CBD and controlled cannabinoids in consumer products

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Agenda

- Background
- The Need
- Collaboration
- Government Chemist CBD Project
  1. Guidance
  2. Wider collaboration & Training
  3. Method development
  4. International ring trial
  5. Impact

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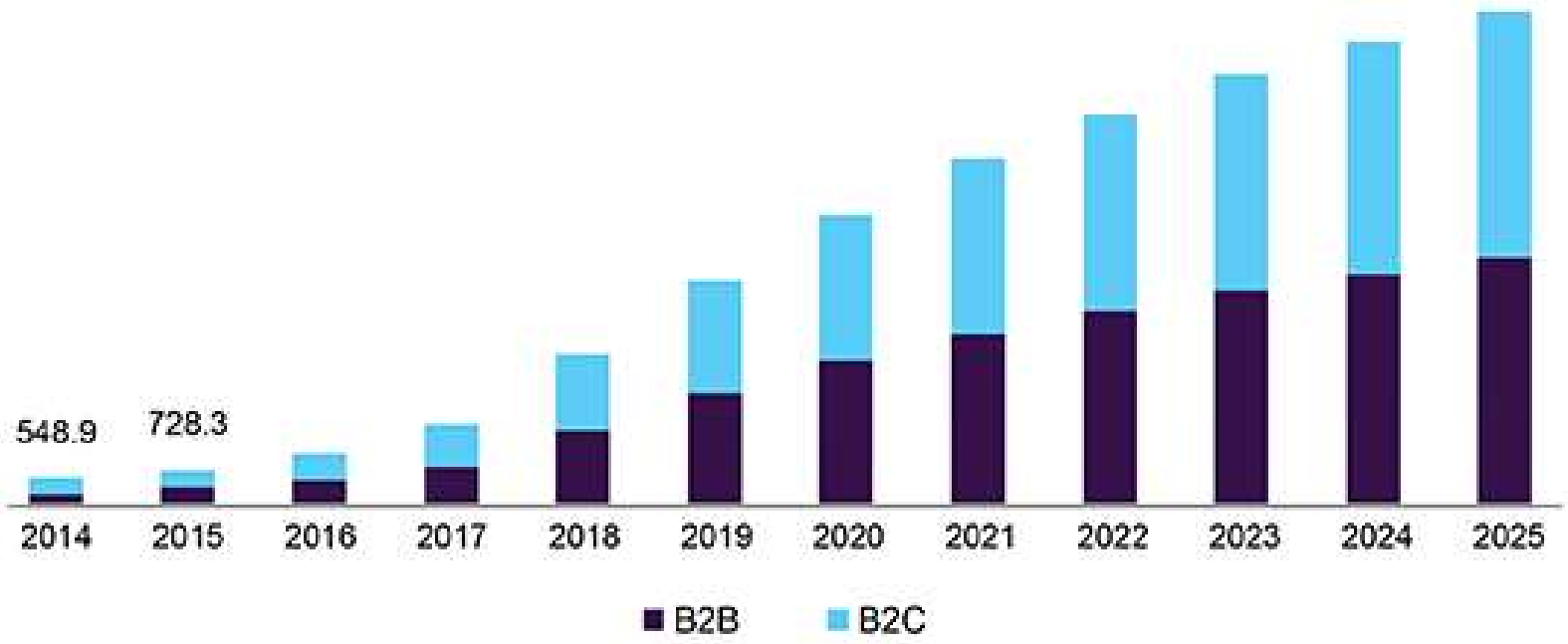
U.S. CBD market, by distribution channel, 2014 - 2025 (USD Million)



Source: www.grandviewresearch.com

Legal Status

Home Office

- CBD as an isolated substance, in its pure form, would not be controlled under the MDA 1971 / MDR 2001
- Very difficult to isolate pure CBD
- High level of sensitivity required to accurately and consistently determine content
- If any controlled cannabinoids present - product would be controlled
- Intention to amend the MDR 2001 to permit CBD products containing no more than a defined percentage trace concentration of certain controlled cannabinoids
- Presumption has to be one of caution - a CBD containing product would be controlled under the MDA 1971 / MDR 2001 due to controlled cannabinoid content
- Home Office definition of an 'exempted product' according to Regulation 2 of the MDR 2001 – 3 limbs - 1mg 'threshold' per pack

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Novel Food Status

- **Hemp & related products not novel**
- **Not the case for CBD extracts in food**
- **Novel food status confirmed in January 2019**
- **Retained European Law states they need to be authorised before placing on market**
- **Novel food application submitted before 31 March 2021**
  - Applicants need to include details of the toxicological studies conducted
  - 1 April 2021: only products with submitted applications (subsequently approved) & were on the market on 13 February 2020 will be allowed to remain on the market
- **List CBD products linked to novel food applications (Eng & Wales)**

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The GC Need

- **GC horizon scanning activities identified**
- **2020 – 2023 programme**
  - Assess the issues related to CBD in foods
  - Develop GC capability to determine CBD in foods
- **GC capability to discharge the statutory function of Referee Analyst in case of submission of referee samples**

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Collaboration

Centre for Medicinal Cannabis
Helping people get the legal access they need

Department for Business, Energy & Industrial Strategy
FUNDED BY BEIS

Food Standards Agency
food.gov.uk

Office for Product Safety & Standards

Home Office

UKAS
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[dstl]
The Science Inside

