



UNIVERSITY OF  
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## Evaluating emerging and existing taste masking technologies for paediatric medicinal development

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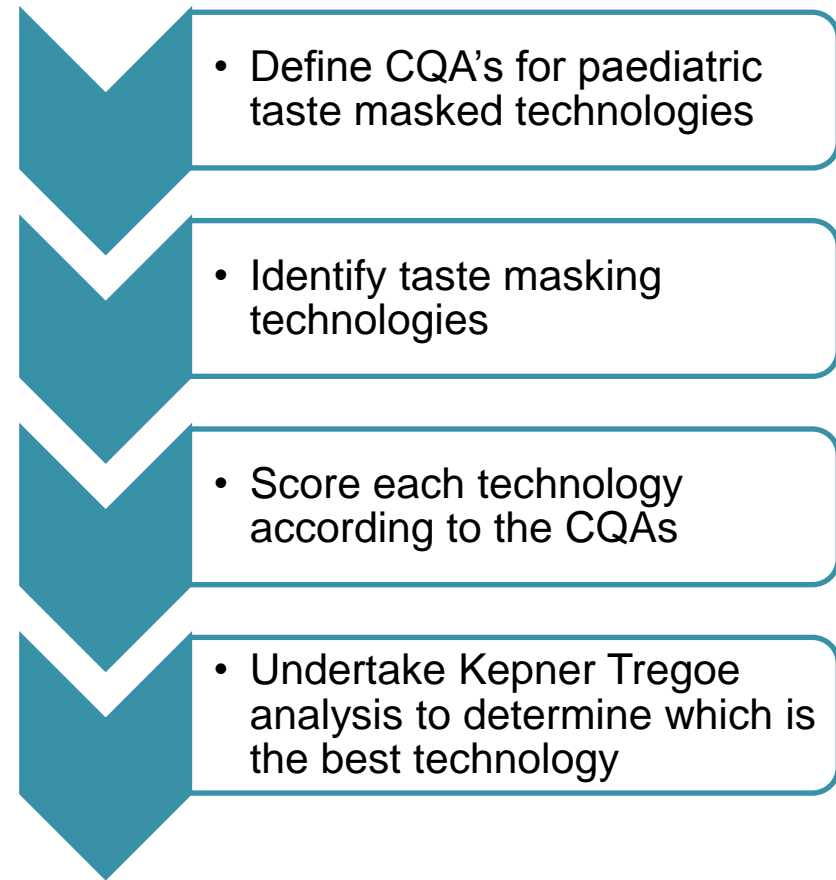
Project co-funded by  
**Innovate UK**



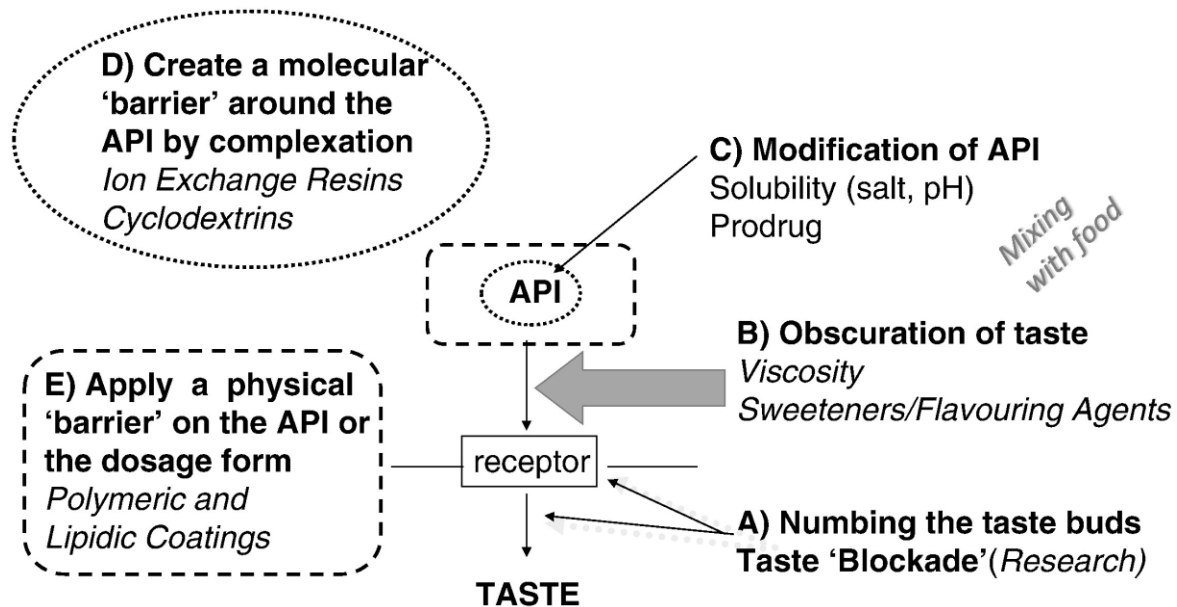
On behalf of an Innovate UK  
co-funded project:  
**'Accelerating Paediatric Formulation Development through  
Smart Design and Predictive Science.'**

