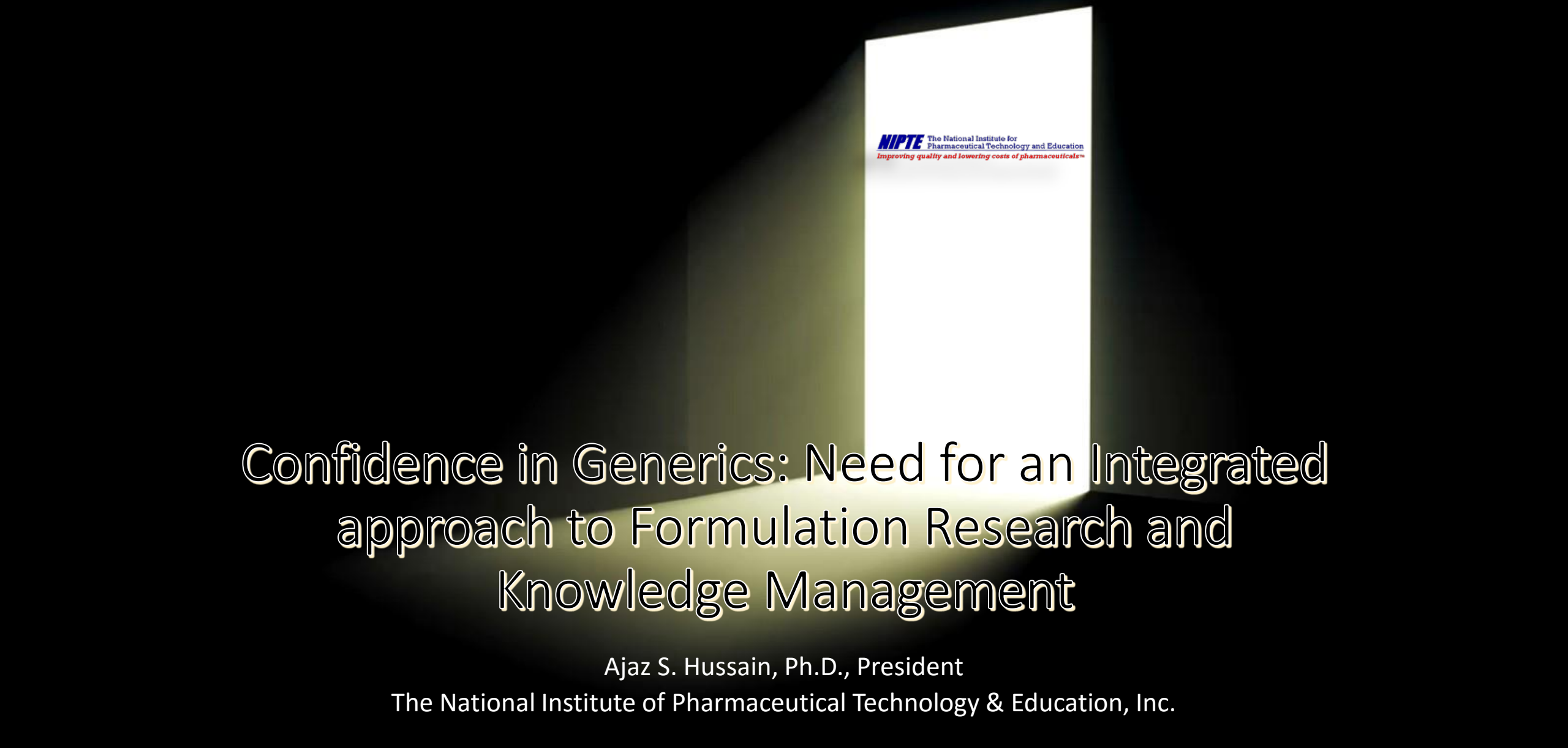
FDA's FY 2016 Regulatory Science Initiatives Part 15 Public Meeting



Confidence in Generics: Need for an Integrated approach to Formulation Research and Knowledge Management

Ajaz S. Hussain, Ph.D., President
The National Institute of Pharmaceutical Technology & Education, Inc.

