Joint Vision and Mission Statement

Vision	▪ *Help Indian Pharmaceutical Manufacturers be the global benchmark in Quality*
Mission	▪ Demonstrate true partnership to customers, patients and regulators by improved quality and reliability ▪ Be the conduit of change – Provide thought leadership, knowledge development and best practice sharing ▪ Measure, benchmark and publicize achievements in Quality ▪ Expand skill and capability of quality talent ▪ Deepen and strengthen industry's relationship with key stakeholders – in and outside India ▪ Provide platform for members and other stakeholders to interact and network

IPA Quality Forum
Near Term Objectives

We have identified and prioritized a set of initiatives to drive the Quality Forum over the next few months:

- Ensuring **data integrity** guidelines are accurately interpreted and adopted
- Developing **right Quality metrics** to benchmark, diagnose and track improvements in Quality performance
- **Building capability** and the right **quality culture**

IPA Quality Forum

Near Term Initiatives to Address the Immediate Priority Topics

Data Integrity and Reliability

- Develop an internal **Data Integrity Guidelines document** that the companies will commit to adhere
- Create a **robust process** to ensure data integrity and reliability in line with global standards
- Develop a **set of tools** to help drive effective implementation

Metrics and Best Practices

- Adopt a **standard metrics** (including FDA metrics) to monitor quality performance and benchmark against Indian and global peers
- Strengthen **key Quality processes (5 in wave 1)** with best-in-class practices
- Standardize and implement common set of processes across organizations

Culture and Capability

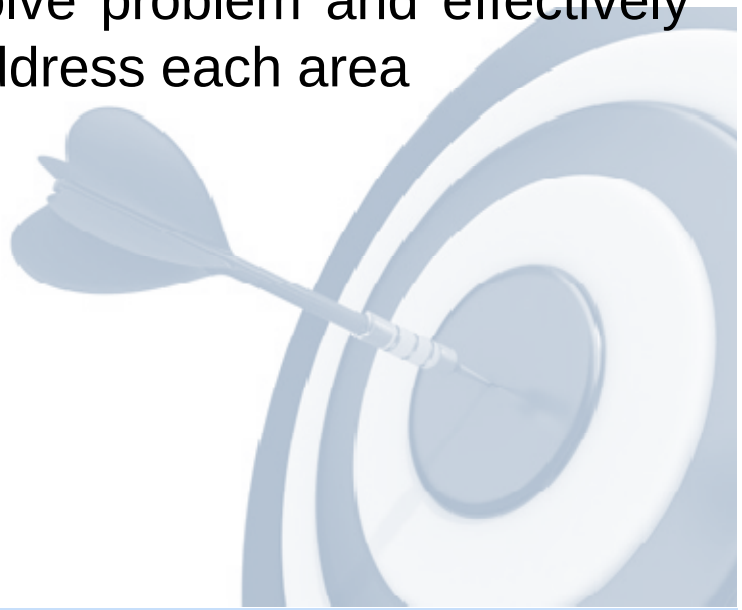
- Develop **framework for training middle management** on leadership and behavioral elements
- Develop framework for **training front line supervisors and operators** on technical skills to ensure quality practices and products
- Define **Quality Culture aspirations** and a set of interventions for driving the change

IPA Quality Forum
Will Track and Measure Impact of These Initiatives

- **Monitor implementation and impact:**
  - **Year 1** - adopt five best practices across companies, data reliability guidelines, metrics, middle management capability building
  - **Year 2 -** show progress on lower 483s for data reliability and five areas of focus
- **Share updates with FDA:**

  Based on individual work stream goals and milestones

- **Objective:**
  - Solicit FDA inputs on the initiative design before and during implementation
  - Seek FDA suggestions to solve problem and effectively address each area



Subgroup 1: Data Integrity and Reliability
Guidelines and Implementations

NOT EXHAUSTIVE

Learn and integrate existing guidelines

Learn and integrate various existing guidances e.g. FDA, MHRA, WHO (draft), PDA etc. and capture the common themes:

- Paper printouts are not "true copies"; System generated data should be retained in electronic form **i.e. Electronic data is the raw data**
- Data must be **ALCOA+** i.e. Attributable, legible and permanent, contemporaneous, original and accurate as well as complete, consistent, enduring and available;
- A **data lifecycle approach** to ensuring data integrity
- If using a computerized system, **the software should prevent** unauthorized modification of data
- Review of electronic data control.

