The following amendments have been made to the original version of the protocol (dated 7 October, 2020).

Version 1.1 (25 November 2020)

- On the title page of the protocol we included the legal entity 11318152 Canada Inc. This was a request from the Study Insurance Broker.
- Appendix 6 Classification of Chronic Pain IASP ICD 11 was developed to further illustrate Subject Inclusion Criteria. The definition of Subject Inclusion Criteria 1. was changed from "Subject ≥ 25 years of age with a diagnosis of chronic non-cancer pain defined as pain lasting or recurring over a period > 3 months (IASP-ICD-11 classification)" to "Subject ≥ 25 years of age with a diagnosis of chronic non-cancer pain defined as pain lasting or recurring over a period > 3 months (IASP-ICD-11 classification, refer to Appendix 6)". Changes were made in several places in the protocol to reflect this change, including in the table of contents (p. 5), the Synopsis (p. 10), Section 6.1 (Subject Inclusion Criteria p. 21), and Appendix 6 (p. 79).
- The ST Discontinuation and Exit Assessment are now two separate assessments. Changes were made in several places in the protocol to reflect this change including in the table of contents (p. 5), the Synopsis (p. 9), in Table 1. (Schedule of Events p. 12), Section 3.1. (Study Design p. 17), in Appendix 4 (ST Discontinuation p. 76) and in Appendix 5 (Exit Assessment p. 78).

Global Registry for the Use of Spectrum Therapeutics Cannabis Products in Subjects with Chronic Pain

Protocol Number:	[710-4502]
Investigational Product(s):	Spectrum Therapeutics Products all formulations: Red, Blue, Yellow, Clear, Orange, Purple, Green
Original Protocol	7 October, 2020
Protocol Amendments	25 Nov, 2020
Development Phase:	Observational Study
Therapeutic Area:	Chronic pain
Sponsor:	Canopy Growth Corporation 1 Hersey Drive Smith Falls K7A 0A8
Legal Entity	11318152 Canada Inc.
Funding Source:	Canopy Growth Corporation
Study Sites:	Canada Germany United Kingdom Australia
Principal Investigator	Dr. Dwight Moulin Email: dwight.moulin@gmail.ca Telephone: 519-685-8661

Confidentiality Statement

SIGNATURES

Sponsor Signature

Signed:  Date: October 19, 2020

Dr. Marcel Bonn-Miller
VP, Human and Animal Research
Canopy Growth Corporation

Investigator Signature

Signed:  Date: October 22, 2020

Dr. Dwight Moulin
Principal Investigator

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SYNOPSIS

Product(s)	Spectrum Therapeutics Products, all formulations: Red, Blue, Yellow, Clear, White, Orange, Purple, Green
Indication:	N/A
Phase:	Real World Evidence
Study Type:	Longitudinal Observational
Sponsor:	Canopy Growth Corporation 1 Hersey Drive Smith Falls K7A 0A8
Protocol Number:	710-4502
Title of Study	Global Registry for the Use of Spectrum Therapeutics Cannabis Products in Subjects with Chronic Pain
Number of sites:	Estimated 50-150 sites
Study Population:	Adults ≥ 25 years of age with chronic non-cancer pain

Purpose and Study Rationale

Chronic pain affects at least 10% of the global population but is often poorly managed, given the variable efficacy of available pharmacological treatments and the limited accessibility of multidisciplinary interventions. The legalization of cannabis in at least 14 countries and the increasing regulatory approval of cannabis preparations and synthetic cannabinoids and analogues have led to a growing interest in the use of medical cannabis products to manage chronic pain. This use is supported by research demonstrating important interactions between cannabinoids and the human endocannabinoid system and pain modulation pathways. While medical cannabis products are increasingly available to practitioners who treat pain, there is little evidence-based guidance for prescribing or titrating these treatments to manage chronic non-cancer pain. This prospective registry aims to assemble real-world data regarding the use of Spectrum Therapeutics (ST) medical cannabis products in subjects with chronic non-cancer pain in countries where these products are commercially available. The registry will also assess treatment outcomes, including pain and related symptoms, global impressions of improvement, and change in concomitant pain medications (opioid use in particular), to better inform the utility of ST products for chronic non-cancer pain management.

Study Objectives

Primary Objective:

- To describe patterns of physician selection of Spectrum Therapeutics (ST) medical cannabis treatment regimen, expressed as average daily dose of THC and CBD (in mg), and mode of administration (ingested or inhaled), in the management of chronic non-cancer pain in countries where these products are commercially available.