ACI

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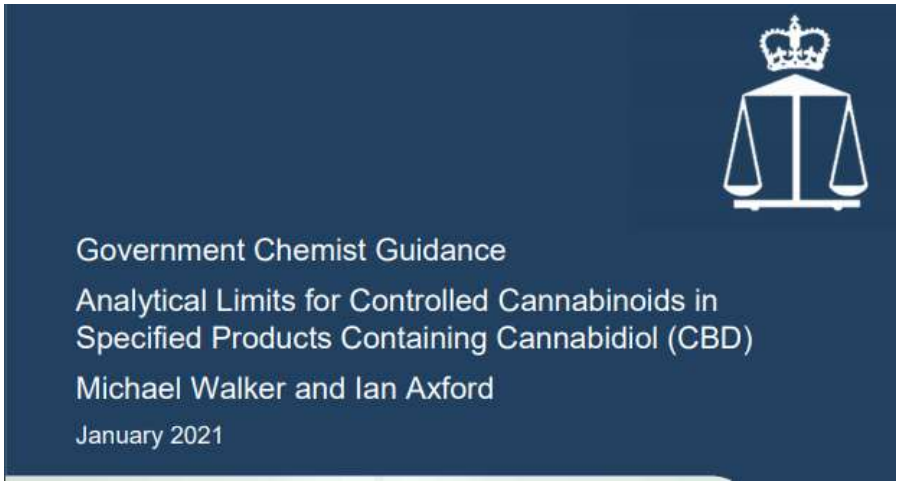
Government Chemist Project on CBD

1. Guidance



Government Chemist team publish a tutorial review of cannabinoids

This tutorial paper offers a review of the common names, abbreviations, regulation, psychoactivity and analytical methodology for the principle cannabinoids

From: Government Chemist
Published 19 May 2021

2. Wider collaboration & Training

- **UKAS CBD Food Product approval Awareness Expert Group**
- **FSA-UKAS-LGC-Fera Group** to discuss the need for the production of a best practice measurement guide for CBD.
- **Joint Knowledge Transfer Framework for Food Standards and Safety**
  - FY 20/21 - Cannabidiol (CBD) in Food Supplements
  - FY 21/22 - Testing of CBD consumer products
- **App based MicroLearning Content Development**

Department for Environment Food & Rural Affairs

Food Standards Agency food.gov.uk

Food Standards Scotland For safe food and healthy eating

Department for Business, Energy & Industrial Strategy

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3. Objectives of GC Laboratory Project

- Development of publicly available methods by January 2021:
  - Determination of CBD in Novel Foods / cosmetics
  - Determination of controlled cannabinoids in Novel Foods / cosmetics
- Transfer methods to UK regulatory (and other) labs via ring trial by March 2021
  - CBD & Controlled cannabinoids
  - Novel Foods & cosmetics