Develop a set of guidelines and tools to help drive effective implementation

Translate common themes, requirements and learnings from various guidelines into one single implementation guideline and associated tools with the following features

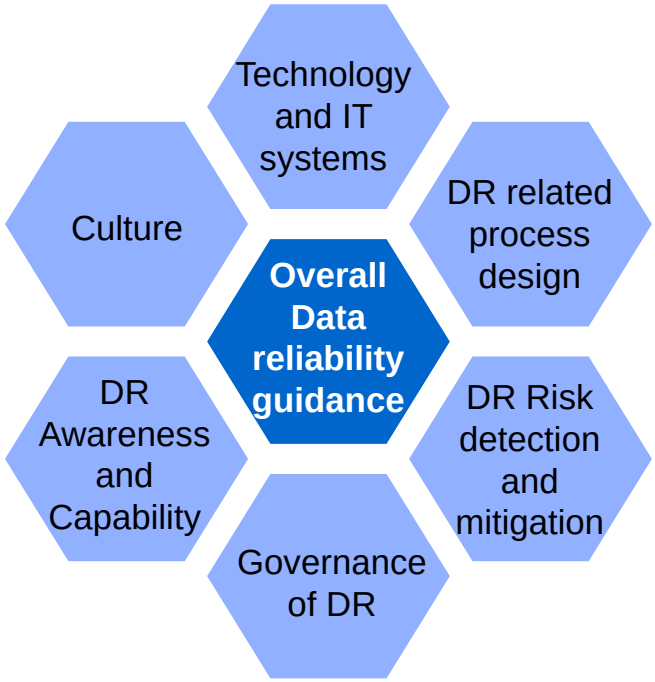
- **Comprehensive** – covering elements such as data integrity related culture, awareness and capability, process design, IT system frameworks, governance and risk mitigation
- **User-friendly** – Presented in a way that can be easily understood through use of innovative delivery forms e.g. infographics, visualization schemes, other technology enabled elements
- **Pragmatic and flexible** – Taking into account current starting position of various companies e.g. separate treatment for IT systems of different maturity levels, practical dos and dont's
- **Proactive** – Developed to be used for proactive reduction, not just post-mortem analysis. Includes working with vendors etc. if required

SOURCE: MHRA, FDA guidelines, Expert interviews, sub-group discussions

Subgroup 1: Data Integrity and Reliability
Seven Elements of the Overall Guideline

