



UNIVERSITY of MARYLAND



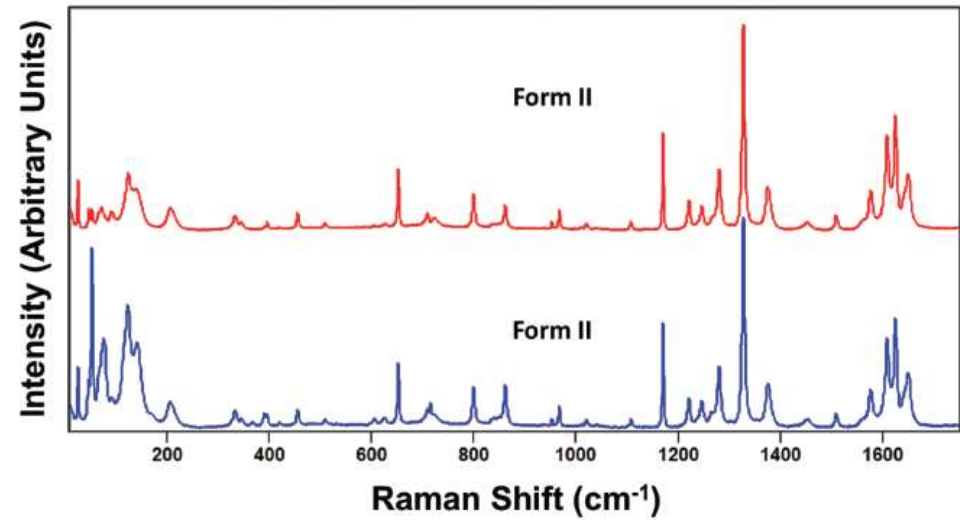
## A Summary of Survey Feedback from Industry Stakeholders

June 23, 2021

[www.complexgenerics.org](http://www.complexgenerics.org)

# Question

- ▶ What research is needed?
- ▶ Greater specificity generally helpful.



# Our Mission

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**“To increase access to safe and effective generic drugs through enhanced infrastructure/communication, education, and research collaboration across industry, academia and the FDA”**

## ***Center for Research on Complex Generics (CRCG) Aims:***



- ▶ **Communication:** Establish core program infrastructure and gain the support of stakeholders to ensure CRCG success.

