Skin and Mucosal Delivery

- Session #1

Critical quality attributes enhance understanding of skin sensory perceptions

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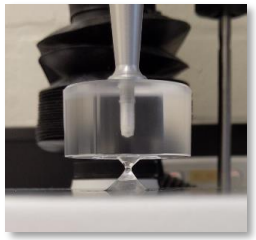
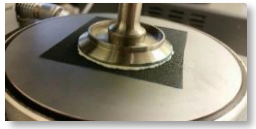
Delivery Science
ACROSS DISCIPLINES

Critical quality attributes (In Vitro) – Sensory panel study (In Vivo)





Experiments

- In vitro: Instrumental analysis
  - Rheology
    - Shear sweep test: μo, σ_y and μ∞
    - Temperature sweep test: μ at 25 °C and 32 °C
    - Amplitude sweep test: G', G'', T_y, T_f, Tan σ
  - Tribology
    - CoF at 25 rad/s
  - Texture analysis
    - Firmness, Spreadability, Adhesiveness, Stringiness
  - Rate of evaporation
    - % weight loss
  - Globule size
    - Diameter and area of globule
- In vivo: Sensory study
  - Human panels
    - 6 sensory attributes

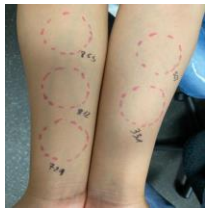
CQAs-Q3 attributes

- Spreadability
- Cooling sensation
- Shine
- Slipperiness
- Stickiness
- Smoothness

Statistical Analysis:

1. One-way/two-way ANOVA with significance level ($p<0.05$)
2. Heat map
3. PCA
4. Hierarchical cluster analysis

- 46 subjects
- Age 18 - 50 years

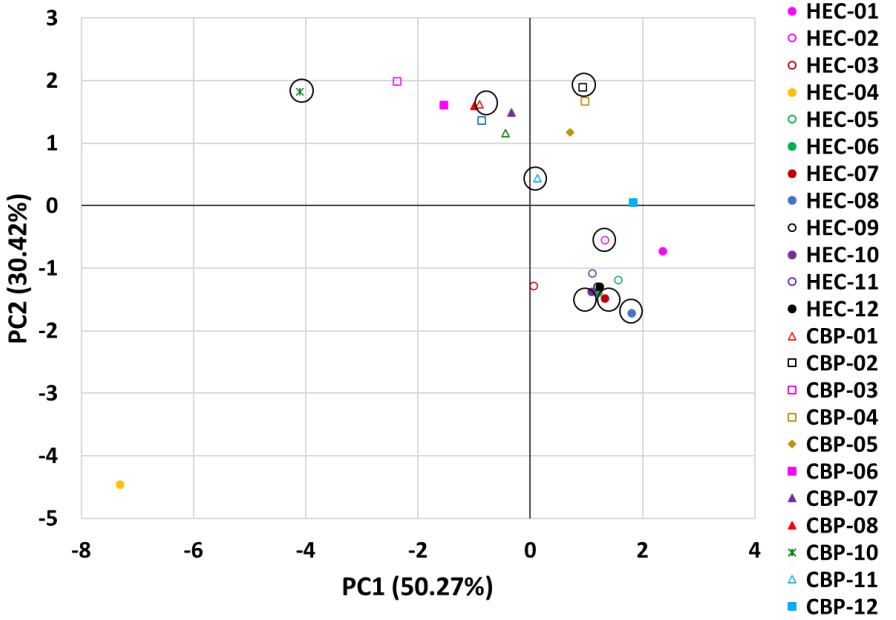


Topical Formulations - Sensory Study

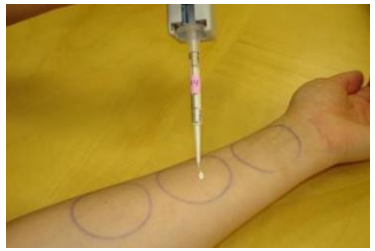
26 formulations

Composition (%w/w)	HEC-01	HEC-02	HEC-03	HEC-04	HEC-05	HEC-06	HEC-07	HEC-08	HEC-09	HEC-10	HEC-11	HEC-12
Hydroxyethyl cellulose	1	2.2	3	5	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2
Ethanol	20	20	20	20	25	30	45	50	20	20	20	20
Propylene glycol	15	15	15	15	15	15	15	15	20	30	40	50
2-Phenoxyethanol	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Water	63.2	62.0	61.2	59.2	57.0	52.0	37.0	32.0	57.0	47.0	37.0	27.0