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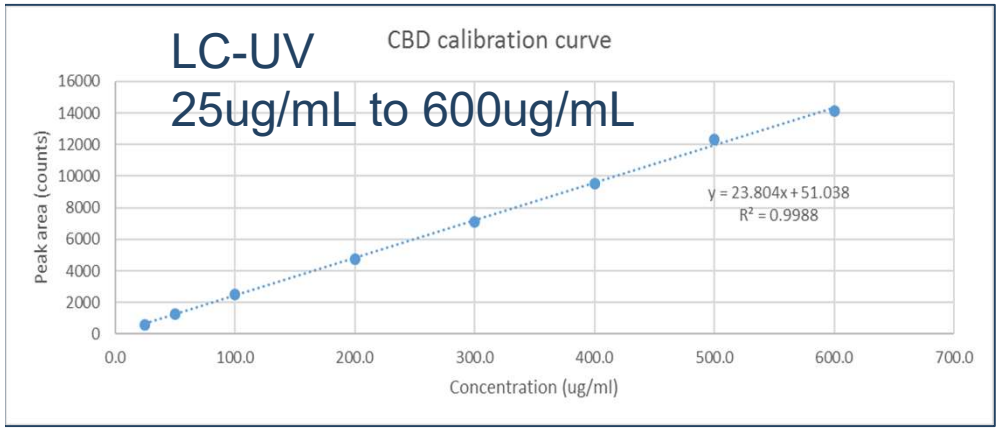
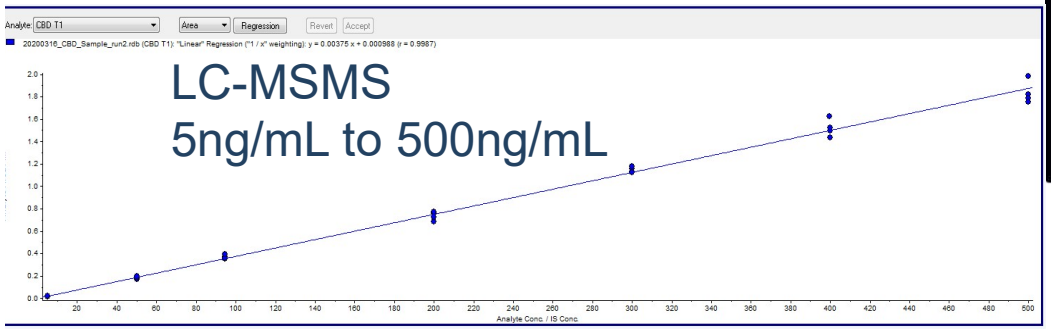
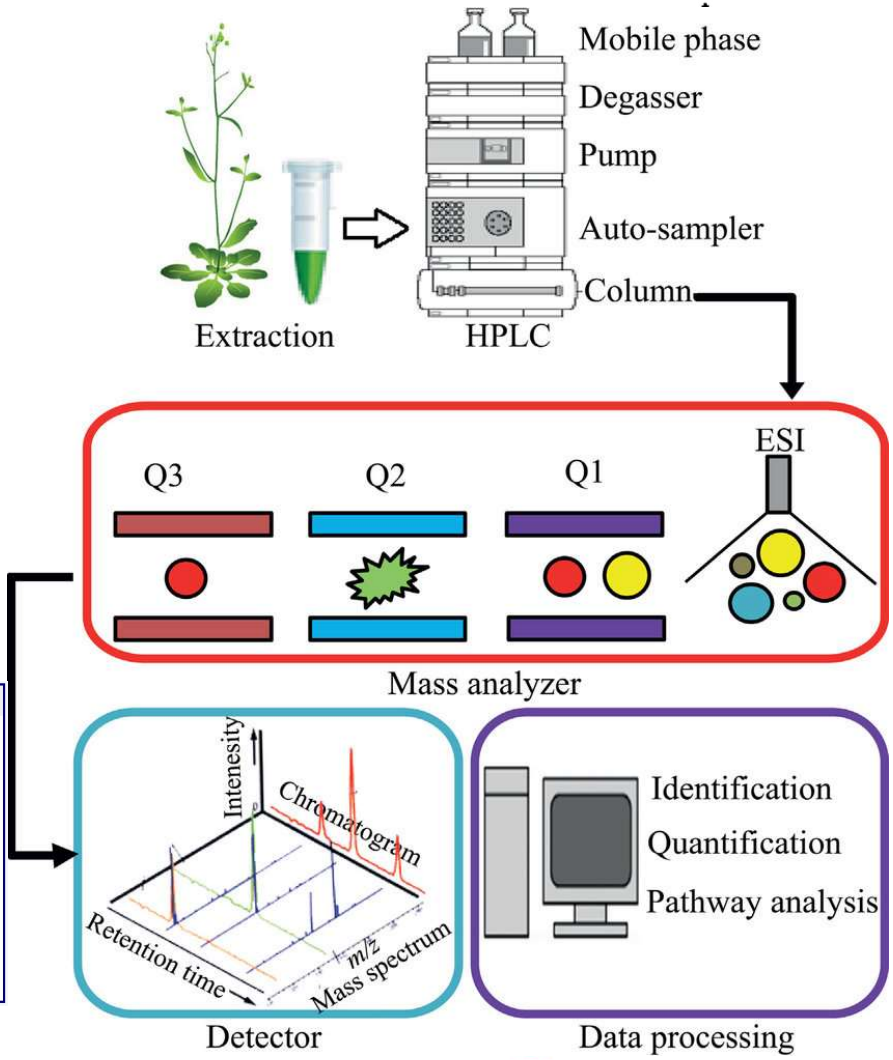
LC-MS/MS methods







Challenges

- Measurement of controlled drugs in presence of CBD
  - Some targets are very chemically similar to CBD
- Reproducibility (day to day, within day) of CBD measurements
  - Some examples of varying results between days
- Traceability of results
  - Good quality standards, high purity CBD
- ‘Matrix’ Interferences
  - Evidence of some formulations/ingredients affecting quantitative data
- Inconsistent Formulations
  - CBD containing products can be difficult to formulate, homogeneity issues

Cannabinoids of Interest

12 Controlled Plant Cannabinoids	
Trans-delta-9-tetrahydrocannabinol-C5	∆9THC
Cis-delta-9-tetrahydrocannabinol-C5	∆9THC
Delta-9-tetrahydrocannabinol-C4	∆9THC-C4
Delta-9-tetrahydrocannabinol-C3 (Delta-9-tetrahydrocannabivarin)	THCV
Delta-9-tetrahydrocannabinol-C1	∆9THC-C1
Delta-8-tetrahydrocannabinol	∆8THC
Cannabinol-C1	CBN-C1
Cannabinol-C2	CBN-C2
Cannabinol-C3	CBV
Cannabinol-C4	CBN-C4
Cannabinol-C5	CBN
Cannabinol methyl ether-C5	CBNM-C5

- **According to the literature:**
  - **most are present at low levels or not naturally occurring**
  - **Not readily available as standards**
- **Four cannabinoids highlighted in orange (∆9THC, THCV, ∆8THC and CBN)**
- **THCA will be also be monitored (not controlled but readily converts into a THC)**

Tetrahydrocannabinolic acid (THCA) as an isolated substance, in its pure form, would not be controlled under the MDA 1971 / MDR 2001. However, it is understood that THCA readily degrades both naturally, and with a catalyst or environmental change to THC which is a Schedule 1 controlled cannabinoid.