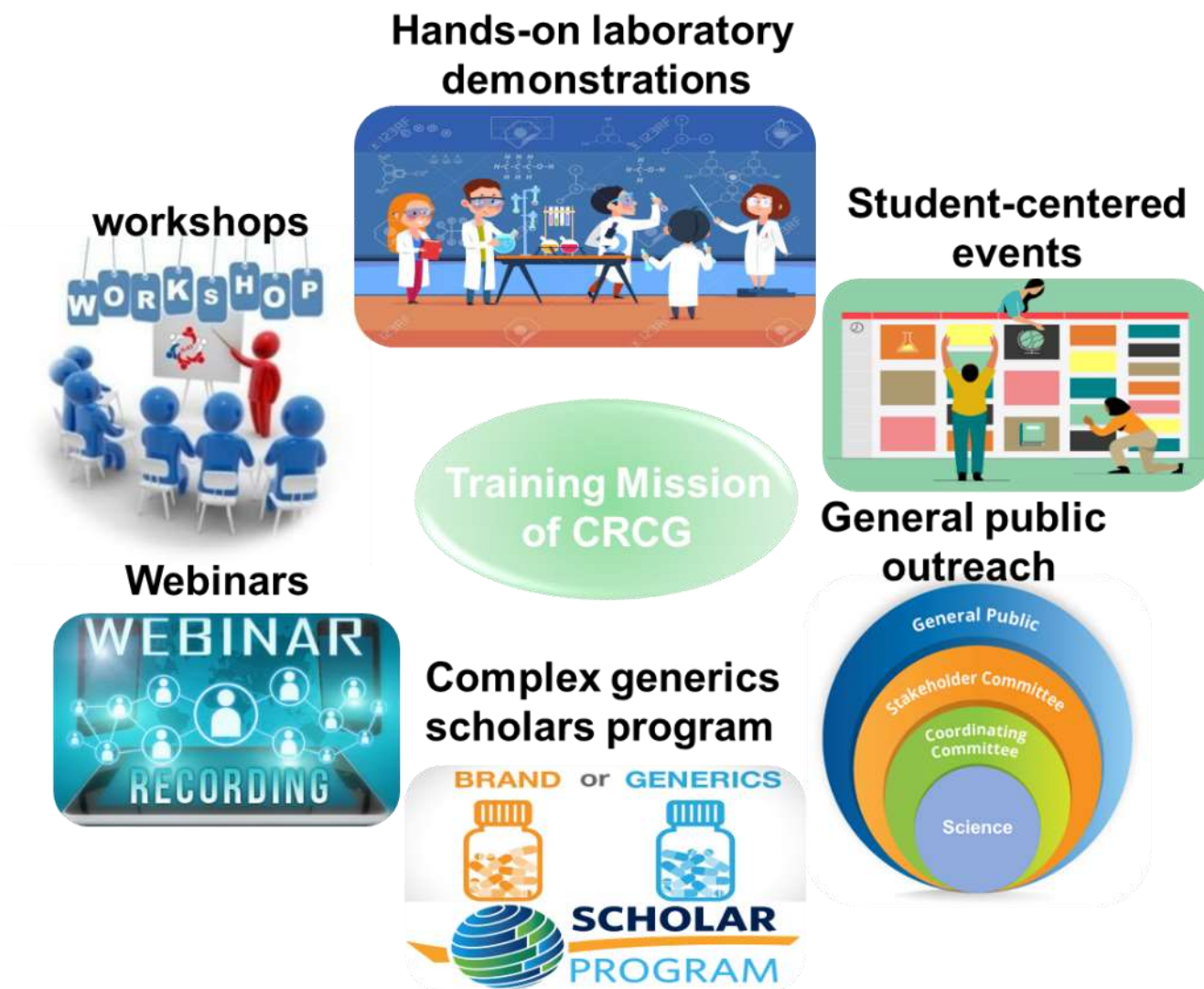


- ▶ **Education:** Promote generic industry training through workshops, webinars and hands-on demonstration, and engage fellows, students and public in complex generics research.



- ▶ **Research:** Conduct collaborative research and technique development that facilitate complex generics.

# Training Mission



# Planned Workshops (online only)

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- ▶ In Vitro Release Test (IVRT) and In Vitro Performance Test (IVPT) Methods: Best Practices and Scientific Considerations for ANDA Submissions
  - Aug 18-20, 2021
- ▶ Regulatory Utility of Mechanistic Modeling to Support Alternative Bioequivalence Approaches
  - Sep 30 and Oct 1, 2021
- ▶ Best Practices for Establishing the Suitability of a Model Integrated Approach to Demonstrate the Bioequivalence of Long Acting Injectable Products
  - Nov 30, 2021





# Research Mission



Research mission  
of CRCG



- ▶ Two projects initiated
- ▶ Incorporating micelle/colloid diffusivity to better parameterized physiologically based pharmacokinetic (PBPK) models for oral drug absorption
- ▶ Reverse engineering of irinotecan liposome injection and development of IVR methodology

# Survey of Scientific Challenges in the Development of Complex Generics

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- ▶ Which complex products (excluding biologics)? (select up to 2)
  - Complex injectables, formulations, and nanomaterials
  - Complex mixtures and peptides
  - Drug-device combination products
  - Inhalation and nasal products
  - Long-acting injectables and implants
  - Ophthalmic products
  - Topical dermatologic drug products
  - Other drug or drug product



# Survey of Scientific Challenges in the Development of Complex Generics

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- ▶ Which analytical techniques (excluding biologics)? (select up to 2)
  - Data analytics and machine learning
  - Locally-acting physiologically-based pharmacokinetic modeling
  - Oral absorption models and bioequivalence
  - Quantitative clinical pharmacology
  - Patient substitution of generic drugs
  - Other analytical techniques and/or drug or drug product