Composition (%w/w)	CBP-01	CBP-02	CBP-03	CBP-04	CBP-05	CBP-06	CBP-07	CBP-08	CBP-09	CBP-10	CBP-11	CBP-12	CBP-13	CBP-14
Carbopol 980	0.5	0.25	0.65	0.25	0.25	0.5	0.5	0.5	0.1	1.0	0.5	0.5	0.5	0.5
Ethanol	-	-	-	-	-	-	20	-	-	-	35	50	10	-
Propylene glycol	15	15	15	25	35	35	15	50	15	15	15	15	15	25
Methyl paraben	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Propyl paraben	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Water	84.4	84.6	84.2	74.6	64.6	64.4	64.4	49.4	84.7	82.5	49.2	34.4	74.3	74.2

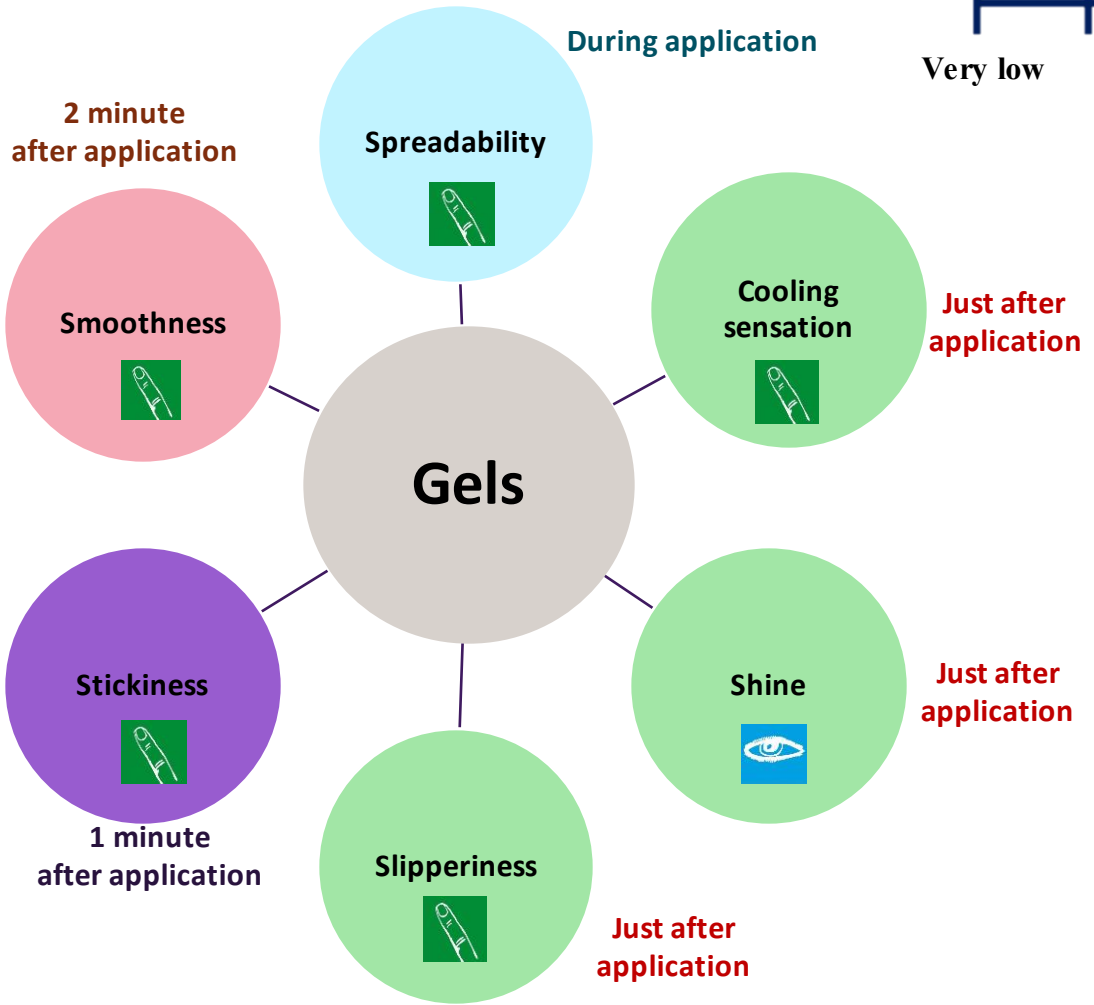


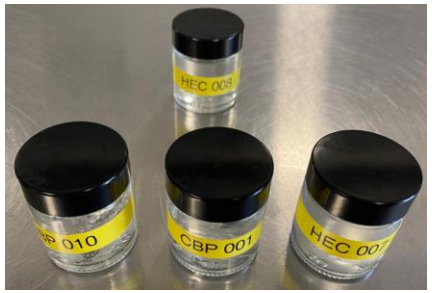
Sensory Intensity Ranking Test



	HEC-007 1	HEC-008 2	CBP-001 3	CBP-010 4	HEC-008 5
1	831	681	441	764	482
2	482	441	764	831	681
3	764	482	681	441	831
4	681	764	831	482	441
5	441	831	482	681	764
6	482	764	441	681	831
7	831	441	681	482	764
8	441	482	831	764	681
9	681	831	764	441	482
10	764	681	482	831	441

metronome

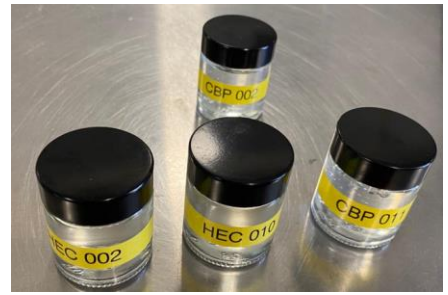




Panel Study – Part 1

CBP-01
CBP-10
HEC-07
HEC-08 (2)