4. International ring trial

- **Samples – All commercially sourced**
  - CBD Hemp Food Oil
  - CBD Food Oil
  - CBD Cosmetic Oil
- **35 Participating Laboratories: 16 UK & 19 International**
- **12 March results deadline**
- **25 March – preliminary review**
- **April – statistical analysis**
- **June - final report published**

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Office for Product Safety & Standards
Food Standards Agency food.gov.uk
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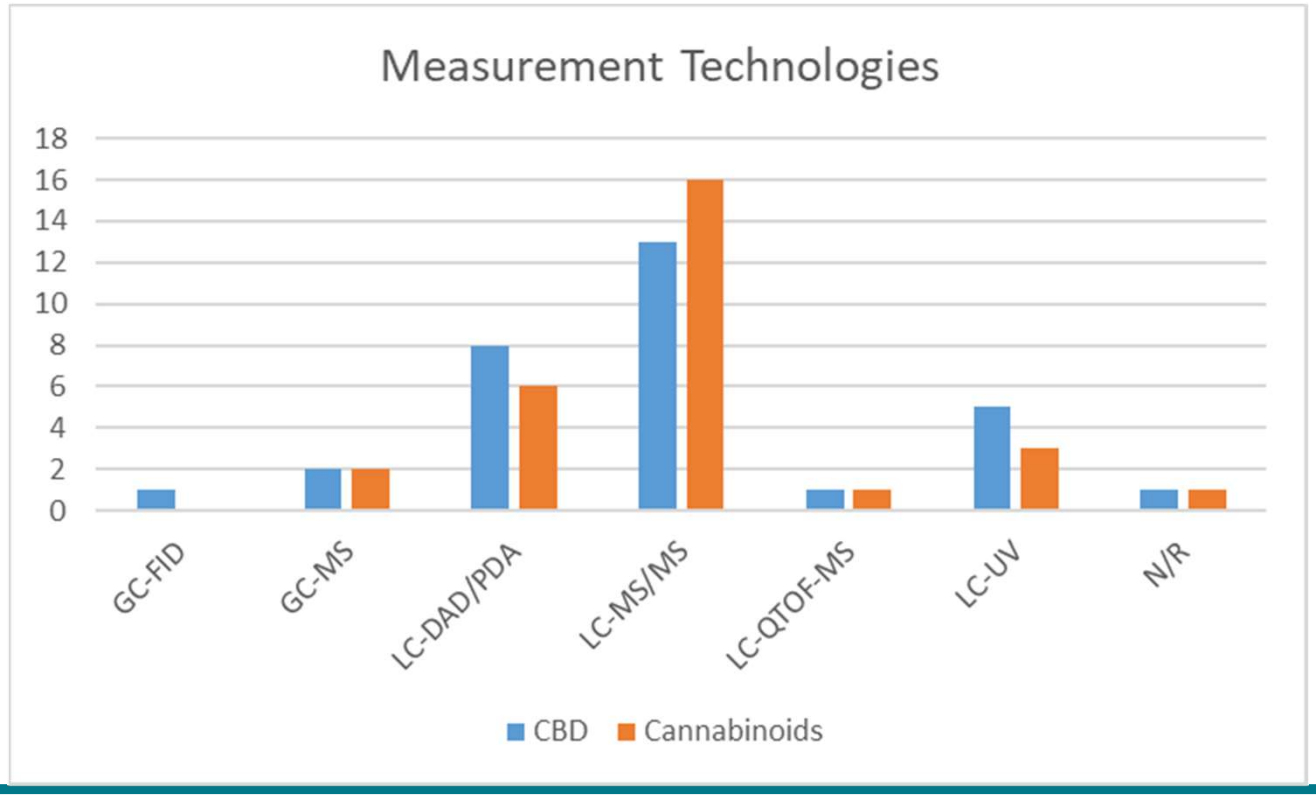
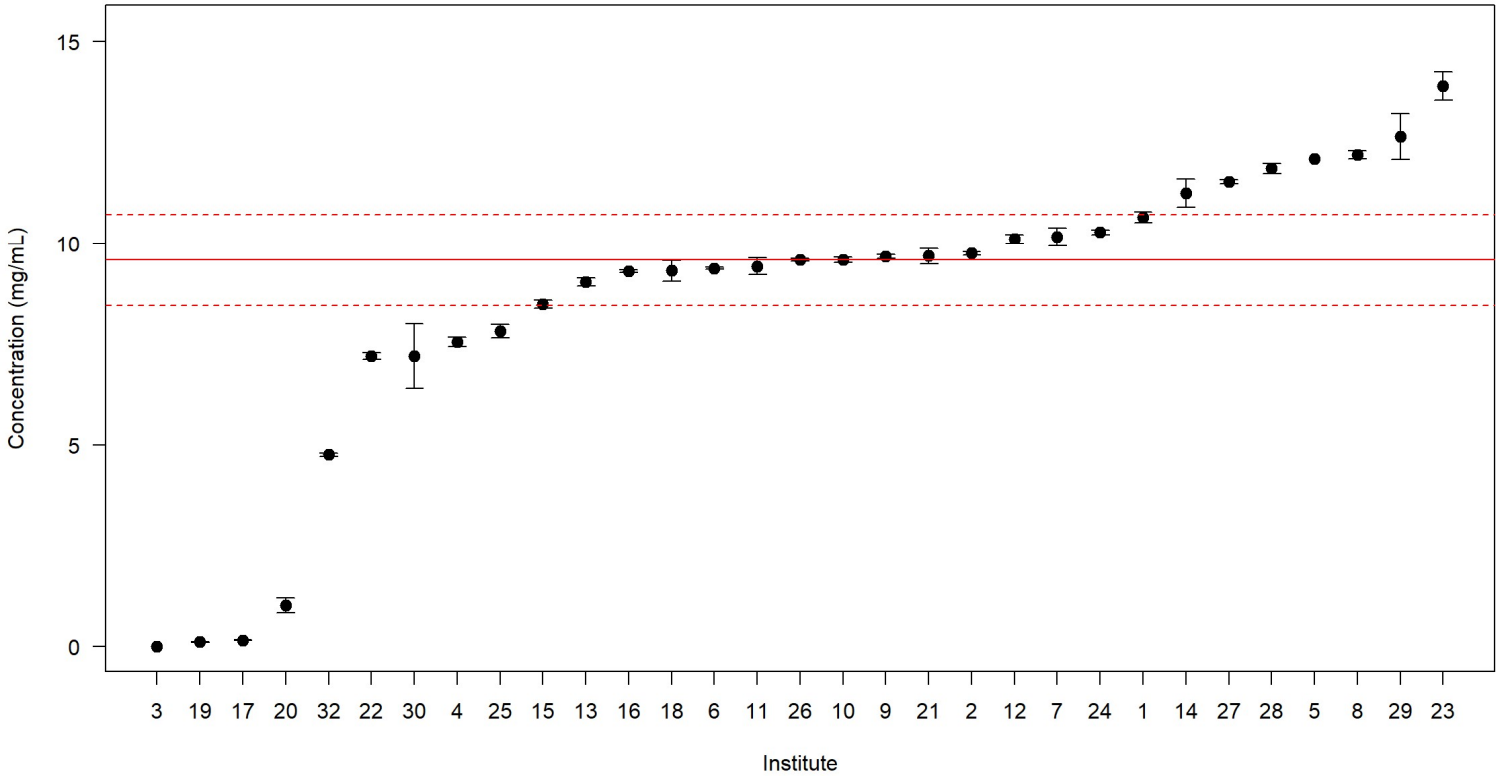
Results - Technologies