# Survey of Scientific Challenges in the Development of Complex Generics

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## ► Which educational topics (excluding biologics)? (Select up to 4)

- Complex injectables, formulations, and nanomaterials
- Complex mixtures and peptides
- Drug-device combination products
- Inhalation and nasal products
- Long-acting injectables and implants
- Ophthalmic products
- Topical dermatologic drug products
- Data analytics, including quantitative methods and Modeling & Simulation
- Locally-acting physiologically-based pharmacokinetic modeling
- Oral absorption models and bioequivalence
- Quantitative clinical pharmacology
- Patient substitution of generic drugs
- Other educational topic



# Survey of Scientific Challenges in the Development of Complex Generics

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## ► Demographic questions

- Are you willing to be a point-of-contact (POC) for your company?
- Employment or perspective (13 options)
  - Generic drug industrial scientist or manufacturing personnel
  - Generic drug executive or management
  - CRO, CMO, or CDMO scientist or manufacturing personnel
  - CRO, CMO, or CDMO executive or management
  - Innovator drug industrial scientist or manufacturing personnel
- Number of employees in your company (7 options)
- Your or your employer's interest (11 options; pick all that apply)
  - API manufacturer
  - Finished dosage form manufacturer
  - Packaging
  - Excipient manufacturer/provider
  - CRO-analytical



# Methods

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- ▶ Three main areas of questioning concerned:
  - Which complex products
  - Which analytical methods
  - Which educational topics merited effort now
- ▶ University of Maryland Baltimore IRB
- ▶ Open to the public from Dec 3, 2020 to Feb 3, 2021
- ▶ CRCG email list; several organizations created awareness of the survey
- ▶ Only required question was the consent question
- ▶ Statistics were performed using SAS
  - Wald (i.e., 2 x 2) chi-square test
  - Bonferroni correction



# Demographics

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- ▶ N=281 examined responses (i.e., provided consent and answered a question)
- ▶ Over half of respondents, including points-of-contact (POCs), were generic drug employees.
- ▶ Respondents were equally distributed between being employees at companies with at most 1,000 employees and at least 1,001 employees, although most POCs were from larger companies.
- ▶ A majority of respondents were employed by a finished dosage form manufacturer, and one quarter by API manufacturer.
- ▶ Comparisons
  - Points-of-contact (POCs) vs non-POCs (never an effect)
  - Employer's interests: e.g., generic vs non-generic (differed in analytical methods)
  - Company size (effect in all three areas)



# Top Three Replies from All Respondents

Rank-order	Complex products	Analytical techniques	Educational topics
First	Complex injectables, formulations, and nanomaterials	Locally-acting physiologically-based pharmacokinetic modeling	Complex injectables, formulations, and nanomaterials
Second	Drug-device combination products	Oral absorption models and bioequivalence	Drug-device combination products
Third	Inhalation and nasal products	Data analytics and machine learning	Data analytics, including quantitative methods and modeling & simulation





# Additional Summary Findings

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## ► Complex products

- POCs and non-POCs did not differ
- Employer interest was not a factor; generic drug employees and non-generic drug employees did not differ
- Companies with more than 10,000 employees differed from all other companies in inhalation and nasal products
- Large vs small companies differed in complex injectables, formulations, and nanomaterials

## ► Analytical methods

- POCs and non-POCs did not differ
- Generic drug industrial scientist (and generic drug manufacturing personnel) differed from all others in locally-acting physiologically-based pharmacokinetic modeling
- Generic drug executive or management differed from all others in “other”
- Large vs small company size differed in locally-acting PBPK modeling



# Additional Summary Findings (continued)

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## ▶ Educational topics

- POCs and non-POCs did not differ
- Employer interest was not a factor; generic drug employees and non-generic drug employees did not differ
- Companies with more than 10,000 employees differed from all other companies in locally-acting physiologically-based pharmacokinetic modeling, as well as data analytics including quantitative methods and modeling & simulation