Secondary Objectives:

- To describe subject product and dose adjustment (under medical follow-up) over time.
- To assess outcomes of treatment, including pain relief and effects on sleep, daily functioning, and quality of life.
- To assess global impressions of treatment effectiveness as reported by subjects and physicians.
- To assess changes in daily dose of opioids, other medications over time.

Safety Objective:

- To assess the safety and tolerability of ST products in subjects with chronic pain.

Study Design

The present study is a prospective, observational registry designed to generate real-world data on the physician-recommended use of ST products for the management of chronic non-cancer pain in countries where these products are commercially available. The study will enroll 1500 subjects from 50-150 sites in geographic regions of ST product distribution, over a 2-year period. Subjects at each site will be followed for one year to collect data on demographics, chronic pain classification, cannabis experience, treatment goals, concomitant medication(s), ST treatment regimen, clinical assessment, subject-reported outcomes, and safety.

The study includes five physician-verified visits (baseline, 2, 4, 8, and 12 months), and four at-home subject-verified follow-ups (months 1, 3, 6, 10). Physician verified follow-ups can be conducted in person or via telemedicine. Additionally, should there be a need, according to the physician's judgement, there may be other unscheduled visits, either in-clinic, or via telemedicine.

All data will be collected using *REDCap Cloud* data management platform, via online electronic case report forms (eCRFs), and questionnaires. During physician-verified visits, online questionnaires will be completed by both the physician and the subject (in the presence of a physician or study site personnel). At-home subject-verified follow-ups will be conducted via the *REDCap Cloud* online portal accessible by computer, tablet, or smartphone.

The following activities will be completed at the Baseline Visit.

- The subject will receive an explanation of the study purpose and procedures, sign the electronic informed consent form (eICF), physician will review eligibility check list, if female of child-bearing potential, subject will complete a urine pregnancy test.
- Together, physician and subject will create an account on *REDCap Cloud*.
- Together, physician and subject will complete the baseline assessment measuring:
    - Demographics;
    - Chronic pain classification;
    - Cannabis experience;
    - Concomitant medications;
    - Treatment goal;
    - ST treatment regimen;
    - Brief Pain Inventory-Short Form (BPI-SF);
    - Euro Quality of Life Assessment (EQ5D-5L).

- The subject will be scheduled for the first physician-verified follow-up visit approximately 2 months after the initiation of treatment with an ST product.

The following activities will be completed at each physician-verified follow-up visit:

- Physician and subject will discuss the overall treatment regimen.
- Physician will review the subject's online *REDCap Cloud* entries.
- Together, physician and subject will complete the follow-up visit assessment measuring:
    - ST treatment regimen
    - Concomitant medications
    - Clinician Global Impression of Improvement (CGI-I)
    - BPI-SF
    - EQ5D-5L
    - Patient Global Impression of Change (PGI-C)
    - Physician adverse events (AEs) form

The following measures are to be completed by the subject for each at-home follow-up:

- ST treatment regimen
- Additional cannabis consumption
- BPI-SF
- EQ5D-5L
- Patient Global Impression of Change (PGI-C)
- Subject adverse events (AEs) log

In the event of ST treatment discontinuation or study dropout, physicians will be asked to attempt to follow-up with subjects for the completion of the ST Discontinuation assessment and Exit assessment. Based on physician answers to the ST Discontinuation Assessment, subjects will either stay enrolled in the study (e.g., discontinue all cannabis treatment, but continue to be monitor by site physician for chronic pain), or be withdrawn (e.g., unwilling to stay in the study, switched cannabis licensed producer).

A complete schedule of events is provided in **Table 1**.

Safety Monitoring:
Spontaneous AE reporting will be entered in *REDCap Cloud* by the subject during subject follow-ups, using the Subject AE log. Physicians will verify and assess all AEs entered at physician follow-ups, using the Physician AEs form. All serious adverse events will be sent directly to Canopy Growth's Global Pharmacovigilance Department (GPVD) in real-time, where they will be reviewed with respect to country specific regulatory requirements. All non-serious adverse events will be sent in a monthly report to GPVD.