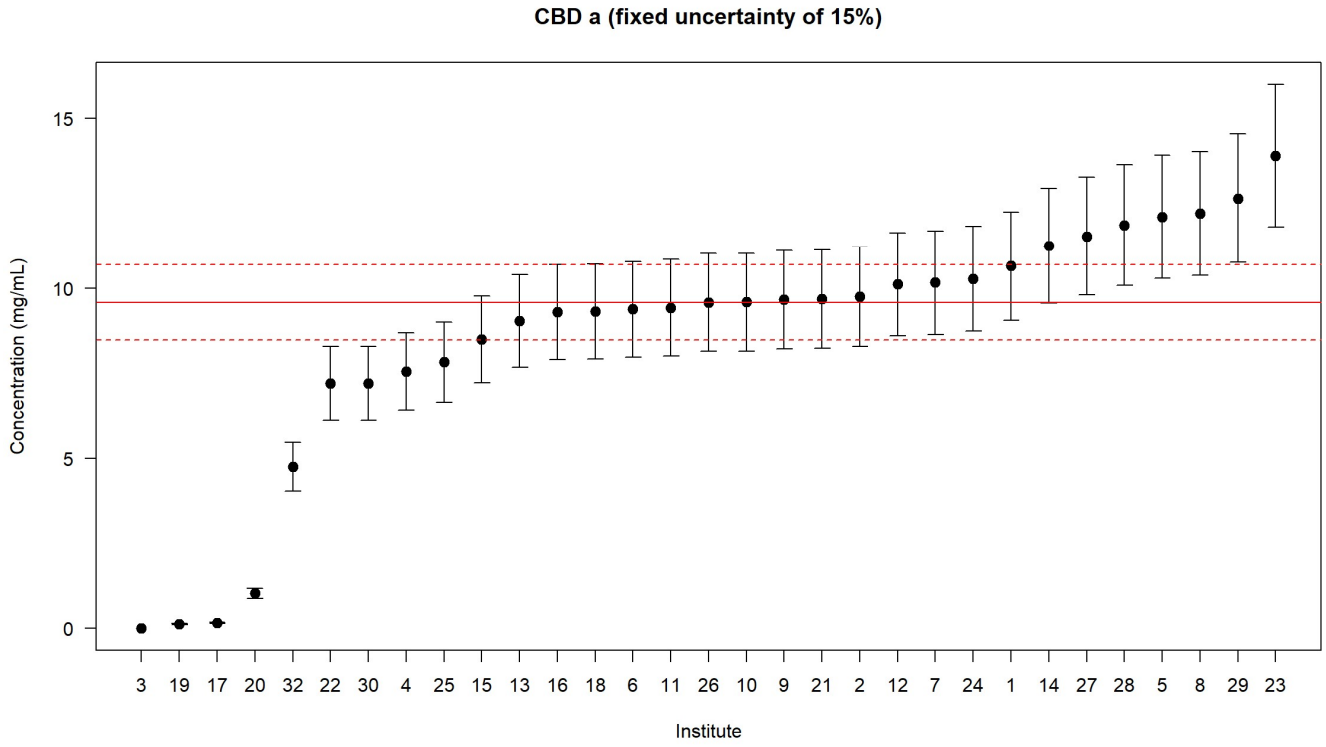


- Good range of technologies employed
- Approx 50/50 MS/spectroscopy

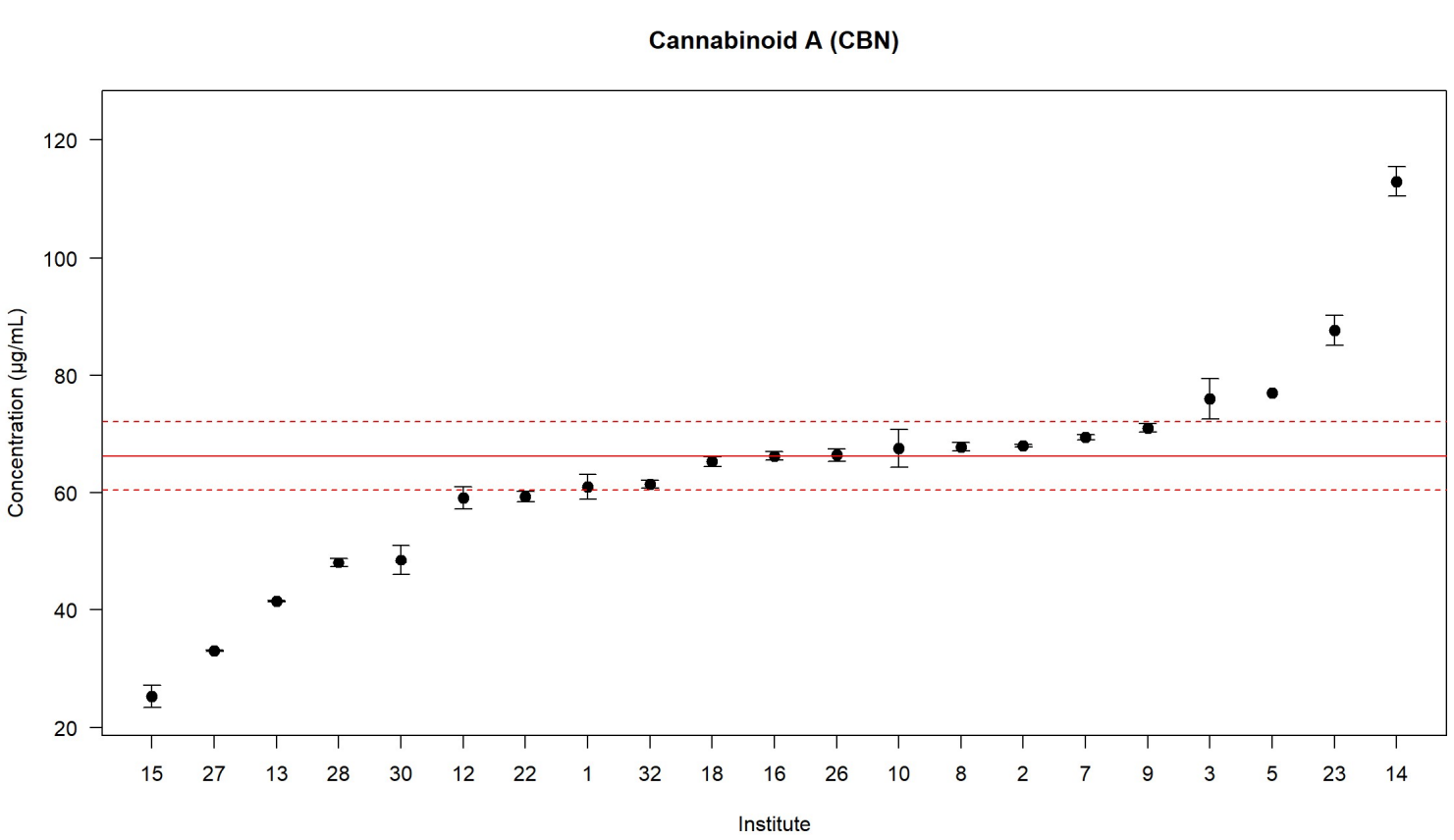
LGC-RT/20/A – Jacob Hooey CBD Oil 5%

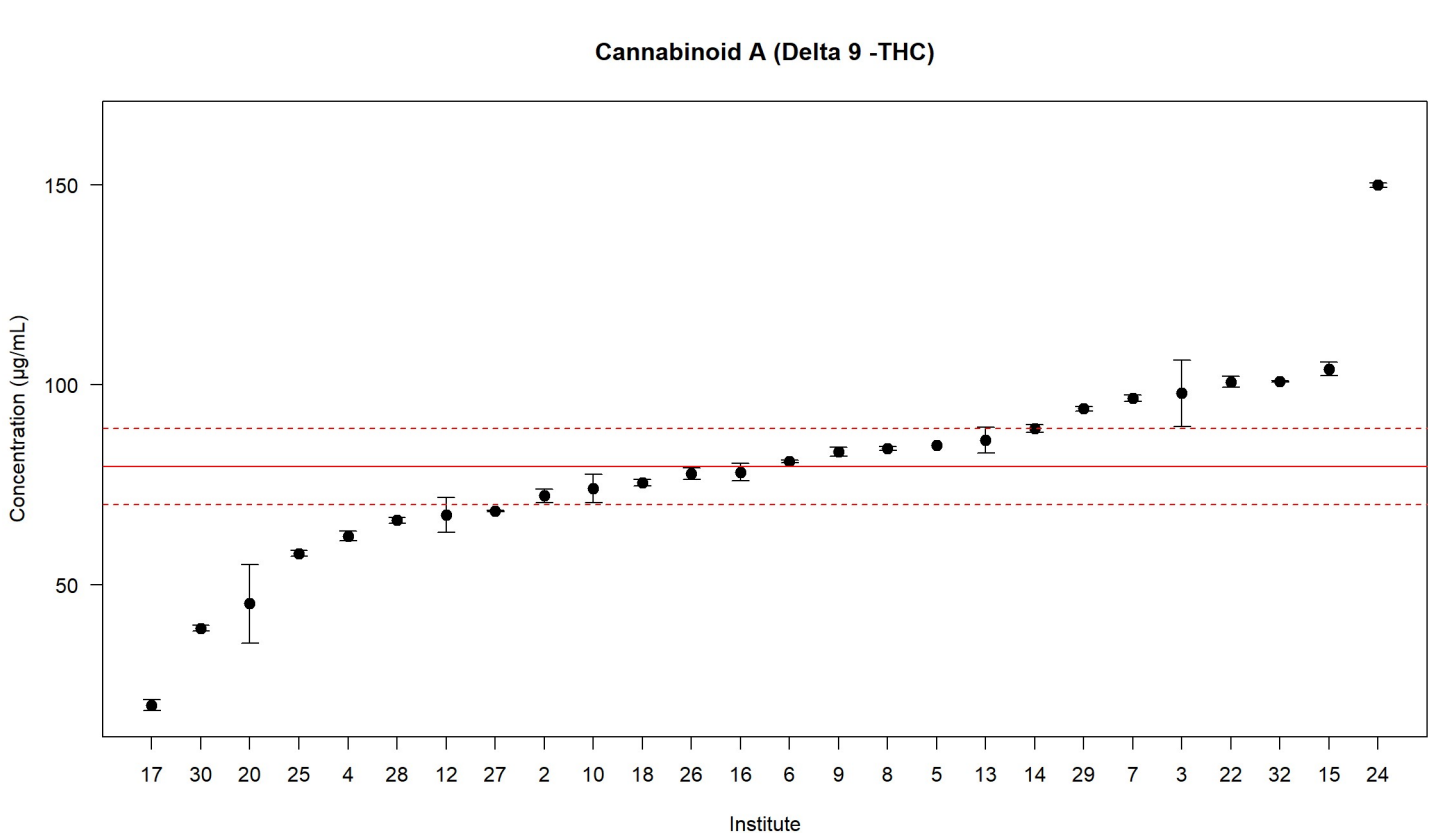


LGC-RT/20/A – Jacob Hooey CBD Oil 5%



- Same data plotted with a fixed 15% measurement uncertainty

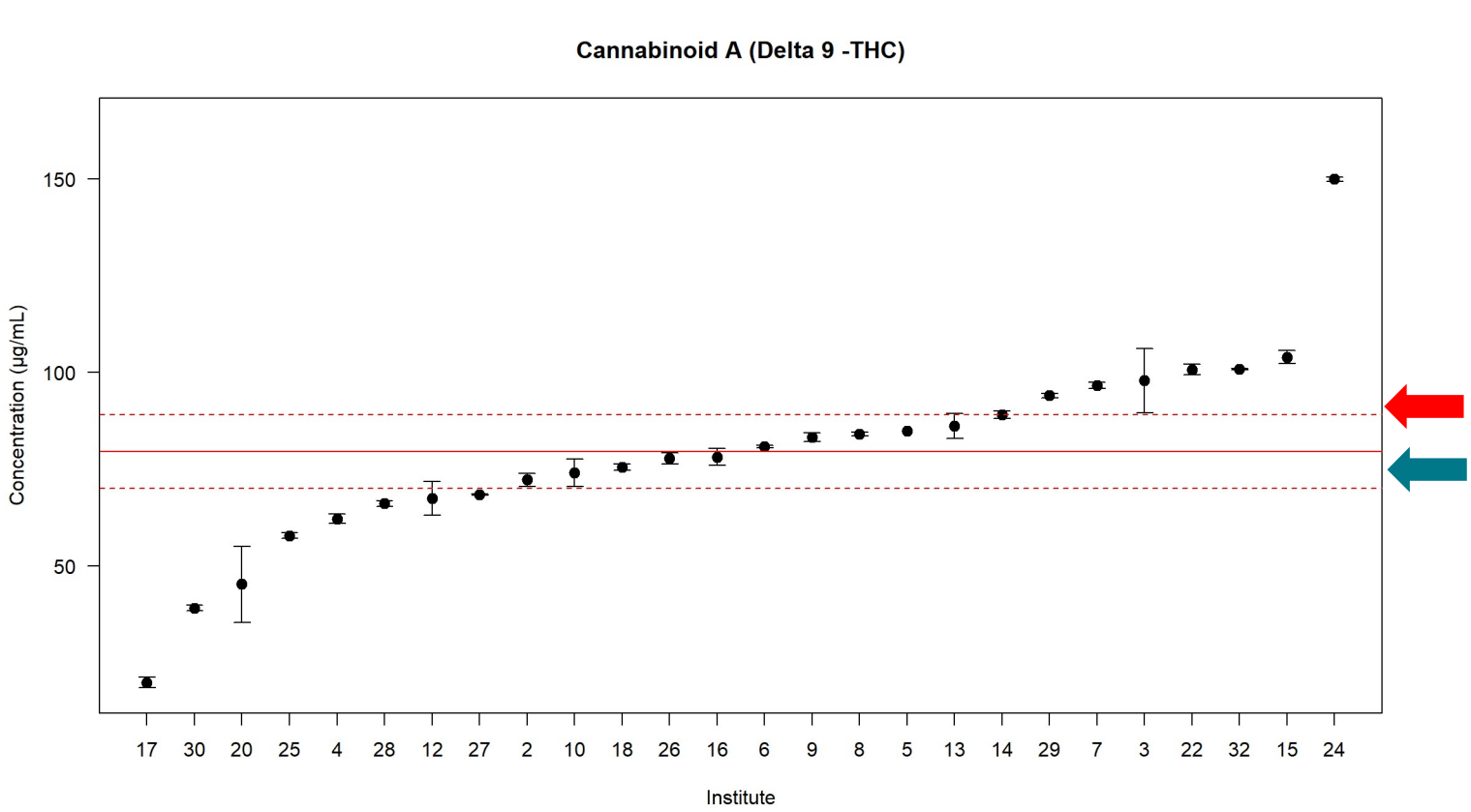

Cannabinoid A (CBN)
Concentration (µg/mL)
120
100
80
60
40
20
15
27
13
28
30
12
22
1
32
18
16
26
10
8
2
7
9
3
5
23
14
Institute


Cannabinoid A (Delta 9 -THC)
Concentration (µg/mL)
150
100
50
17 30 20 25 4 28 12 27 2 10 18 26 16 6 9 8 5 13 14 29 7 3 22 32 15 24