## ▶ Harmonization highly supported

## ▶ Results will help prioritize the CRCG's research and training efforts



## Which Complex Products? (select up to 2)

Complex product	All respondents (n=278)
Complex injectables, formulations, and nanomaterials	54.3%
Complex mixtures and peptides	19.4%
Drug-device combination products	29.5%
Inhalation and nasal products	25.2%
Long-acting injectables and implants	22.3%
Ophthalmic products	12.9%
Topical dermatologic drug products	14.7%
Other drug or drug product	6.5%

# Which Complex Products: By Number of Employees

Complex product	1 (n=10)	2-25 (n=26)	26-100 (n=27)	101-1,000 (n=35)	1,001-10,000 (n=39)	More than 10,000 (n=50)
Complex injectables, formulations, and nanomaterials	50.0%	50.0%	37.0%	48.6%	64.1%	68.0%
Complex mixtures and peptides	30.0%	15.4%	22.2%	14.3%	23.1%	20.0%
Drug-device combination products	20.0%	26.9%	53.6%	34.3%	28.1%	24.0%
Inhalation and nasal products	30.0%	19.2%	14.8%	20.0%	23.1%	46.0%

## Which Analytical Techniques? (selected up to 2)

Analytical technique	All respondents (n=252)
Data analytics and machine learning	32.5%
Locally-acting physiologically-based pharmacokinetic modeling	49.2%
Oral absorption models and bioequivalence	36.1%
Quantitative clinical pharmacology	17.9%
Patient substitution of generic drugs	26.2%
Other analytical techniques and/or drug or drug product	15.1%





# Which Analytical Techniques: By Type of Employer

Analytical technique	Generic drug industrial scientist or manufacture (n=51)	Generic drug executive or management (n=60)	CRO, CMO, or CDMO executive or management (n=19)	Innovator drug executive or management (n=15)	Health care professional (n=11)	Academic (n=13)
Data analytics and machine learning	47.1%	36.7%	31.6%	33.3%	27.3%	0.0%
Locally-acting physiologically-based pharmacokinetic modeling	66.7%	48.3%	31.2%	33.3%	63.6%	23.1%
Oral absorption models and bioequivalence	35.3%	31.7%	36.8%	33.3%	9.1%	46.2%
Quantitative clinical pharmacology	5.9%	11.7%	26.3%	26.7%	54.5%	23.1%
Patient substitution of generic drugs	13.7%	20.0%	26.3%	20.0%	27.3%	53.8%
Other analytical techniques and/or drug	7.8%	28.3%	15.8%	26.7%	9.1%	23.1%

# Which Analytical Techniques: By Number of Employees

Analytical technique	1 (n=10)	2-25 (n=26)	26-100 (n=27)	101-1,000 (n=35)	1,001-10,000 (n=39)	More than 10,000 (n=50)
Data analytics and machine learning	50.0%	23.1%	25.9%	25.7%	38.5%	50.0%
Locally-acting physiologically-based pharmacokinetic modeling	50.0%	50.0%	22.2%	45.7%	<u>43.6%</u>	<u>76.0%</u>
Oral absorption models and bioequivalence	10.0%	26.9%	37.0%	45.7%	33.3%	26.0%
Quantitative clinical pharmacology	20.0%	15.4%	18.5%	20.0%	23.1%	8.0%
Patient substitution of generic drugs	20.0%	26.9%	33.3%	25.7%	28.2%	14.0%
Other analytical techniques and/or drug or drug product	20.0%	30.8%	22.2%	14.3%	12.8%	18.0%

## Which Educational Topics? (select up to 4)

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<b>Educational topic</b>	<b>All respondents (n=240)</b>
<b>Complex injectables, formulations, and nanomaterials</b>	<b>58.3%</b>
<b>Complex mixtures and peptides</b>	26.3%
<b>Drug-device combination products</b>	<b>50.0%</b>
<b>Inhalation and nasal products</b>	25.0%
<b>Long-acting injectables and implants</b>	31.3%
<b>Ophthalmic products</b>	19.2%
<b>Topical dermatologic drug products</b>	19.2%
<b>Data analytics, including quantitative methods and modeling &amp; simulation</b>	<b>41.7%</b>
<b>Locally-acting physiologically-based pharmacokinetic modeling</b>	29.6%
<b>Oral absorption models and bioequivalence</b>	25.8%
<b>Quantitative clinical pharmacology</b>	9.6%
<b>Patient substitution of generic drugs</b>	20.0%
<b>Other educational topic</b>	4.5%