4 + 1

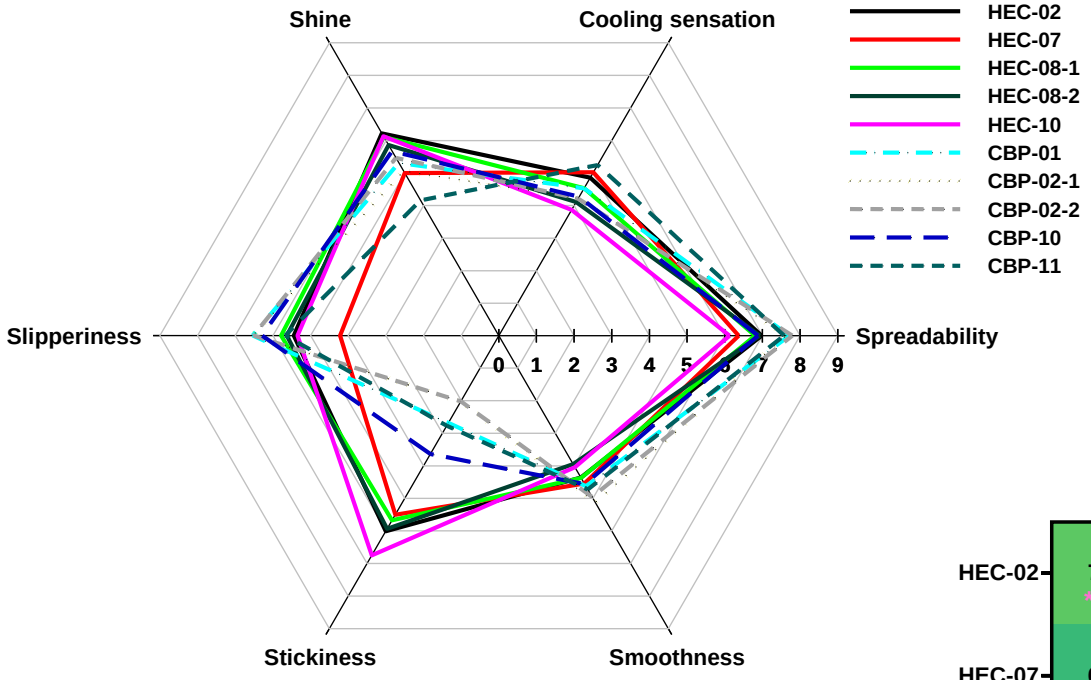


Panel Study – Part 2

CBP-02 (2)
CBP-11
HEC-02
HEC-10

4 + 1

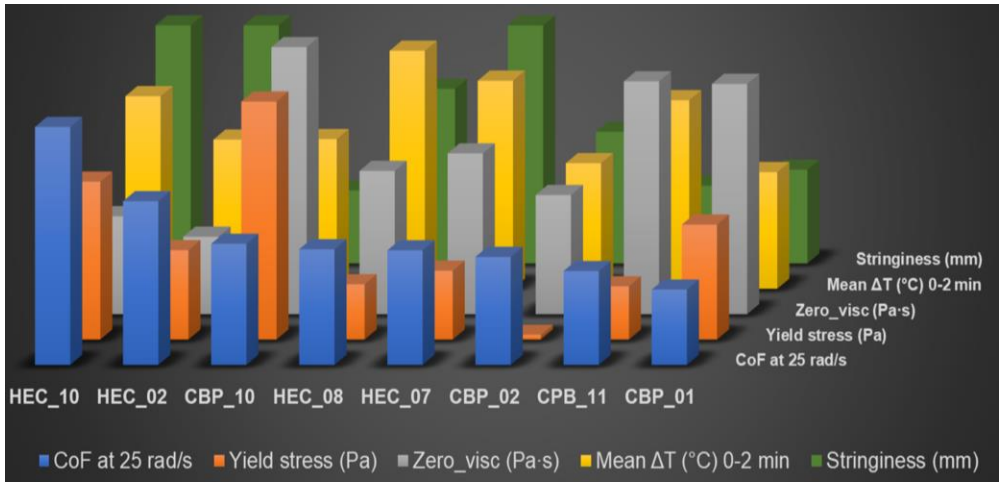
Q2 - Q3 - In Vivo Properties



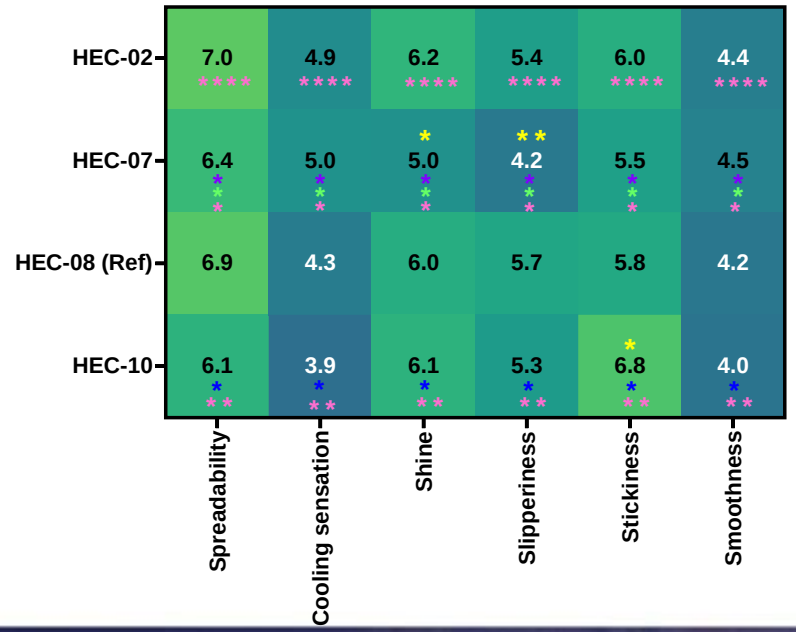
Composition (%w/w)	HEC-10	HEC-02	HEC-07	HEC-08
Hydroxyethyl cellulose	2.2	2.2	2.2	2.2
Ethanol	20	20	45	50
Propylene glycol	30	15	15	15
2-Phenoxyethanol	0.8	0.8	0.8	0.8
Water	47	62	37	32