Outline

- A note on NIPTE
- US FDA's strategic response to maximizing how generics meet public health needs
- Some considerations for navigating multifaceted challenges
- Summary
- References

About NIPTE

A 501(c)(3) Non-profit organization

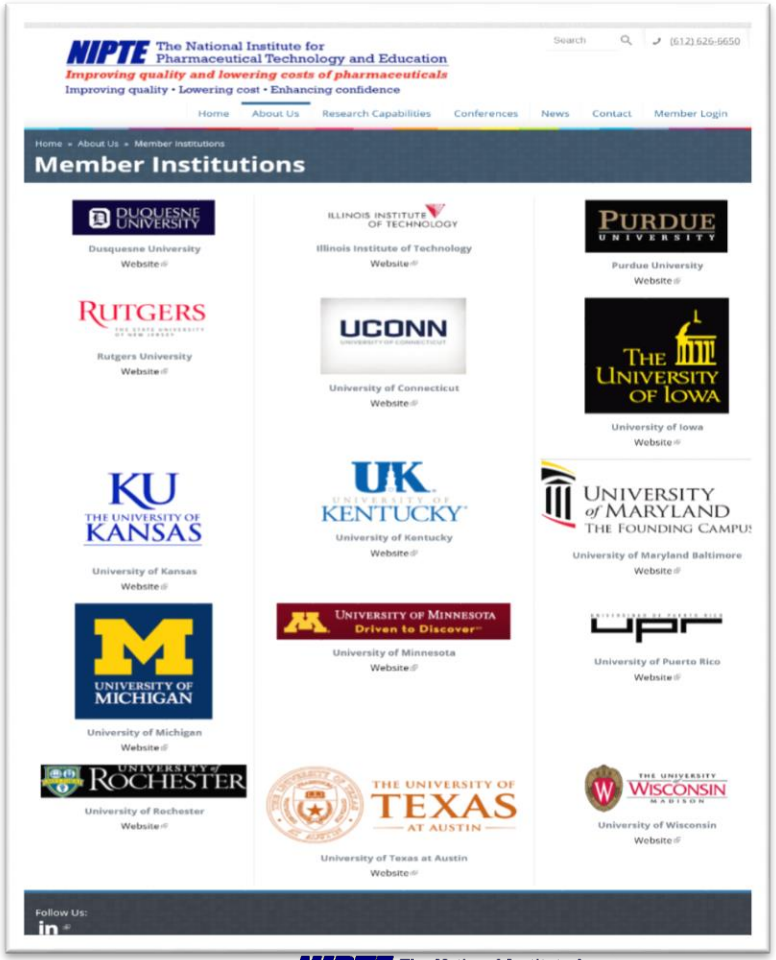
Founded in 2005

Incorporated in 2007

Headquarters: Minneapolis, MN

12 Schools of Pharmacy, 3 Schools of Engineering, 1 Medical School

Improving Quality and Lowering Costs with Confidence



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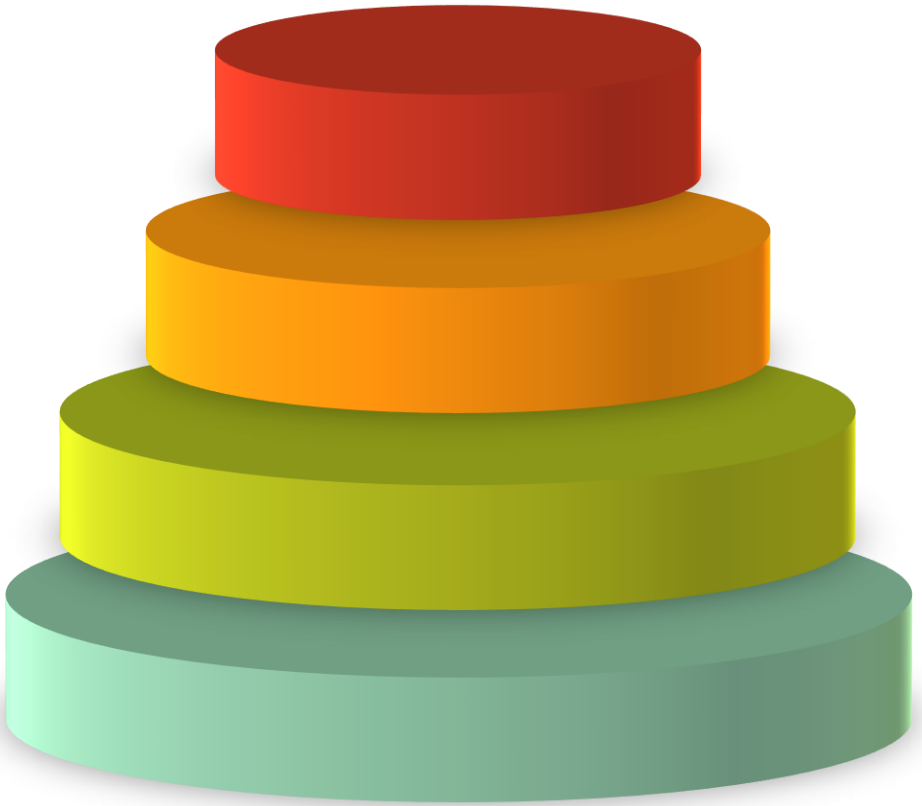
US FDA's strategic response to maximizing how generics meet public health needs