# Project Purpose

- ❑ The need for taste masking technologies in paediatric medicines is recognised
- ❑ Many taste masking technologies exist and considerable effort is required to select the most appropriate technology
- ❑ The presented research entails investigations linked to Innovate UK's industrial project, "Accelerating paediatric formulation development through smart design and predictive science"
- ❑ This provides an independent critical evaluation of several taste-masking technologies



# Existing and emerging taste masking techniques In Industry; past 10 years



# Kepner-Tregoe principles

- ▷ Allows the evaluation of alternatives against an agreed framework, thus providing an impartial prioritisation process
- ▷ Framework is formed by the CQAs identified
- ▷ Scoring should be simple but accurate
- ▷ Classify musts and wants
- ▷ Weighted analysis: allows more emphasis to be placed on certain CQAs

# Defining the CQA's for technologies

<b>Regulatory acceptability of excipients</b>	<ul style="list-style-type: none"><li>•Excipients available and approved for use in children's medicines</li><li>•STEP Database; FDA Access data</li></ul>
<b>TRL (Technology Readiness level)</b>	<ul style="list-style-type: none"><li>•Technology has previously been produced at commercial scale</li><li>•Availability of evidence of taste masking in humans</li></ul>
<b>Complexity and manufacturing cost</b>	<ul style="list-style-type: none"><li>•Use of standard processes and equipment</li></ul>
<b>Dosage forms</b>	<ul style="list-style-type: none"><li>•Availability of a range of dosage forms that offer flexibility in dosing to children</li></ul>
<b>Independent evaluation</b>	<ul style="list-style-type: none"><li>•Source of evidence regarding technology – peer reviewed publication or independent evaluation is preferred</li></ul>
<b>Availability/freedom to operate</b>	<ul style="list-style-type: none"><li>•Is technology widely available for use by anyone</li></ul>

Scoring scales were from 1 →3 with 3 being highest

# Scoring system developed

<b>CQA</b>	<b>Score = 3</b>	<b>Score = 2</b>	<b>Score = 1</b>
Regulatory Excipients	Excipients approved for use in paediatrics	Excipients approved for use in medicines	Novel excipients
TRL (Technology Readiness Level)	Technology on the systematic TRL scale between 7—9	Technology on the systematic TRL scale between 4—6	Technology on the systematic TRL scale between 1—3
Complexity and manufacturing cost	Low excipient load; simple manufacturing process	High excipients and complex manufacturing process	Change in API chemistry; novel process
Dosage forms	Suitable for use with solid and liquid products	Only limited products available yet appropriate for paediatric use	Only single dosage form available; typically used in adults (eg tablets)
Independent evaluation	Information available in peer-reviewed journal	Information available in sources outside the company	Information limited to patent and company web pages

Ability/freedom to operate = Score 1 if available for use and 0 if not available

# Technologies included

OXPzero	Oxford Pharmascience Group PLC	Oral Suspension - Novel salt coupled with encapsulation inside layered matrix structure based on Inulin
Bio-dar microencapsulation	Biodar Pharmaceuticals	Microencapsulation using HPMC Phthalate (300 micron microcapsules) in soft, sweet matrix
Instek	Inventia Healthcare	Conventional melt/orodispersible tablets with taste making using fumed silica
aaiPharma TMT	AAI Pharma Services	Formation of an absorbate w/ magnesium aluminium silicate and calcium carbonate
Cima TMT	Cima Labs	Polymeric coating; comprises a small proportion of a water soluble polymer formulated with non-water soluble polymer.
Elan Cyclodextrin	Alkermes	Blending of drugs with cyclodextrins without pre-formation of the complex.
Gattefosse Lipid based	Gattefosse	Precirol® ATO 5 (Gattaphen® T and Gattecoat) High-melting point lipid based coating applied to particulates
SRI TMT	Southern Research Institute	Solvent based microencapsulation
Panacea TMT	Panacea Biotec Ltd	Non-sugar sweetener, and non-sugar sweetener in mucoadhesive slow release copolymer matrix (PVA/MA)
Redpoint TMT	Redpoint Bio corporation	TRPM5 taste receptor inhibitors comprising nucleotides
Abbott Lipid based TMT	Abbott Laboratories Inc.	A uniform dispersion in aqueous medium of droplets comprising: (a) a core comprising water, a non-toxic C2-C5 alkanol, a water-soluble drug, and a surfactant, and (b) a coating surrounding the core comprising oils.