Key elements

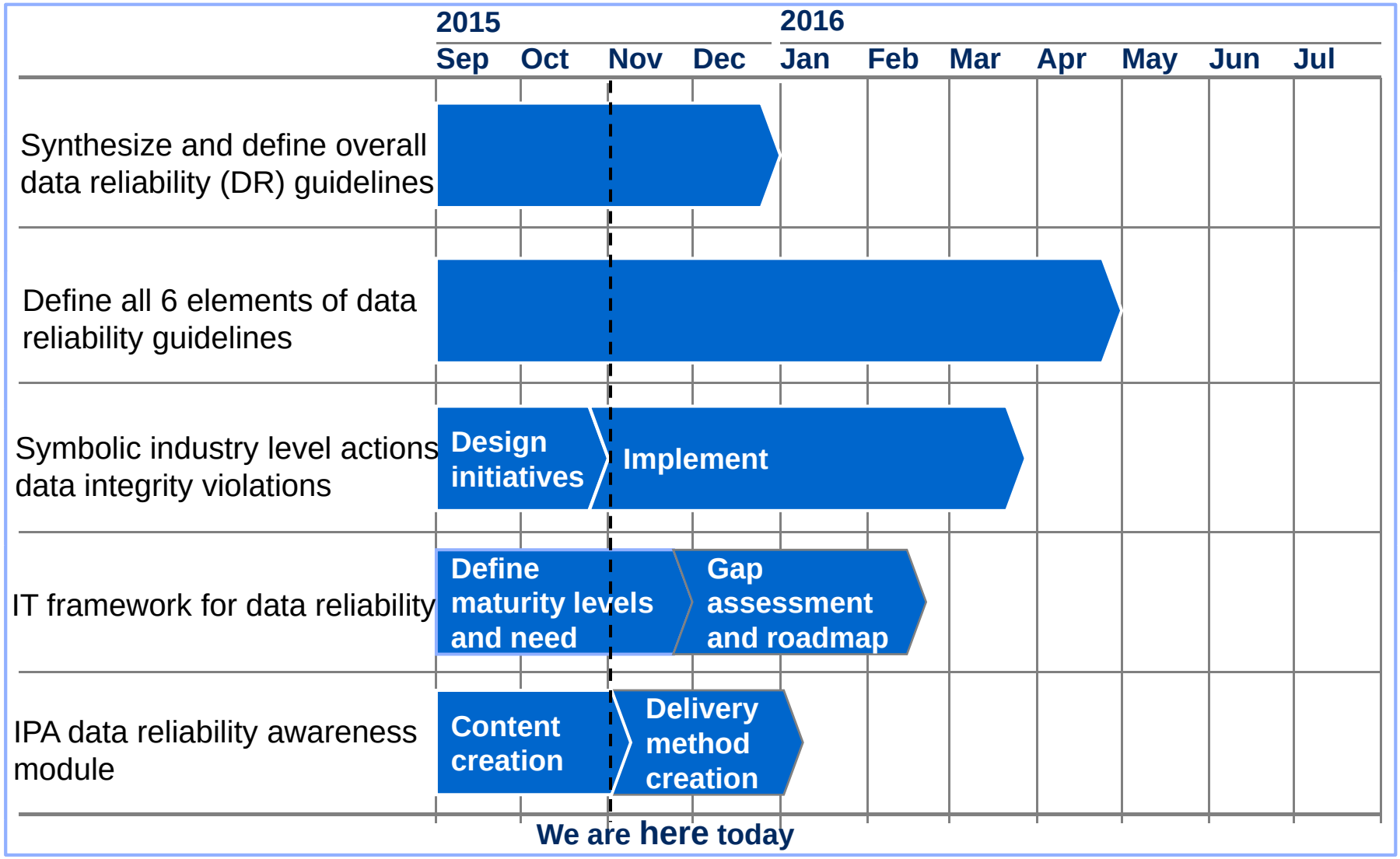
- Supporting elements
- Core guideline



Definitions

1 **Overall DR guidance**	A set of overall guidelines laying out requirements for data integrity. Supporting elements lay out how to achieve these requirements
2 **DR related process design**	Features of quality process design – both general and with deep dive into 3-4 critical processes required to minimize data reliability risk and recommends an approach to achieve this desired end state
3 **DR risk de-tection and mitigation**	Approach and tools to assess and mitigate risks
4 **Governance of DR**	Key elements of governance e.g. data owners, management responsibility and best practices
5 **DR aware-ness and capability**	DR specific skill sets required across different job profiles; Best practices in designing and delivering content; Capability module based on this content
6 **Culture**	Key mindsets and behaviors critical for data integrity; A mandate for different job profiles; Portfolio of initiatives based on best practices
7 **Technology and IT systems**	Technical requirements and standards and solutions to achieve them

Subgroup 1: Data Integrity and Reliability
Develop a Draft Version by End-April 2016



SOURCE: Sub-group 1 discussion

Subgroup 2: Best Practices and Metrics
Context, Vision and Objectives

Context

- Quality Forum realizes the need to benchmark Quality processes in India with international best practices and refine metrics-based performance tracking in-line with the recent FDA draft guidelines
- IPA offers an ideal platform for companies to leverage their collective wisdom / expertise in these areas, and lead the journey of Quality transformation for Indian pharma industry

Our vision

- To lead the Indian pharma industry in transformation of quality processes and performance
- Establish consistent set of metrics and methodology to benchmark the quality performance across the core companies
- Strive to achieve best-in-class Quality systems and processes globally

Objectives

- **Best practice processes:**
  - Identify and strengthen key Quality processes with best-in-class practices
  - Standardize and implement best practices/processes across organizations
- **Metrics:**
  - Adopt a standard set metrics to monitor quality performance and benchmark against Indian and global peers
  - Identify performance gaps and come up with set of interventions to achieve best-in-class quality performance