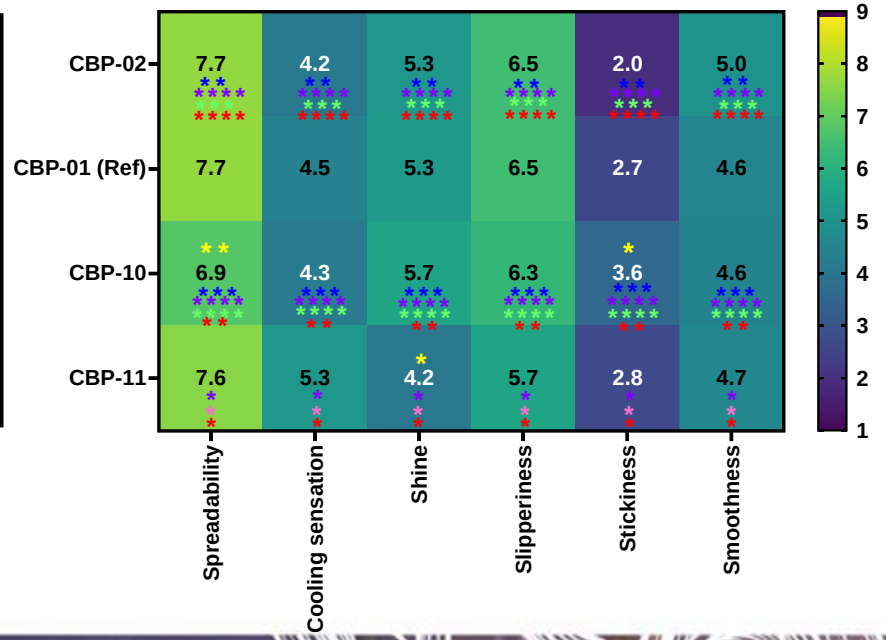
Composition (%w/w)	CBP-02	CBP-01	CBP-11	CBP-10
Carbopol 980	0.25	0.5	0.5	1
Ethanol	-	-	35	-
Propylene glycol	15	15	15	15
Methyl paraben	0.1	0.1	0.1	0.1
Propyl paraben	0.03	0.03	0.03	0.03
Triethanolamine	q.s.	q.s.	q.s.	q.s.
Water	84.62	84.37	49.21	82.47

Selected physicochemical and structural (CQAs-Q3) properties (normalized for different units)