# Technologies included

Prolamine Coatings	Abbott Laboratories Inc.	A uniform dispersion in aqueous medium of droplets
BMS oral suspensions	Bristol Myers Squibb Co.	The dry powder is formed of drug (e.g. des-quinolone), and a pH modifying agent, etc. L-arginine
Aventis TMT	Sanofi	15 to 30 % of an active substance mixed with 60 to 80 % of glycerol ester/ fatty acid. Spray-cooling to produce granules >350 microns.
Eisai TMT	Eisai Co Ltd	Complexation of basic drugs with anionic polymers such as carrageenan, chondroitin sulphate etc.
Lts Buccal Wafers	LTS Lohmann Threapie-Systems	Rapidly disintegrating buccal film . forming polymer (e.g. HPMC, PVA) and 7-20% of carbon dioxide - ion exchange resin as a primary taste mask.
Takeda ODT-1	Takeda Pharmaceutical Co .Ltd	Fast melt/ODT Comprises oil + bitterness-relieving agent consisting of a sweetener and/or an acidic phospholipid or lyso-derivative.
Bend LMPs	Bend Research	Lipid multiparticulates produced by melt spray congealing. Additional coating (multiple layers) – via fluid bed coating
Super-critical fluids	Crystec Pharma	Particle formation w/ supercritical fluids provides the opportunity to apply a coating drug particulates.
Exines	Sporomex	Plant pollens / spores and removes the internal genetic material by a chemical or enzyme process. Leaving a porous, inert, elastic shell (skeleton) called an exine
Capricorn	Capricorn Pharma Inc.	TM pharmaceutical resin- complexed granules for water soluble drugs.
Redpoint TMT	Redpoint Bio corporation	TRPM5 receptor to block taste buds





# Individually assessed TMT scored data collection

Panacea biotech: non-sugar sweetener, and non-sugar sweetener in mucoadhesive slow release copolymer matrix (PVA/MA)

CQA	Score	Justification	References
<b>Regulatory Excipients</b>	3	Mannitol, sorbitol, xylitol - already used in TMT	web
<b>TRL</b>	3	3 commercial products available; Nimulid MD, Toff MD and Awayke MD	web
<b>Complexity and manufacturing cost</b>	3	Conventional melting processes and orodispersible tablet formulation methods	Patent
<b>Dosage forms</b>	2	Tablets forms; ODT	Patent
<b>Independent evaluation</b>	3	Independent information on technology available	References in article, journal

aaPharma- U.S: formation of an adsorbate w/ magnesium aluminium silicate and calcium carbonate

CQA	Score	Justification	References
<b>Regulatory</b>	3	Excipient Regulatory approval; (silicates)	patent
<b>TRL</b>	1	Used to prepare H2 Receptor antagonist medicines but no evidence of human taste assessment	patent
<b>Complexity and manufacturing cost</b>	2	Granulation, drug adsorbate methods	patent
<b>Dosage forms</b>	2	Chewy or solid tablet or powder-filled capsule form	patent
<b>Independent evaluation</b>	1	Little, unreliable information of technology accessed.	majority of source from patent



# Overall Results

Technology name/description	Provider	Availability (0 = no; 1 = yes)	REGULATORY/ EXCIPIENTS	TRL	COMPLEXITY/ COST	DOSAGE FORMS	INDEPENDENT EVALUATION	Overall
OXPzero	Oxford Pharmascience Group PLC	1	3	3	3	3	3	16
Bio-Dar Microencapsulation for Taste Masking	BioDar Pharmaceuticals	0	2	2	2	3	1	11
INSTEK	Inventia Healthcare	1	3	3	2	2	2	13
aaipharma Taste Masking Technology	AAI Pharma Services	1	3	1	2	2	1	10
Cima Taste Masking Technology	Cima Labs	1	3	3	2	2	3	14
Elan Cyclodextrin Based Taste Masking Technology	Alkermes - based on finding the technology from Elan pharmaceuticals	0	3	2	3	2	1	11
Gattefosse Lipid Based Taste Masking Technology	Gattefosse	1	3	1	2	2	3	12
SRI Taste Masking Technology	Southern Research Institute	0	1	1	1	1	1	5
Capricorn Taste Masking	Capricorn Pharma Inc.	1	1	2	1	1	1	7
Panacea Taste Masked Fast Melt	Panacea Biotec Ltd	1	3	3	3	2	3	15
Redpoint Taste Masking Technology	Redpoint Bio corporation	0	1	1	2	3	2	9
Panacea (non - ODT )	Panacea Biotec Ltd	1	2	2	3	1	1	10
Prolamine Coatings for Taste Masking	Abbott Laboratories Inc.	1	3	3	3	3	3	16
Aventis Taste Masking Composition	Sanofi	0	3	3	2	2	2	12
Eisai Taste Masking	Eisai Co Ltd	1	3	3	2	3	1	13
LTS Taste Masked Buccal Wafers	LTS Lohmann Threapie-Systeme	0	3	1	1	1	2	8
Takeda Taste Masked ODT-1	Takeda Pharmaceutical Co. Ltd	1	3	3	3	2	1	13
Bend Research Lipid multiparticulates (LMPs)	Bend Research	1	3	3	2	2	2	13
Super-critical fluids	Crystec Pharma	0	3	1	2	2	1	9
Exines	Sporomex	1	2	2	1	2	1	9