Subgroup 2: Best Practices and Metrics
Initiatives to Achieve Objectives

Quality processes

- Identified an exhaustive list of processes to be shared, harmonized and improved across the companies
- Four processes prioritized for 1st wave of best-practices
  - Process validation[1]
  - Investigations and root-cause assessment
  - Media fill + Environment monitoring and recording of results
  - Good laboratory practices e.g., documentation, analyst qualification, data review, batch testing records[2]
- Shared practices with the forum, generating ideas internally and engaging with the subject matter experts to benchmark processes with global best practices

Metrics

- Defined 5 metrics, in-line with recent FDA draft guidelines, to be calculated and tracked periodically. These are:
  - Lot acceptance rate
  - Product quality complaint rate
  - Invalidated OOS rate
  - Annual product review / product quality review time rate
  - CAPA Effectiveness rate[3]
- Currently being implemented at 2-3 pilot sites per company. Will be rolled out across the network subsequently

Additionally, developing a collective response to FDA draft guidelines.

1 Pre requisite, environmental, scalable machines harmonization unit operation wise
2 Additionally QbD in Analytical method development (capturing observation during sample preparation, during validation batches analysis)
3 To be calculated based on re-trainings (as per FDA draft guidance) as well as based on repetition of failures

Subgroup 2: Best Practices and Metrics
Implementation of Work Plan

	Sept 2015	Oct – mid Nov 2015	mid Nov – Dec 2015	Jan-Mar 2016
Best-practice processes	▪ Identify and prioritize processes for best-practices ▪ **Share current practices across the Quality Forum**	▪ Develop draft master SOPs based on current practices to brainstorm improvement ideas ▪ **Engage with SME's and cross-functional teams to develop final SOPs**	▪ Finalize best practice SOPs / Protocols across diff dosage forms and API ▪ **Implement best-practices and train employees**	▪ Identify 3-4 additional process for best-practices
Metrics	▪ **Finalize metrics, definitions and pilot sites**	▪ **Launch pilot at 10-12 pilot sites across six companies** ▪ Share response with FDA on draft metrics guidelines	▪ **Plan to scale up metric pilot and IT-enablize**	▪ Analyze outcome of metrics pilot ▪ **Scale to other sites including Non-orals and API** ▪ Identify additional metrics to be taken up

Subgroup 3: Culture and Capability Building
Findings

Major Findings

- We note **cultural/behavioral challenges** and **technical/training gaps**
- **Cultural/behavioral gaps** lay in areas such as: accountability and ownership, openness and transparency, discipline and professionalism as well as managerial courage to dissent.
- **Technical/training gaps** in Investigation management, Sterility Assurance, Regulatory requirements, Facility & equipment lifecycle management, Data integrity.
- **Urgent** need to close the above cultural and technical shortcomings.

Subgroup 3: Culture and Capability Building
Measures

Suggested Measures to overcome the problem areas

- Measure 1: Run a structured gap assessment survey, aimed at substantiating and validating major findings (gaps) with granular fact-based data.
- Measure 2: Generate cultural/behavioral shifts at plant management level, by focused sessions during which current individual and group behavior will be analyzed. Then, desired behaviors will be defined and piloted. This will be followed by company-wide roll out of these new behaviors.
- Measure 3: Close technical gaps by developing joint training modules, emphasizing theory, regulatory expectations and case studies. A total of 15 subjects are identified where technical gaps exist.
- Measure 4: Perform relevant effectiveness checks focusing on the above capability building efforts. Identification of continuous improvement plans.

Subgroup 3: Culture and Capability Building
Implementation Timelines

The training programs will first target middle management in six of India's leading companies and subsequently be spread more widely across the industry

	November 2015	December 2015	Q1 CY 2016	Q2 CY 2016	Q3 CY 2016
Technical	Launch of modules: ▪ Data integrity ▪ Regulatory Requirements	Launch of modules: ▪ Investigations ▪ Facility and Equipment Qualification Lifecycle	Launch of module: ▪ Sterility Assurance	Offer the modules to other Companies Phase 2 modules	
Behavioral	▪ Launch gap survey (to validate gap findings and establish baseline)	▪ behavior shift forums covering ~70 managers of two plants per company	▪ continue with behavior shift forums with more plants per company	Offer the modules to other companies	