Outcome Assessments:

- The BPI-SF is a 9-item self-report questionnaire that includes 6 pain items (e.g., location, 24-hour worst pain, 24-hour average pain, pain right now); 2 treatment items; and 1 (7 part) pain interference item.
- EQ5D-5L is a 5-category questionnaire (total of 6 questions) assessing mobility, self-care, usual activities, pain/discomfort, anxiety/depression, and overall health on a scale from 0-100 (where 100 denotes the best, and 0 the worst health).
- The PGI-C is a 1-item self-report outcome question that measures a subject's overall impression of improvement during treatment using a 7-point Likert-type scale. The PGI-C shows good performance in subjects with chronic pain and is often more responsive than primary measures of pain intensity.
- The CGI-I is a 1-item clinician-reported outcome question, similar to the PGI-C, that measures a clinician's overall impression of subject improvement in response to treatment using a 7-point Likert-type scale. The CGI-I typically correlates well with the PGI-C.

Duration of Subject Participation and Treatment: Subjects will be followed for one year, unless the subject withdraws early, either independently or in response to physician recommendation. ST treatment will continue for as long as subjects and physicians agree that there is a benefit and treatment is tolerated.

Study Population

Subject Inclusion Criteria:

Subjects must meet all of the following criteria to be eligible for enrollment into the study:

1. Subject ≥ 25 years of age with a diagnosis of chronic non-cancer pain defined as pain lasting or recurring over a period > 3 months (IASP-ICD-11 classification, refer to Appendix 6).
2. Subject is, in the physician's opinion, a candidate for medical cannabis treatment. Candidate status will be determined based on local regulations, common clinical practice, available guidelines and scientific literature, and the physician's expertise or experience with medical cannabis products.
3. Subject received a prescription/authorization for a product in the medical channel of Spectrum Therapeutics.
4. Subject is able to read and understand the informed consent form and complete the study questionnaires.

Subject Exclusion Criteria:

Subjects meeting any of the following criteria will not be eligible for participation in the study:

1. Subject refuses to provide informed consent or participate in any aspect of the study.
2. Subject is pregnant or lactating.
3. Subject has a history of psychosis or schizophrenia (or other significant psychiatric disorder), including among first-degree relatives.
4. Subject has a suspected or confirmed cardiovascular disease.
5. Subject is a liver transplant recipient or has severely compromised liver function.

Endpoints:

Primary endpoints

- Physician selection of Spectrum Therapeutics (ST) medical cannabis treatment regimen and changes over time in:
  (1) average daily dose of THC and CBD (in mg);
  (2) route of administration (inhaled or ingested).

Secondary endpoints

- Subject selection of ST treatment regimen and changes over time in:
  (1) average daily dose of THC and CBD (in mg);
  (2) route of administration (inhaled or ingested).
- Change in BPI-SF responses from baseline.
- Change in EQ5D-5L responses from baseline.
- PGI-C for the target treatment goal.
- CGI-I for the target treatment goal.
- In subjects taking an opioid, changes in opioid use over time (calculated as milligram morphine equivalents [MME]/day).
- Among subjects taking other medication, total daily dose change over time.

Safety endpoint

- Incidence of AEs stratified by product and formulation.

Statistical Methods:

The Sponsor will perform statistical analyses. The Sponsor or designee will extract and analyze descriptive data every 6 months. This will be done to keep sites apprised of study progress. A de-identified summary report will be generated and delivered to all registered site physicians.

The report will indicate:

- The number of physician-collaborators stratified by country.
- The number of subjects enrolled stratified by country.
- Subject demographics, chronic pain classification, and treatment goal.
- Subject concomitant medication use.
- Subject ST treatment regimens.
- Incidence of AEs per individual ST product.

Upon database lock a series of analysis will be conducted to address study objectives. For each analysis, the normality of the data distributions will be ascertained using the Shapiro-Wilk test of normality and Levene's test of equality of error variance. Descriptive statistics (frequencies, means, and standard deviations for normally distributed parametric data; medians and interquartile ranges for nonparametric data) will be used to characterize the sample. Outcome analyses will include a change in ST regimen; a change in reported opioid consumption in MME/day; change in daily dose of other medications, including analgesics, sedatives, and benzodiazepines; change in responses to BPI-SF items and EQ-5DL items; initial PGI-C and changes over time; and initial CGI-I and changes over time. For the safety endpoint, AEs will be tabulated descriptively. Detailed analyses are outlined in the Statistical Analysis Plan.

Number of Subjects (Planned):

Given a continuous enrollment design, the study will include two enrollment milestones over the 2-year study period. Milestone 1, targeted for the end of year 1 will be to recruit 750 subjects. Milestone 2, targeted for the end of year 2 will be to recruit 750 subjects. To enroll a total of up to 1500 subjects. The number of subjects may vary based on the real-life use of ST products. Sites will be recruited from countries where ST products are available: Canada, United Kingdom, Germany, and Australia. Sites from additional countries may be included as ST products are rolled out in those countries and based on site feasibility.