# Use of database with KT analysis

▷ Top 3 existing technologies for a multitude of dosage forms

▷ Prolamine Coatings

▷ Abbott Laboratories Inc.

▷ A uniform dispersion in aqueous medium of droplets

▷ Eisai TMT

▷ Eisai Co Ltd

▷ Complexation of basic drugs with anionic polymers such as carrageenan, chondroitin sulphate etc.

▷ Redpoint TMT

▷ Redpoint Bio corporation

▷ TRPM5 receptor to block taste buds

▷ Top 3 technologies for standard manufacturing techniques

▷ OXPzero

▷ Oxford Pharmascience Group PLC

▷ Oral Suspension - Novel salt coupled with encapsulation inside layered matrix structure based on Inulin

▷ Takeda ODT-1

▷ Takeda Pharmaceutical Co .Ltd

▷ Fast melt/ODT Comprises oil + bitterness-relieving agent consisting of a sweetener and/or an acidic phospholipid or lyso-derivative.

▷ Eisai TMT

▷ Eisai Co Ltd

▷ Complexation of basic drugs with anionic polymers such as carrageenan, chondroitin sulphate etc.

# Summary of taste-masking technologies

- ▷ 21 taste masking technologies were identified and evaluated
- ▷ 18 technologies worked by reducing dissolution within the oral cavity
  - ▷ 2 by inhibition of taste receptors
  - ▷ 1 by balancing bitterness with other flavours
- ▷ Only 4 technologies were appropriate for use in liquid products
- ▷ 14 reported technologies are available for use

# Independent analysis of TMTs for paediatric use: Conclusions

- ▷ This analysis used information available within the public domain
- ▷ An independent evaluation of technologies is presented
- ▷ This database can be mined to determine which TMT is most appropriate for a given application
- ▷ Further work is required to supplement these technologies and to further validate these scores

Thank you!  
**Any questions?**

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## Weighted for those that are readily available:

Technology name/description	Provider	Availability (0 = no; 1 = yes)	REGULATORY/ EXCIPIENTS	TRL	COMPLEXITY/ COST	DOSAGE FORMS	INDEPENDENT EVALUATION	Overall
OXPzero	Oxford Pharmascience Group PLC	1	3	3	3	3	3	19
Bio-Dar Microencapsulation for Taste Masking	BioDar Pharmaceuticals	1	2	2	2	3	1	13
INSTEK	Inventia Healthcare	1	3	3	2	2	2	16
aaiPharma Taste Masking Technology	AAI Pharma Services	1	3	1	2	2	1	10
Cima Taste Masking Technology	Cima Labs	1	3	3	2	2	3	17
Elan Cyclodextrin Based Taste Masking Technology	Alkermes - based on finding the technology from Elan pharmaceuticals	0	3	2	3	2	1	0
Gattefosse Lipid Based Taste Masking Technology	Gattefosse	1	3	1	2	2	3	13
SRI Taste Masking Technology	Southern Research Institute	0	1	1	1	1	1	0
Capricorn Taste Masking	Capricorn Pharma Inc.	1	1	2	1	1	1	9
Panacea Taste Masked Fast Melt	Panacea Biotec Ltd	1	3	3	3	2	3	18
Redpoint Taste Masking Technology	Redpoint Bio corporation	0	1	1	2	3	2	0
Panacea (non - ODT )	Panacea Biotec Ltd	1	2	2	3	1	1	12
Prolamine Coatings for Taste Masking	Abbott Laboratories Inc.	1	3	3	3	3	3	19
Aventis Taste Masking Composition	Sanofi	0	3	3	2	2	2	0
Eisai Taste Masking	Eisai Co Ltd	1	3	3	2	3	1	16
LTS Taste Masked Buccal Wafers	LTS Lohmann Threapie-Systeme	0	3	1	1	1	2	0
Takeda Taste Masked ODT-1	Takeda Pharmaceutical Co. Ltd	1	3	3	3	2	1	16
Bend Research Lipid multiparticulates (LMPs)	Bend Research	1	3	3	2	2	2	16
Super-critical fluids	Crystec Pharma	0	3	1	2	2	1	0
Exines	Sporomex	1	2	2	1	2	1	12