1. **What is the data they are using to support its use in "untreatable" pain?**

   As mentioned in our presentation, this is a list of conditions that was decided by the legislature. We do not know the data used in support of adding or omitting debilitating medical conditions. That being said, chronic, untreatable or intractable pain is not an uncommon qualifying condition across the nation's 30 medical cannabis programs. Additionally, Minnesota has a medical cannabis program that is similar to ours when one compares allowed forms and qualifying conditions. They have done surveys with their physician and patient populations, and assembled the following document based on the findings, which this group may find helpful: Intractable Pain Patients in the Minnesota Medical Cannabis Program

2. **How do you decide which strain of cannabinoid is going to be used in the product since they are vastly different?**

   Our administrative rules prohibit any current or future manufacturer from advertising or marketing strains or varieties of cannabis. Our manufacturer has selected genetic varieties that develop to produce greater amounts of either THC or CBD. Following extraction and refinement, these separate oils are formulated into different ratios of THC:CBD (10:1, 1:2, 1:1 and 1:20) before being formulated into final products. Each ratio is recommended for different therapeutic utility for different conditions.

3. **Could you provide any background regarding why HIV was included as a qualifying debilitating medical condition?**

   As mentioned in our presentation, this is a list of conditions that was decided by the legislature. However, in terms of background for justification, the symptoms of HIV/AIDS typically include weight loss, loss of appetite, and peripheral neuropathy, and the side effects of antiretroviral therapies include nausea, vomiting, loss of appetite and pain. HIV/AIDS is currently a qualifying condition in every state-based medical cannabis program, which is likely due to a "compassionate use" perspective in the potential mitigation of some of these symptoms and side effects.

4. **With the number of different formulations being proposed, what data will be used to demonstrate that CBD or THC is actually absorbed through skin or oral mucosa?**

   I cannot answer the question for "what data will be used" to demonstrate the absorption for a given route of transmission, this will ultimately be up to the physician and patient. However, I can present data that are currently available for these routes of transmission and why they are used. For ingested cannabinoid preparations, the bioavailability for both THC and CBD is only around 6%, although this is variable and dependent on multiple factors. This is largely due to cannabinoids, after ingestion, going through a first-pass metabolism in the liver before being distributed to the body. As both THC and CBD are highly-lipophilic molecules, sublingual or buccal administration has been shown to improve the bioavailability of cannabinoids, although much will still be ingested and go through first-pass metabolism. THC and CBD's highly lipophilic qualities are also applied to the trans-cutaneous route of transmission to avoid first-pass metabolism. The justification for vaporization (not allowed in Iowa) in some medical cannabis programs is also due to bioavailability, which has been shown to be between 30-56%, creating a more fast-acting, titratable dose. Some research behind these pharmacokinetics can be reviewed in the following studies:

   - JAMA – Cannabinoids for Medical Use: A Systematic Review and Meta-analysis

- NIH – Human Cannabinoid Pharmacokinetics

5. How do you envision patients in hospice or long term care facilities gaining access?

Patients who are in long-term care facilities and/or are immobilized will have a primary caregiver. This is a person designated by the patient's healthcare practitioner to purchase and administer medical cannabidiol on the patient's behalf. The primary caregiver goes through the registration process and receives a registration card in a similar process that a patient does. In our program, one patient may have many caregivers, or a caregiver may be responsible for many patients. How this is carried out will be determined by healthcare facility.

6. Does affirmative defense apply to pharmacists?

The affirmative defenses are extended to IDPH, the Iowa Department of Transportation, patients, primary caregivers, health care practitioners, and any authorized agent or employee of a health care practitioner. Currently, there are no affirmative defenses for pharmacists written into our statute. This is likely due to our legislature not designating a role for pharmacists in the program. If there comes a time when this legislation matures and a role were to be created, it is likely that affirmative defenses would be created.

7. What happens to the program if the DEA reschedules cannabis?

While impossible to know, I will answer this as I understand it. There is an important distinction to draw between the upcoming scheduling of Epidiolex, and the scheduling of CBD, CBD extracts, or cannabis in other forms. Although Epidiolex is the first marijuana plant-based drug to pass FDA approval, this does not mean the scheduling of other forms of marijuana or CBD extracts by the DEA are in any way bundled into this. Rescheduling of any kind is a complex and lengthy process. In terms of *cannabis* or *marijuana*, there have been five petitions to reschedule marijuana since the controlled substances act (CSA) went into effect. The first petition (1972) took 22 years before a decision was issued; the second (1995) took six years; and a 2002 petition was not decided until 2011. The most recent petitions (2009 and 2011) were decided in 2016. *Marijuana* or *cannabis* in plant or any form is still a schedule I drug, and is likely to remain and be regulated as such in state-based cannabis programs for the foreseeable future. This situation could be more complex for CBD or CBD extracts, as there are over-the-counter forms and now a pharmaceutical form. However, the DEA recently rejected a challenge of the CSA's definition of marihuana extracts, which is defined to include any extract "containing one or more cannabinoids that has been derived from any plant of the genus Cannabis." The over-the-counter CBD industry recently attempted to challenge the CSA's marijuana extract definition citing the 2014 Farm Bill, but was denied. Without standards and research, it is unlikely to expect the scheduling of CBD as a category to change in the immediate future, or for there to be any type of federal policy avalanche-effect because of it. As the situation stands, we are not preparing for any policy issues to drastically affect our program in the near future.