The present study has an observational design that poses low-burden for subjects, as the number and frequency of in-clinic (telemedicine) visits represent those necessary for adequate monitoring of treatment for chronic pain and at-home follow-ups will be completed using a simple online app and take no longer than 15 minutes to complete. On this premise, we did not restrict the sample size based on an estimated minimum required sample. Furthermore, the observational nature of the primary endpoint (daily average dose [in mg] of THC and CBD and mode of administration [inhaled or ingested]), did not permit an a priori power analysis to estimate sample size. A sample size of 1500 subjects is consistent with similar previous observational registry studies.

Table 1. Schedule of Events

	Day 1	Month 1 (+/-7d)	**Month 2** (+/-7d)	Month 3 (+/-7d)	**Month 4** (+/-7d)	Month 6 (+/-7d)	**Month 8** (+/-7d)	Month 10 (+/-7d)	**Month 12** (+/-7d)	Un-scheduled visit
	Physician Baseline Visit	Subject-verified Follow-up 1	**Physician Follow-up 1**	Subject-verified Follow-up 2	**Physician Follow-up 2**	Subject-verified Follow-up 3	**Physician Follow-up 3**	Subject-verified Follow-up 4	**Physician Follow-up 4**	
Electronic Informed consent form (eICF)	X									
Pregnancy Test	X									
Review eligibility criteria check list	X									
Create subject *REDCap Cloud* account	X									
Demographics	X									
Concomitant medications	X		X		X		X		X	X
Chronic Pain Classification	X									
Cannabis experience	X									
Treatment goal	X									
ST treatment regimen	X	X	X	X	X	X	X	X	X	X
Additional cannabis consumption		X		X		X		X		
BPI-SF[1]	X	X	X	X	X	X	X	X	X	X
EQ5D-5L[2]	X	X	X	X	X	X	X	X	X	X
PGI-C		X	X	X	X	X	X	X	X	X
CGI-I			X		X		X		X	X
Subject AE[3] log		X		X		X		X		
Physician AE[3] form			X		X		X		X	X
ST discontinuation assessment										X
Exit assessment										X

Abbreviations: AE, adverse event; BPI-SF, Brief Pain Inventory-Short Form; CGI-I, Clinical Global Impression-Improvement; PGI-C, Patient-Global Impression of Change; eICF, electronic informed consent form; EQ5D-5L-European QoL; ST, Spectrum Therapeutics.

1. The subject-verified visits will only include numeric rating scale pain items from the BPI.
2. EQ5D-5L- QoL (5 category questionnaires to be completed by the subject)
3. AEs recorded by the subject at subject-verified follow-ups will be assessed by the physician at physician verified follow-up.

ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation/Term	Definition
AE	Adverse event
BMI	Body mass index
BPI-SF	Brief Pain Inventory-Short Form
CBD	Cannabidiol
CGI-I	Clinician Global Impression-Improvement
eCRF	Electronic case report form
ECS	Endocannabinoid system
eICF	Electronic informed consent form
EQ5D-5L	Euro Quality of Life (QoL)
GCP	Good Clinical Practice
GPVD	Global Pharmacovigilance Department
IASP	International Association for the Study of Pain
ICF	Informed consent form
ICH	International Council for Harmonization
IME	Important Medical Event List
MME	Milligram morphine equivalents
MSL	Medical science liaison
NRS	Numeric rating scale
PGI-C	Patient Global Impression of Change
SAE	Serious adverse event
SD	Standard deviation
ST	Spectrum Therapeutics

1. BACKGROUND INFORMATION AND STUDY RATIONALE

1.1 Background

Chronic pain, defined by the International Association of Pain (IASP) as pain persisting or recurring for more than three months, refers to a complex and heterogeneous group of disorders that produce significant disability and emotional distress.[1–5] Studies suggest that chronic pain affects at least 10% of the worldwide population, with estimates approaching 20–25% in some regions[6].

According to IASP[27], chronic pain is the "parent code" for 7 other codes that compromise the most common clinically relevant groups of chronic pain conditions (Top-level diagnosis): (1) chronic primary pain; (2) chronic cancer-related pain; (3) chronic post-surgical or post-traumatic pain; (4) chronic neuropathic pain; (5) chronic secondary headache or orofacial pain; (6) chronic secondary visceral pain; and (7) chronic secondary musculoskeletal pain. Within the primary pain syndrome, pain is conceived as a disease or health condition, whereas in secondary pain syndromes, pain is regarded as a symptom.