Institute

Δ^9-THC

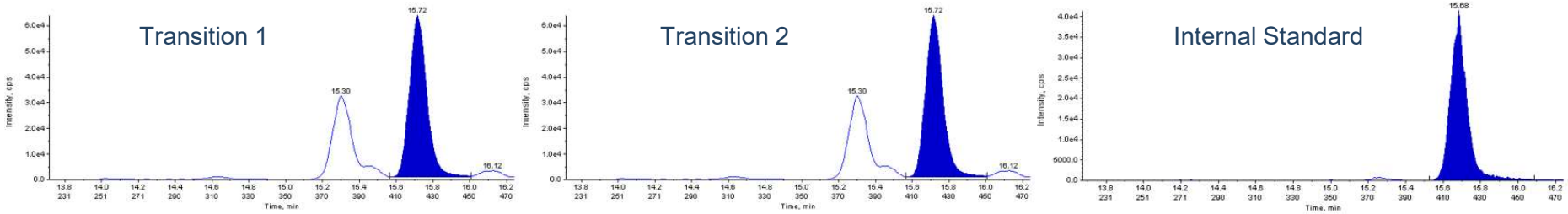
- Using the LGC supplied method Δ^9-THC cannot be confirmed in LGC-RT/20/A and LGC-RT/20/B as the MRM Transition 1/ Transition 2 values do not meet acceptance criteria
- LGC reported Δ^9-THC as 'not confirmed' for both these samples
- These samples were later run on a longer and more complex method to calculate a value for Δ^9-THC

Sample	Method	Δ^9-THC Concentration (µg/ml)	Meets Acceptance Criteria
LGC-RT/20/A	LGC proprietary method	64.8	Yes
LGC-RT/20/A	LGC protocol method	94	No
LGC-RT/20/B	LGC proprietary method	1.8	Yes
LGC-RT/20/B	LGC protocol method	3.9	No