Dr. Woodcock's testimony to the US Congress, 4 February 2016

GDUFA II negotiations a pre-ANDA process?
Submission quality - Multiple review cycles (on average 4)

Several programs in OPQ, One Quality Voice
Need for additional quality regulation to "better assure quality in an increasingly globalized industry"



"First Generics" Public Health Priority
GADUFA goal date (15 months – to shorter)

GDUFA research funding prioritization (this meeting)
Need for research; Research to policy to practice - time and effectiveness.

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Recognizing multifaceted challenges

Topics and Points of View

Topics for FY 2016 Regulatory Science Initiatives

1. Opportunities for scientific or technical advancements that would help to overcome specific barriers for industry that currently limit the availability of generic drug products.
2. Innovative approaches to pre-approval development of generic drugs, including new methodologies for product design and manufacturing, and design and conduct of in vitro, ex vivo, and clinical studies and identification of scientifically robust strategies for demonstration of bioequivalence for various product classes.
3. Innovation in scientific approaches to evaluating the therapeutic equivalence of generic drug products throughout their lifecycle.
4. Identification of high-impact public health issues involving generic drugs that can be addressed by the prioritized allocation of FY 2017 funding for regulatory science research.
5. Identification of specific issues related to generic drug products where scientific recommendations and/or clarifications are needed in developing and/or revising FDA's guidance for industry.
6. Strategies for enhancing quality and equivalence risk management during generic drug product development, during regulatory review, and/or throughout the drug product's lifecycle.

NIPTE point of view

1. Integrated approach for evolving standard for analytical characterization - case example excipient variability (Eric Munson)
2. Integrated approach for evolving standards for formulation design - case example NTI's (Ken Morris)
3. Two talks (above) also relevant to this topic
4. Confidence in Generics: Need for an Integrated approach to Formulation Research and Knowledge Management (Ajaz Hussain)
5. The talk above also illustrates some challenge
6. Mechanism for an integrated approach to Formulation Research, Knowledge Management, & Knowledge sharing with FDA & Industry (Steve Byrn)

Describing multifaceted challenges

Need for integration with clarity & consistency

Integrated Analysis & Synthesis

- Public perceptions are shaped by the few errors, recalls, etc.
- Stark reminders & reasons to pay attention to perceptions (e.g., color, shape, etc.)
- 'Totality of Evidence' is increasingly the dominant path for complex generics; complexity is increasing, generally; there is a need for integration with clarity & consistency

Needed to optimally address multifaceted challenges

- Therapeutic equivalence increasingly demands notable attention to integration of product/process design & development, orthogonal analytical characterization, in vitro and, when necessary, evidence of in vivo equivalence
- Knowledge bases and decision-making processes pertaining to integration of evidence (specifically – product/process design & development and orthogonal analytical characterization), need to grow, mature and progress.

Need for integration with clarity & consistency

Illustrative examples

To facilitate more optimal policy considerations, to more rapidly recognize innovative proposals by companies, to reduce scientific disputes,…

Formulation Science?

Does subject-by-formulation interaction variance, derived from a general population, provide adequate assurance ?

Evidence based on underlying mechanisms (e.g., failure modes)

Delayed release tablet dissolution related to coating thickness by terahertz pulsed image mapping. Journal of pharmaceutical sciences, 97(4), pp.1543-1550. (2008)

Right Question at the Right Time

Timely integration of formulation and process design, analytics & in vivo evidence can and must be facilitated

Nov. 2014 Draft Guidance on Methylphenidate Hydrochloride

Subject-by-Formulation Interactions?