Given the limited access to physical and psychological interventions for chronic pain[7–9] and the variable efficacy and tolerability of currently available medications[10,11], there is a growing interest in the use of cannabinoids (medical cannabis and cannabis-based medicines) for chronic pain management. The legalization of cannabis in at least 14 countries and regulatory approval of cannabis extract preparations, as well as the emergence of synthetic cannabinoids and analogs, is expected to herald an increase in the number of individuals seeking cannabinoids as a means of pain relief. A recent European Pain Federation position paper provided a series of recommendations surrounding cannabis-based medicines to this effect[12].

Cannabis has a long history of therapeutic use for pain and other indications. Research into the pharmacology of cannabinoids and their mechanisms of action[13] has led to the identification of an endocannabinoid system (ECS) in humans, composed of endogenous cannabinoids, the proteins responsible for their synthesis, release and degradation, their associated metabolites, and cannabinoid receptors[14]. Of more than 120 cannabis-derived phytocannabinoids, the majority of cannabis' effects are attributed to two compounds: delta-9-tetrahydrocannabinol (THC), the main psychoactive cannabinoid in cannabis, and cannabidiol (CBD), a non-euphoric cannabinoid that has been investigated in pre-clinical studies for effects on anxiety, cognition, inflammation, and pain[15,16]. Both THC and CBD have been demonstrated to bind and modulate various receptors within the ECS to mediate their proposed therapeutic effects.

Despite accumulating experimental and clinical evidence both for and against the use of cannabis products in subjects with chronic pain, there are limited guidelines or standards of care to facilitate the safe and effective prescription of cannabinoid formulations by physicians who treat subjects with chronic pain. This study aims to establish a Spectrum Therapeutics (ST) Chronic Pain Registry that will collect descriptive, clinical, and outcome data on the use of ST medical cannabis products in subjects with chronic pain. These real-world data will provide insights regarding physician-recommended treatment regimens, titration, safety, and changes in self-reported pain relief, daily function, and quality of life. Additionally, data generated from the registry will aid in the development of further controlled clinical studies, market access initiatives, educational programs, and future publications.

1.2 Rationale

Primary chronic pain and chronic musculoskeletal pain are the most common reasons people cite for using medical cannabis products [13, 17-20]. Rapid changes in the global regulatory landscape regarding medical use of cannabis and cannabinoids have had a significant impact on health care professionals who currently receive little or no education on medical cannabis[19]. Appropriate knowledge about the use of medical cannabis and evidence to support the development of clinical guidelines is essential for the effective use of medical cannabis by health care professionals. This sentiment parallels requests for the development of research in this area by professionals and the media [20, 21].

2. STUDY OBJECTIVES AND PURPOSE

2.1 Objectives

The overall scope of this research is to collect prospective real-world data on the physician-recommended use of ST products for chronic pain in countries where ST products are commercially available. This effort will yield a data generation platform to meet primary and secondary study objectives and establish a research framework for future efforts.

2.1.1 Primary Objective

- To describe patterns of physician selection of Spectrum Therapeutics (ST) medical cannabis treatment regimen expressed as average daily dose of THC and CBD (in mg), and mode of administration (ingested or inhaled) in the management of chronic non-cancer pain in countries where these products are commercially available.

2.1.2 Secondary Objectives

- To describe subject product and dose adjustment (under medical follow-up) over time.
- To assess outcomes of treatment including pain relief and effects on sleep, daily functioning, and quality of life.
- To assess global impressions of treatment effectiveness as reported by subjects and physicians.
- To assess changes in daily dose of opioids, other medications over time.

2.1.3 Safety Objective

- To assess the safety and tolerability of individual ST products in subjects with chronic pain.

3. STUDY DESIGN

3.1 Description of the Study

The present study is a prospective, observational registry designed to generate real-world data on the physician-recommended use of ST products to manage chronic pain in countries where these products are commercially available. The study will enroll up to 1500 subjects from 50-150 sites in geographic regions of ST product distribution over a two-year period. Physicians will recruit subjects during routine care visits and assess whether subjects with chronic pain are candidates for medical cannabis treatment. Once enrolled, subjects will be followed for 1 year to collect data on demographics, chronic pain classification, cannabis experience, treatment goals, concomitant medication(s), ST treatment regimen, clinical assessment, subject-reported outcomes, and safety.

