Future Plans at the National Institute of Standards and Technology for Hemp Quality Assurance Program and Reference Materials

Walter B. Wilson, Charles A. Barber, Melissa M. Phillips, Catherine A. Rimmer, and Laura J. Wood

Chemical Sciences Division, Material Measurement Laboratory, National Institute of Standards and Technology, Gaithersburg, Maryland 20899, USA

NIST is developing a Hemp QAP to help improve hemp measurements for testing laboratories and product manufacturers, while supporting the development of new hemp and hemp-derived RMs. The initial Hemp Quality Assurance Program (QAP) exercises will focus on the analysis of the highly targeted analytes within the hemp community. Hemp QAP participants will receive information regarding the accuracy and precision of their results, as well as concordance within the community. Detailed study reports and certificates of completion will be provided for participants, and workshops and webinars will be held to discuss results as well as methodological advancements in the area of hemp measurements.

Similarly, NIST has recently established the Health Assessment Measurements Quality Assurance Program (HAMQAP) to identify, understand, and address community-wide measurement challenges for other botanical materials. This program helps to improve measurement accuracy by providing an opportunity for laboratories to assess their in-house measurement performance and to demonstrate an effort to comply with applicable regulations. Standardization programs, proficiency testing, interlaboratory comparisons, and participation in QAPs, in conjunction with the use of reference materials (RMs), are all essential in order to improve the comparability and precision of data over time. The breakdown of participants for the first set of HAMQAP exercises are shown in Figure 1, which may be a good indicator of the participants for a Hemp QAP.

A potential lifecycle for the initial Hemp QAP exercise is illustrated in Figure 2. Once the overall measurement performance within the hemp community has been explored for a plant material, accuracy and precision can be improved through use of RMs, which can be used to validate methods, establish traceability, provide quality control when producing in-house RM, or produce scientific data that can be referred readily to a common base. Hemp QAP will help support the development of characterized RMs that are value assigned for chemical composition, by incorporation of candidate RMs into the studies. NIST has previously produced numerous RMs for chemical composition of foods, dietary supplements, and botanical authenticity, by incorporating these materials into QAPs. The initial exercises of a Hemp QAP and RM development will focus on several targeted analyte groups discussed in detail below for a dried plant material. These materials will also be screen for total yeast, mold, and microbiological contaminants.