# Which Educational Topics: By Number of Employees (1 of 2)

Educational topic	101-1,000 (n=35)	1,001-10,000 (n=39)	More than 10,000 (n=50)
<b>Complex injectables, formulations, and nanomaterials</b>	54.3%	64.1%	60.0%
<b>Complex mixtures and peptides</b>	17.1%	35.9%	20.0%
<b>Drug-device combination products</b>	42.9%	43.6%	66.0%
<b>Inhalation and nasal products</b>	25.7%	23.1%	24.0%
<b>Long-acting injectables and implants</b>	34.3%	30.8%	28.0%
<b>Ophthalmic products</b>	8.6%	17.9%	22.0%
<b>Topical dermatologic products</b>	20.0%	15.4%	8.0%



# Which Educational Topics: By Number of Employees (2 of 2)

Educational topic	101-1,000 (n=35)	1,001-10,000 (n=39)	More than 10,000 (n=50)
Data analytics, including quantitative methods and modeling & simulation	37.1%	43.6%	58.0%
Locally-acting physiologically-based pharmacokinetic modeling	28.6%	25.6%	54.0%
Oral absorption models and bioequivalence	37.1%	25.6%	18.0%
Quantitative clinical pharmacology	17.1%	10.3%	6.0%
Patient substitution of generic drugs	25.7%	17.9	8.0%
Other educational topic	5.7%	5.1%	2.0%





# Harmonized International Approach for Complex Generics Requirements

Level of agreement	Percentages of responses
Strongly agree	68.7%
Agree	26.7%
Disagree	3.3%
Strongly disagree	0.0%
Unable to judge	1.2%



# Acknowledgements

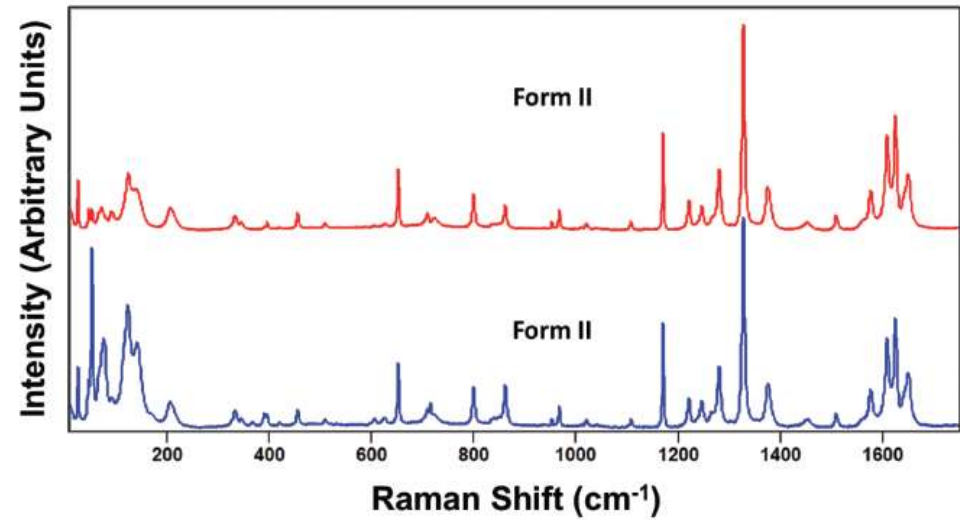
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- ▶ Survey respondents
- ▶ Several organizations created awareness of the survey
- ▶ Thank you!



# Question

- ▶ What research is needed?
- ▶ Greater specificity generally helpful.



# Contact Us !

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