The study includes five physician-verified visits (baseline, 2, 4, 8, and 12 months), and four at-home subject-verified follow-ups (months 1, 3, 6, 10). Physician verified follow ups can be conducted in person or via telemedicine. Additionally, should there be a need, according to the physician's judgement, there may be other unscheduled visits, either in-clinic, or via telemedicine. All data will be collected using *REDCap Cloud* via online eCRFs. The study time-points were selected based on the typical timeframe of titration in routine care, and adverse event (AE) emergence for the use of cannabis products in new subjects; a majority of titration occurs within the first month of taking a new cannabis product[29]. Visits were also spaced out so that subject retention may be maximized, and treatment adjusted in a timely manner. Later time-points are designed to capture longer-term treatment-related outcomes while screening for AE emergence and medication use changes in the long term.

At the first visit (Day 1), subjects will complete the informed consent. A pregnancy test will be administered to women of childbearing potential, and the site physician or study site personnel will confirm subject eligibility criteria. Following this, the site physician or study site personnel trained in the use of *REDCap Cloud* will assist each subject in creating a *REDCap Cloud* account and completing the baseline assessment (Appendix 1). The first visit (Day 1) will assess important baseline information, including demographics, chronic pain classification, cannabis experience, concomitant medications, treatment goal, and ST treatment regimen. Subjects will complete the Brief Pain Inventory-Short Form (BPI-SF) and Euro- Quality of life Assessment (EQ5DL) at this visit.

At each subsequent physician-verified visit (a total of 4), the site physician or study site personnel will assist with the completion of physician follow-up assessment (Appendix 2) via *REDCap Cloud*, and reassess ST treatment regimen, concomitant medications, effectiveness and tolerability of the ST treatment regimen (including AEs & SAEs). Subjects will complete the BPI-SF, EQ5DL, and Patient Global Impression of Change (PGI-C) and physicians will complete the Clinical Global Impression-Improvement (CGI-I).

Four subject-verified follow-up assessments will be completed by subjects via the *REDCap Cloud* online portal (Appendix 3). Subjects will receive an automated email one week prior and the day of subject-verified follow-up with a reminder to complete the online assessment. The subject-verified online assessment will include questions about their ST treatment regimen, additional cannabis consumption, numeric rating scale (NRS) pain items of the BPI-SF, the EQ5D-5L, and the PGI-C.

Spontaneous AE reporting will be entered in *REDCap Cloud* by the subject during subject follow-up assessments, using the Subject AE log (Appendix 3). Physicians will verify and assess all AEs entered at physician follow-ups, using the Physician AE form (Appendix 2). All serious adverse events will be sent directly to Canopy Growth's Global Pharmacovigilance Department (GPVD) in real-time, where they will be reviewed with respect to country specific regulatory requirements. All non-serious adverse events will be sent in a monthly report to GPVD.

In the event of ST treatment discontinuation, or study dropout, physicians will be asked to follow-up with subjects to complete the ST Discontinuation Assessment and Exit assessment (Appendix 4). Based on physician answers to ST Discontinuation Assessment , subjects will either stay enrolled in the study (e.g., discontinue all cannabis treatment, but continue to be monitored by site physician for chronic pain), or be withdrawn (e.g., unwilling to stay in the study, switched cannabis licensed producer).

A complete schedule of events is provided in **Table 1**.

4. STUDY MEDICATION

For the purposes of this study, subjects enrolled will have been prescribed/authorized Spectrum Therapeutics products that are commercially available in participating countries. It is important to note that product availability varies from country to country. No country except Canada, has access to the full ST medical portfolio (e.g., only flowers are available in Germany).

The full repertoire of Spectrum Therapeutics products is outlined here (see Figure 1). It encompasses six "colors" (order from Red to Yellow follows the descending THC:CBD ratio), and five types of formulations: soft gels, spray*, oil, flowers and vapes). Refer to webpage for the most up to date products available per country *https://www.spectrumtherapeutics.com/canada/en/patients/products.*

Figure 1. Repertoire of Spectrum Therapeutics Products.

Cannabinoid Content for Spectrum Therapeutics Products

Spectrum Product	Percentage of THC & CBD per gram of weight **Dried flower (%)**	Milligram of THC & CBD per milliliter of **Oil (mg/ml)**	Milligram of THC & CBD per **Soft gel (mg)**
Red	(17-23) THC : (< 0.7) CBD	(26.3) THC : (<1) CBD	(2.5-10) THC : (<1) CBD
Orange	(10-14) THC : (<1) CBD	NA	NA
Purple	(8-11) THC : < (0.7) CBD	NA	NA
Blue	(6-10) THC : (8-11) CBD	(10) THC: (12-15) CBD	(2.5 – 10) THC : (1.75-15) CBD
Green	(4-7) THC: (7-10) CBD	NA	NA
Yellow	(<1) THC : (10-14) CBD	(<1) THC : (20) CBD	(<1) THC: (5-20) CBD

*Spray formulation is the most recent addition to the formulations and not yet featured on the web site.