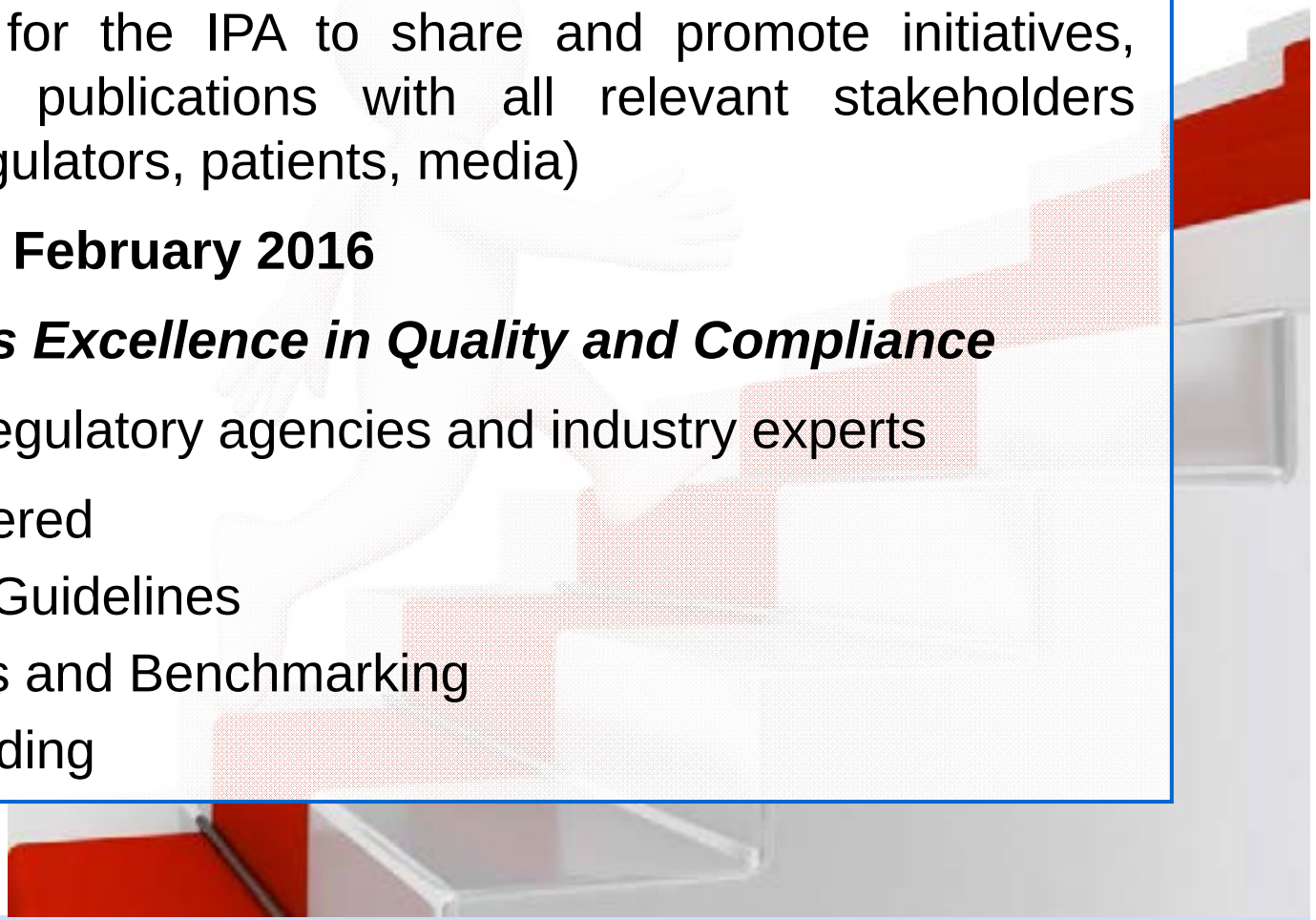
1st IPA Annual Conference
Focus on Quality

Purpose of the Annual Conference

- Marquee event for the IPA to share and promote initiatives, knowledge and publications with all relevant stakeholders (government, regulators, patients, media)

1st Conference in February 2016

- Theme: ***Towards Excellence in Quality and Compliance***
- Speakers from regulatory agencies and industry experts
- Topics to be covered
  - Data Integrity Guidelines
  - Quality Metrics and Benchmarking
  - Capability Building



THANK YOU

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