Sept 2012 Draft Guidance on Mesalamine

Applicant should provide evidence of high variability in the bioequivalence parameters

Sept 2015 Draft Guidance on Mometasone Furoate Monohydrate

In vitro BE, Pharmacokinetic (PK) BE and Clinical Endpoint BE

Considering potential impacts

Complexity is increasing generally

- Increasingly a more complex environment; a disproportionally higher risk posed to maintaining/improving confidence in generic drugs
- Protracted and costly development, multiple review cycles, and/or delayed launch dates (for reasons beyond IP issues)
- Limited competition, even among generics
- Increased risk of continued challenges to approved generics (e.g., based on comparisons utilizing novel analytics)
- More reasons for significant delays; particularly in approval of "first generic"

Specific consideration

- In their allocation of FY 2017 funding for regulatory science research, the FDA is urged to consider prioritizing efforts towards development of knowledge bases and standards to guide optimal development & integration of multifaceted scientific evidence of Therapeutic Equivalence.

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Summary

Confidence in generic drugs is built upon an optimal integration of evidence derived from formulation and process design, analytical characterization and, when necessary, in vivo assessment

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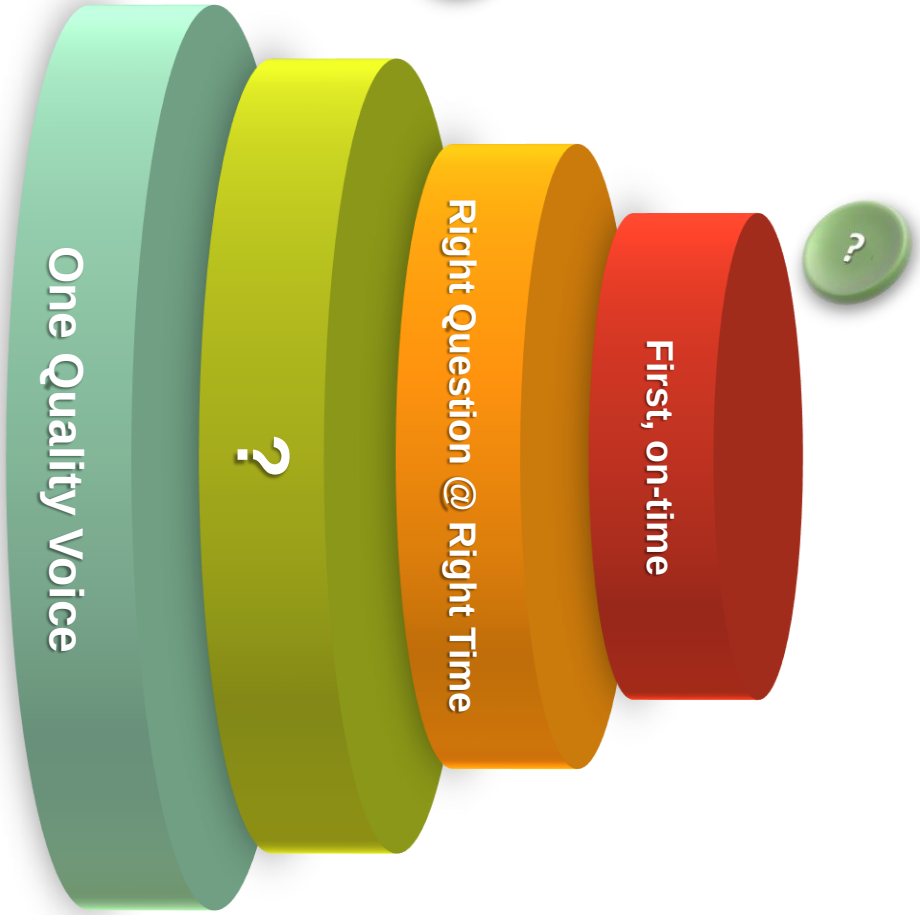

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References

- FY 2016 Regulatory Science Initiatives Part 15 Public Meeting.
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- Draft Guidance on Methylphenidate Hydrochloride.
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- Draft Guidance on Mesalamine.
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- Draft Guidance on Mometasone Furoate Monohydrate.
  - http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM461141.pdf (accessed 5/12/2016)