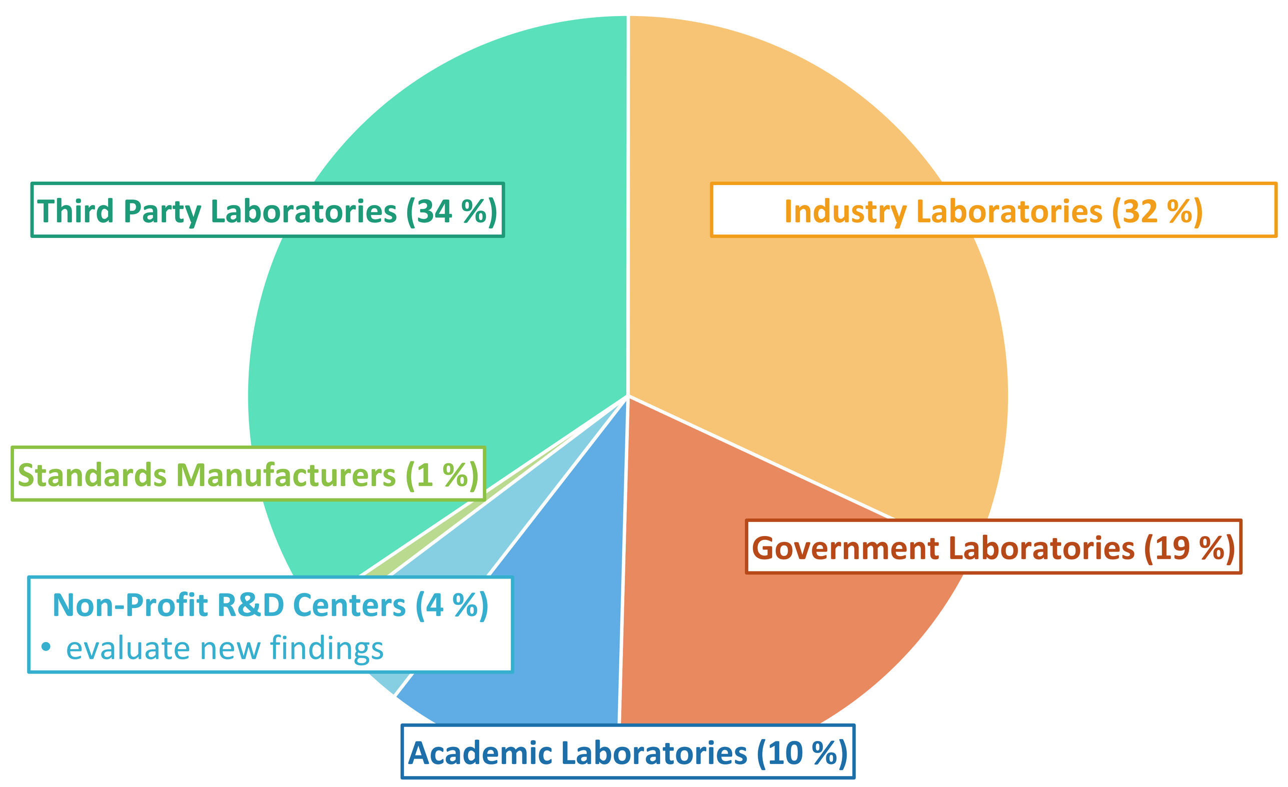


Figure 1: HAMQAP participants breakdown for the first set of exercises.

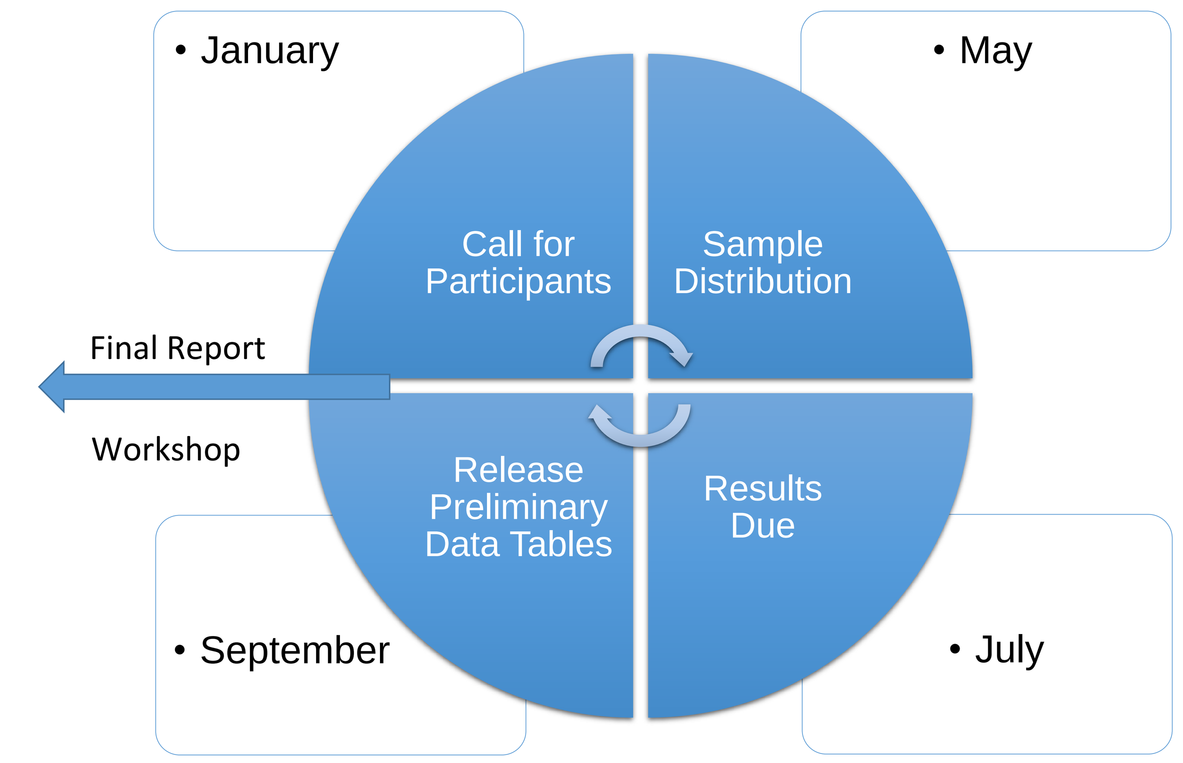


Figure 2: Potential Hemp QAP exercise lifecycle over 12 months.