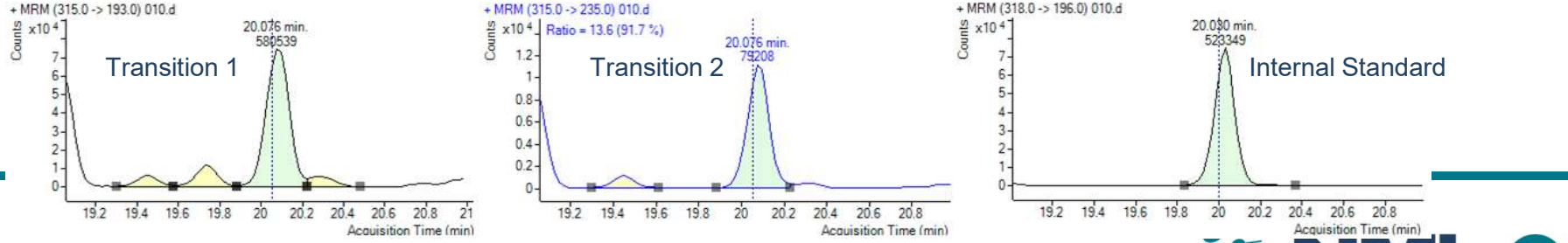

Cannabinoid A (Delta 9 -THC)
Concentration (µg/mL)
150
100
50
17 30 20 25 4 28 12 27 2 10 18 26 16 6 9 8 5 13 14 29 7 3 22 32 15 24
Institute

LGC-RT/20/A - Δ^9-THC

Protocol method



LGC complex proprietary method



Ring Trial Conclusions

- CBD and controlled cannabinoid measurements are not straight forward
  - Interferences
  - Robustness
  - Product variance
- Methods developed by December 2020
- Cross government successful international ring trial executed within 8 weeks
- National and international capability for:
  - CBD in foods & cosmetics
  - Controlled cannabinoids (positive bias observed for Δ9-THC but method fit for screening purposes)

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5. MP wrote back to thank us for:

- Copying him in on the letter to the Chair
- Informing him of the role as Government Chemist and the ongoing work regarding CBD
- "….your valuable contributions on this subject"
- Invitation to present to the Home Office Advisory Committee for the Misuse of Drugs Working Group on CBD
- GC inputted into ACMD call for evidence for by providing international ring trial data for Δ9THC, THCV, Δ8THC, CBN & THCA

Acknowledgements

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