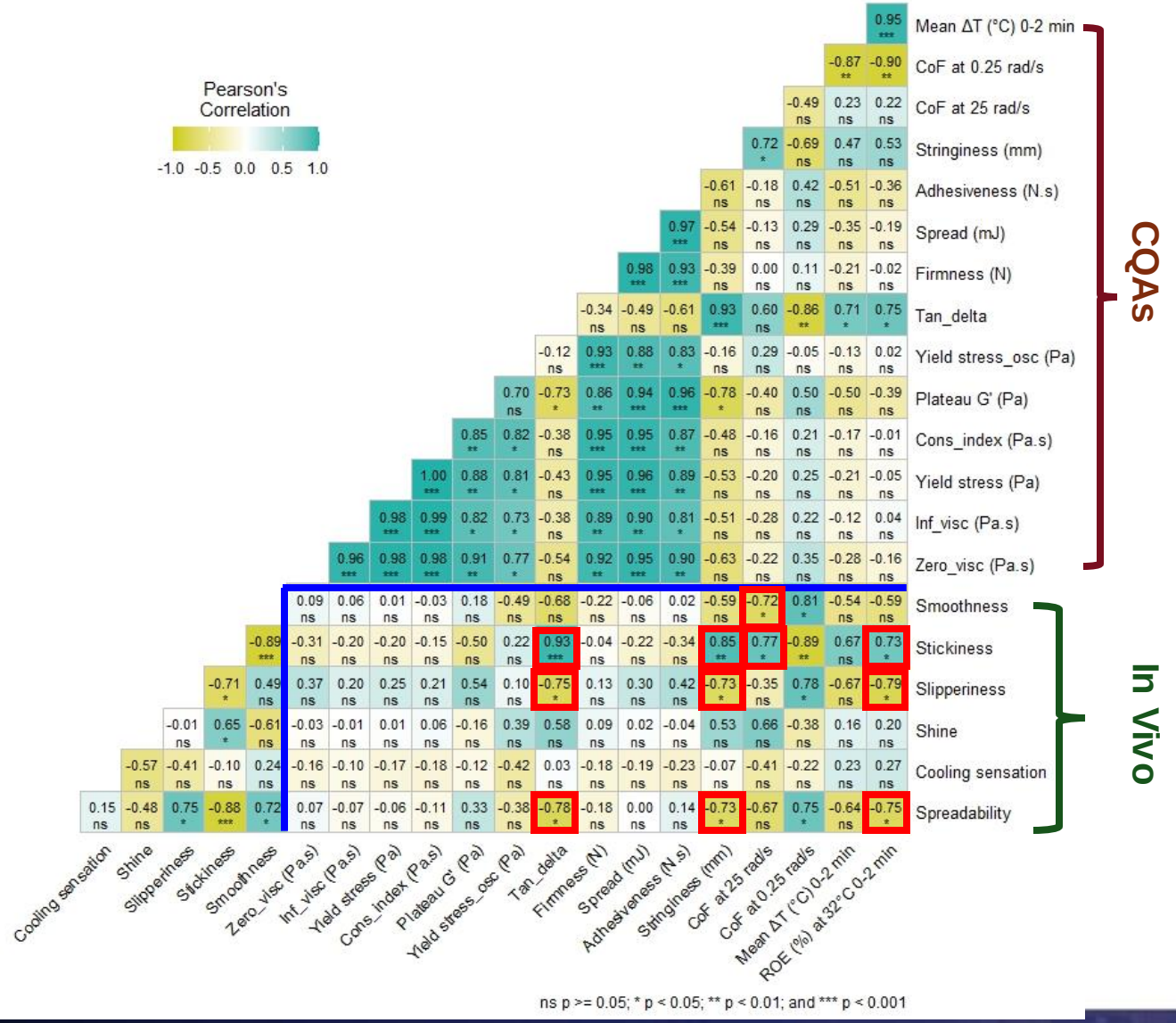


Color code	Parameters
Yellow "*"	Sensory perceptions
Blue "*"	CoF at 25 rad/s
Purple "*"	Yield stress (Pa)
Green "*"	Zero shear viscosity (Pa.s)
Pink "*"	Mean temperature difference (°C) in 0-2 min
Red "*"	Stringiness (mm)





Correlations: sensorial perceptions & instrumental properties



- **Spreadability negatively correlated with Tan_delta (G”/G’), stringiness, ROE at 32°C**
- **Slipperiness negatively correlated with Tan_delta (G”/G’), stringiness, ROE at 32°C**
- **Stickiness positively correlated with Tan_delta (G”/G’), stringiness, CoF at 25 rad/s, ROE at 32°C**
- **Smoothness negatively correlated with CoF at 25 rad/s**