1. Developing New Capabilities for Hemp at NIST

Δ^9-THC, THCA, Total THC, and Moisture

Hemp was legalized with the passage of the 2018 Farm Bill by removing it from the Schedule 1 controlled substance list making it possible for all analytical laboratories ability to do hemp research with no DEA license requirements. The bill also defined hemp by the Δ^9-THC concentration of not more than 0.3 % on a dry weight basis. However, THCA is the primary component of THC in the cannabis plant, which can be converted into Δ^9-THC through decarboxylation as shown in Figure 3.

A typical packaging label for cannabis will show the percentage of Δ^9-THC, THCA, and total THC. The reported values could be significantly different when determining the "potency" of a cannabis material. Total THC is not calculated through the addition of THC and THCA values because Δ^9-THC has a smaller molecular weight than THCA and conversion of THCA to Δ^9-THC is not always 100 % efficient. The best way to calculate the theoretical maximum percent dry weight value for the total THC is below.

$$\text{Total THC} = (0.877 \times \%\ \text{THCA}) + \%\ \text{THC}$$

NIST plans for all RM or QAP materials (plant, extracts, or finished products) shipped from NIST will not only have a Δ^9-THC concentration ≤ 0.3 %, but a total THC value ≤ 0.3 %. These samples no matter the target analytes of analysis will be accompanied with some form of documentation summarizing the mass fraction, uncertainties with 95 % confidence, and analytical procedure for measuring total THC. Since the true value for total THC will lie within the assigned uncertainty, the upper confidence limit for total THC will be ≤ 0.3 %.

Moisture measurements will play a critical role in assigning values on a dry-mass basis. Currently moisture measurements depend on the requirement of the state. All QAP and RM dried plant materials will have moisture measurements using standard approaches employed at NIST (*i.e.* oven drying, desiccator drying, and/or Karl Fischer).

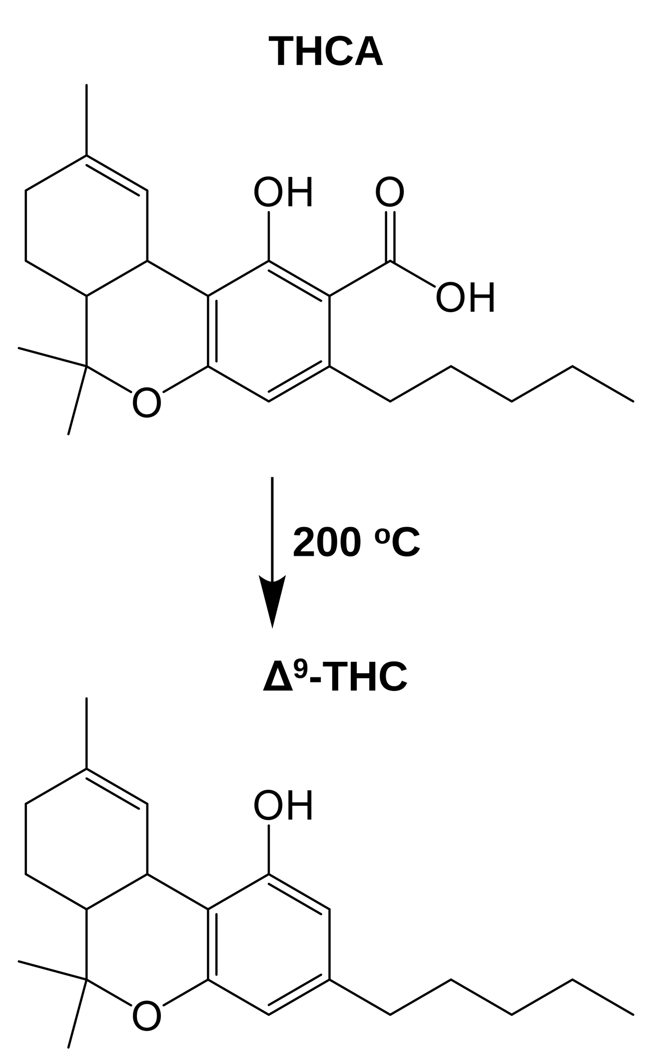


Figure 3: Conversion THC into Δ^9-THC.