4.1 Study Medication Prescribing/Authorization

Medical cannabis is accessible to subjects via different authorization or prescription pathways, in different regional jurisdictions. Authorization and prescription are the two most common pathways.

In Canada, Spectrum Therapeutics products are authorized via the physician specifying the amount (in grams) of THC and/or CBD, and the subject is free to choose the product, licensed producer, and formulation on their own. Likewise, subjects have the freedom to switch from one product or producer to another, at will.

In other countries, such as Germany, medical cannabis products are prescribed, and physicians are specific in this process regarding parameters such as the licensed producer, mode of administration, and cannabinoid content (THC:CBD).

This protocol does not assign a specific intervention. The prescription of medical cannabis is decided by the subject and his or her physician prior to enrolling the subject in the study. The principal investigator has no control over the prescribing/authorization or administration of the cannabis product.

4.2 Study Medication: Cannabinoid Content Calculation

On entering study medication information into *REDCap Cloud*, the preprogrammed algorithm will calculate the intake amount of mgs of THC and CBD for all formulations, and whether it was inhaled or ingested. Only limited data exist on the plasma concentration of circulating cannabinoids and their metabolites resulting from inhalation of cannabis products. It is known that factors influencing this include, but are not limited to, pattern of smoking or vaping (length of inhalation), as well as the flower combustion temperature. It is possible that these data may be calculated in retrospect (unlike other formulations that will allow for real time mg calculation), if more structured studies are conducted to evaluate the cannabinoid intake from smoked and/or vaped products, from different flower varieties.

4.3 Study Medication Safety Information

Cannabis and cannabinoids are generally considered to be well-tolerated, although there is a large degree of individual difference in the side effects seen. A review of medical cannabis trials found that 96.6% of side effects were not serious, with the most common side effects of acute use being[22]:

- Somnolence
- Dizziness
- Drowsiness
- Fatigue
- Tachycardia (increased resting heart rate)
- Temporary impairment of sensation and body functions
- Intoxication or feeling “high”
- Nausea
- Vomiting
- Cough
- Abdominal Pain

Withdrawal symptoms from chronic use of cannabis can occur, usually within 1-2 days following discontinuation. The most common withdrawal symptoms include irritability, anxiety, sleep difficulties, craving, headache, restlessness, and anger or aggression, which usually resolve within 1-2 weeks.

5. RECRUITMENT

5.1 Site Eligibility

Potential sites will be identified by Spectrum Therapeutics regional medical teams (ST MSL), based on feasibility criteria. Sites expressing interest in study participation will undergo an extensive feasibility evaluation. All sites will be required to satisfy the following eligibility criteria:

1. Site physician profile (pain specialist, rheumatologist, neurologist, general practitioner);
2. Site must recruit a minimum of five new chronic non-cancer pain subjects per month, or large chronic non-cancer pain database willing to start subjects on Spectrum Therapeutics products;
3. Previous experience with observational or clinical studies (has been a site, or enrolled subjects in a registry);
4. Access to, willing to participate in, an ethics review;
5. Minimum structure (required SOPs, internet access, *REDCap cloud* support) and human resources (study site personnel);
6. Interest in participating in Real World Data collection;
7. Experience with authorizing/prescribing medical cannabis.

To ensure a consistent approach to the subjects and the study, all participating site physicians will be required to complete ICH GCP training (unless already in possession of ICH GCP certificate).

Suggested resource**:** *https://about.citiprogram.org/en/series/good-clinical-practice-gcp/*

Sites who risk ineligibility for insufficient enrollment or compliance will be contacted by the Sponsor for possible remedial action.

5.2 Investigator Training

After completing the feasibility evaluation, and upon attaining site-specific ethics approval, and ICH GCP certificate, site physicians and any study site personnel, will attend a live Investigator training webinar, or follow a recording of a live webinar. A certificate of attendance will be issued upon (1) completion of the training modules and (2) successful passing of a training-focused quiz. Investigator training will be available in the native language of the site physician. Completion of the training is required prior to enrolling subjects. The investigator training objectives will include the following.