Conclusion and learning objectives

- CQAs assessed instrumently are valuable in understanding sensorial characteristics in vivo
- Significant differences in instrumental attributes (e.g. rheological, tribological behaviour, texture properties) are likely to be perceptible to human subjects
- Data from selected instrumental techniques to evaluate CQAs can be predictive of sensory properties of topical products

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Thank You!

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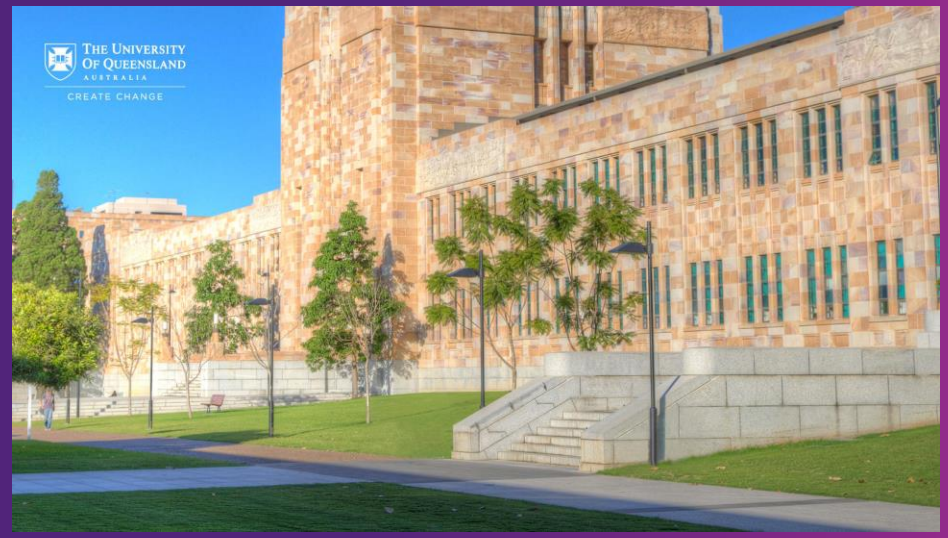
Vice-Chair - American Association of Pharmaceutical Sciences, (TTC)



With

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