Additional Natural and Synthetic Cannabinoids

AOAC currently has a working group developing a Standard Method Performance Requirements (SMPR) document for the quantitation of cannabinoids in hemp plant materials. The proposed SMPR includes the requirement of measuring CBD, CBDA, and CBN in addition to Δ^9-THC and THCA. Nine additional cannabinoids are included as desirable (CBC, CBCA, CBDVA, CBG, CBGA, CBDV, Δ^8-THC, THCV, THCVA), which would allow for any separation method to provide a chromatographic profile of the cannabinoids in any hemp or hemp-derived product.

Preliminary studies have been conducted at NIST looking at the different retention characteristics for the 14 cannabinoids listed in the proposed SMPR as shown in Figure 4. The cannabinoids were separated using a C_{18} column with the dimensions of 150 mm x 4.6 mm; 3 µm average particle diameter. The separation conditions included a 1.0 mL/min flowrate, 15 ºC column temperature, and isocratic elution at 75 % acetonitrile or 79 % methanol (both in 0.1 % formic acid) and water mobile phases. Significant retention difference were observed for multiple cannabinoids.

Synthetic cannabinoids are a concern moving forward as the market grows and changes. Development of generic LC-MS/MS or GC-MS methods for identifying them in real samples would be useful for the industry and addition of their mass spectra to the NIST database.

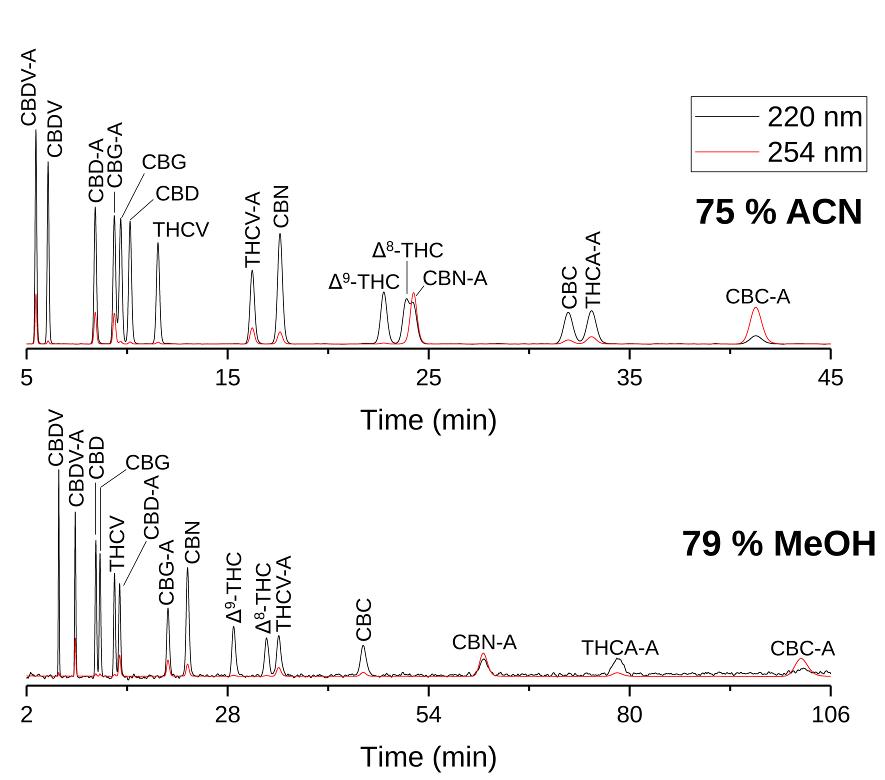


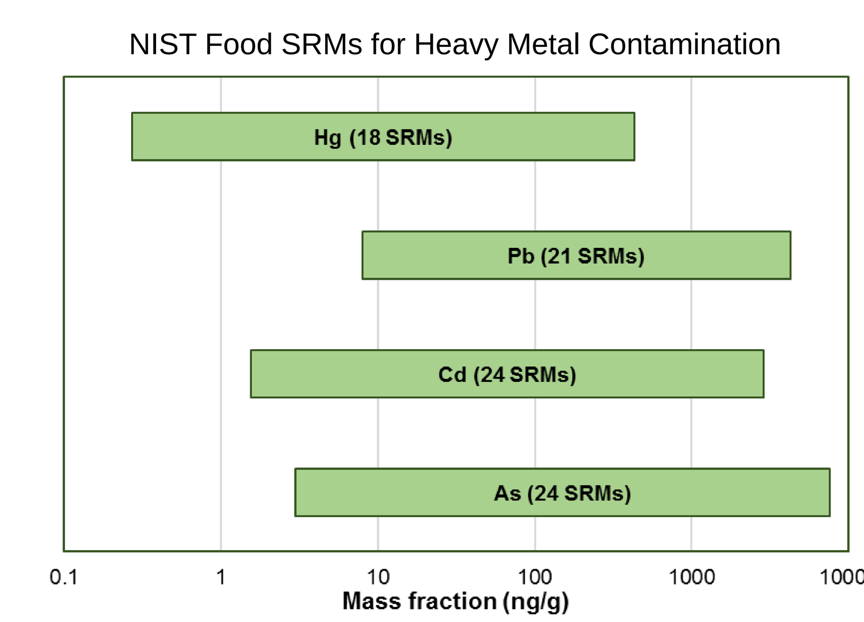
Figure 4: RPLC-UV chromatogram of 15 cannabinoid reference standards.

2. NIST Capabilities to be Extended for Contaminants in Hemp

Toxic Heavy Metals

Heavy metals are one of the most highly targeted contaminants in cannabis materials. Commonly the key metals of importance include cadmium (Cd), arsenic (As), lead (Pb), and mercury (Hg), which fall into the FDA class 1 category. These metals are considered highly toxic because the human body is unable to remove these metals efficiently after exposure. NIST currently has a large number of SRMs with assigned values for these toxic metals as illustrated in Figure 5.

The FDA recommends these four elements be evaluated during the risk assessment for all forms of food and supplements; however, the literature is lacking direct studies on health effects of toxic metals in hemp. NIST is looking to expand past these four metals to also include five additional heavy metals recommend by the FDA in tobacco products: beryllium, chromium, cobalt, nickel, and selenium.



Available materials include grains, meats, and processed foods

NIST Botanical Supplement SRMs with Heavy Metal Values

	SRM 3232 Kelp Powder	SRM 3246 *Ginkgo* Leaves	SRM 3247 Ginkgo Extract	SRM 3248 *Ginkgo* Tablets	SRM 3262 St. John's Wort	SRM 3398 Ginger Rhizome
As	X		X	X	X	X
Cd	X	X	X	X	X	
Hg	X	X	X	X	X	X
Pb	X	X		X	X	X

Figure 5: Some NIST SRMs providing heavy metals values.

Mycotoxins

NIST has developed a new SRM that can be used to identify mycotoxins in corn products that allow analytical scientists to make reliable measurements for these poisonous compounds that are produced by mold.

Mycotoxins are naturally occurring and often form when grains and cereals are stored in areas of high humidity or in rye and wheat crop fields, which can cause economic losses for farmers and food producers if left undetected and allowed to spread.

The assigned mass fraction values are summarized in Figure 6 through measurements made at NIST, FDA, and an interlaboratory study. NIST plans to apply the same analytical approaches developed for the corn measurements to dried hemp plant material at ppb levels.

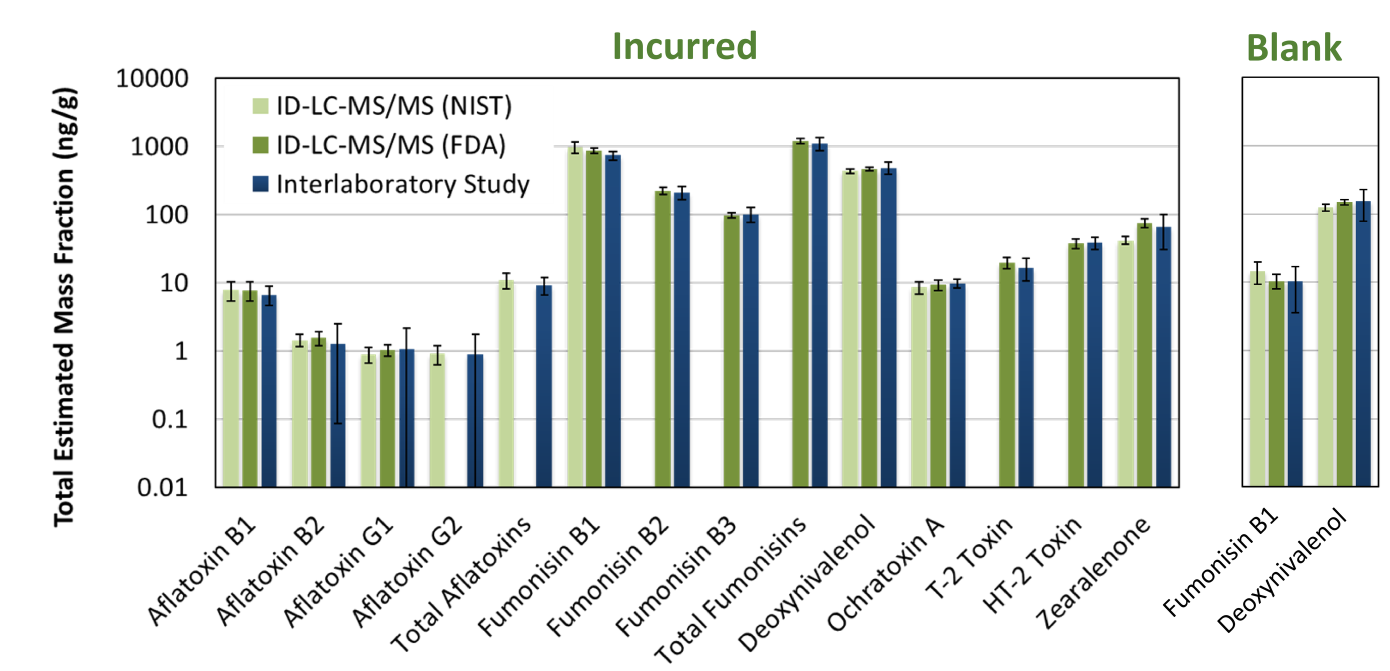


Figure 6: Mass fraction value comparisons for mycotoxins in corn (SRM 1565).

Pesticide Residues

Hemp and marijuana samples obtained from retail shops or dispensaries may be contaminated with pesticides used to eliminate or prevent infestations. Currently, there aren't any federal regulations on pesticide use for cannabis and the laws vary widely from state to state. Pesticides are introduced either by the growers, through contaminated soil, and/or airborne chemical spread from other farms.

NIST has recently started developing analytical methods for measuring pesticides in a variety of plant and food materials. Research has focused on the determination of glyphosate in organic and non-organic oat cereals as illustrated in Figure 7. Low levels of glyphosate were measured in the organic materials.

Multiple screening methods have been developed at NIST to identifying 207 pesticides through the combination of QuEChERS and LC-MS/MS analysis of honey oats cereal, kale, apple sauce, and frozen fruits. This same approach will be utilized for future pesticide analysis of hemp QAP or RM plant materials.

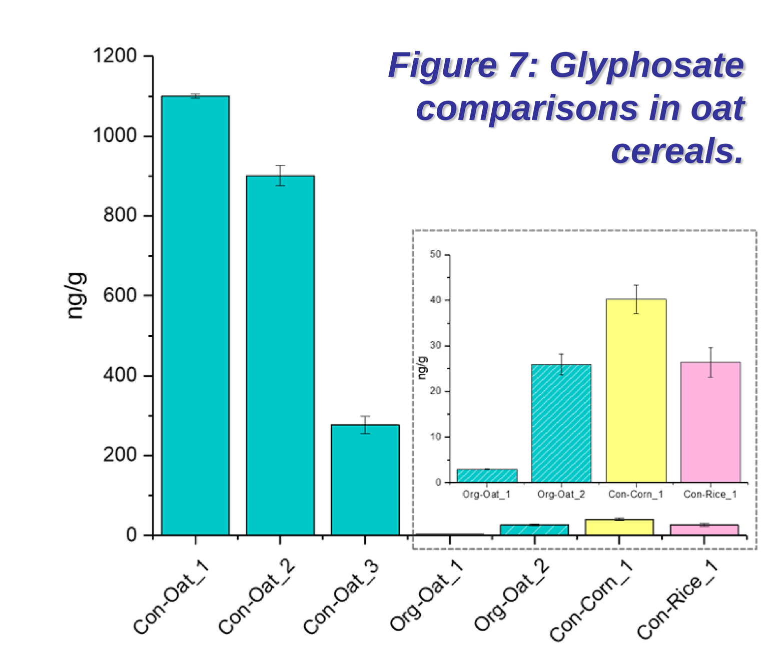


Figure 7: Glyphosate comparisons in oat cereals.