1. Overview of medical cannabis in chronic pain.
2. Overview on Real World Evidence and research methods.
3. Overview of the registry Protocol, and other study documents.
4. Spectrum Therapeutics Safety training (common AEs, contraindications, and information about local regulatory reporting requirements).
5. Overview of the Investigator Communication Platform.
6. Overview of *REDCap Cloud* data management system.

On-site support from the ST MSL team will be continuously available to sites throughout the study.

6. SUBJECT SELECTION AND WITHDRAWAL CRITERIA

6.1 Subject Inclusion Criteria

Subject eligibility will be assessed after subjects have signed and dated the eICF. Subjects must meet all of the following criteria to be eligible for enrollment into the study:

1. Subject is ≥ 25 years of age with a diagnosis of chronic non-cancer pain defined as pain lasting or recurring over a period > 3 months (IASP-ICD-11 classification[27], refer to Appendix 6).
2. Subject is, in the physician's opinion, a candidate for medical cannabis. Candidate status will be determined based on local regulation, common clinical practice, available guidelines and scientific literature, and the physician's expertise or experience with medical cannabis products.
3. Subject received a prescription/authorization for a product in the medical channel of Spectrum Therapeutics.
4. Subject is able to read and understand the informed consent form and complete the study questionnaires.

6.2 Subject Exclusion Criteria

Subjects meeting any of the following criteria will not be eligible for participation in the study:

1. Subject refuses to provide informed consent or participate in any aspect of the study.
2. Subject is pregnant or lactating.
3. Subject has a history of psychosis or schizophrenia (or other significant psychiatric disorder), including among first-degree relatives.
4. Subject has a suspected or confirmed cardiovascular disease.
5. Subject is a liver transplant recipient or with severely compromised liver function.

6.3 Subject Withdrawal from Study Participation

Subjects are free to withdraw from the study at any time. Subjects who start taking medical cannabis from another licensed producer or withdraw consent for study participation will be contacted by the site physician or study site personal to complete an Exit assessment as soon as possible.

Subjects that have received ST products and started using them for treatment of chronic pain, will be entered in the data analysis population, unless they have withdrawn consent together with withdrawing from the study. This is described in more detail, in the Statistical Analysis Plan.

The site physician, by joining the study, confirms commitment to subject retention through coaching, counseling, and education.

The site physician may withdraw a subject from the study in the following circumstances:

- Subject experiences a serious adverse event (SAE) or other safety concerns.
- Subject does not benefit from ST product treatment.
- Subject meets any exclusion criteria.
- Noncompliance with the study protocol.
- Administrative reasons or study termination (e.g., Sponsor decision).
- Other factors determined by the physician to affect the eligibility of subjects to continue.

A record of the reason for withdrawal will be maintained for reporting and publication. Subjects who are withdrawn or removed from the study will be replaced if the study is still in enrollment.

7. OUTCOME ASSESSMENTS

7.1 Study Endpoints

Primary endpoints

- Physician selection of Spectrum Therapeutics (ST) medical cannabis treatment regimen and changes over time in:
  (1) average daily dose of THC and CBD (in mg);
  (2) route of administration (inhaled or ingested).

Secondary endpoints

- Subject selection of ST treatment regimen and changes over time in:
  (1) average daily dose of THC and CBD (in mg);
  (2) route of administration (inhaled or ingested).
- Change in BPI-SF responses from baseline.
- Change in EQ5D-5L responses from baseline.
- PGI-C for the target treatment goal.
- CGI-I for the target treatment goal.
- In subjects taking an opioid, changes in opioid use over time (calculated as milligram morphine equivalents [MME]/day).
- Among subjects taking other medication, total daily dose change over time.

Safety endpoint

- Incidence of AEs stratified by product and formulation.

7.2 Study Assessments

7.2.1 EQ5D-5L- Euro QoL

EQ5D-5L is a 5-category questionnaire (with a total of 6 questions) assessing mobility, self-care, usual activities, pain/discomfort, anxiety/depression, and overall health on a scale from 0-100 (where 100 denotes the best, and 0 the worst health)[28].

7.2.2 BPI-SF

The BPI-SF is a 9-item self-report questionnaire that is quickly and easily administered to subjects with chronic pain. The questionnaire includes 6 pain items that assess the spatial and temporal characteristics of pain (e.g., location, 24-hour worst pain, 24-hour average pain, pain right now); 2 items that ask about current treatments assumed for chronic pain and pain relief; and 1 pain interference item (with parts A–G) were respondents rate the level of interference of pain with general activity, mood, walking ability, normal work, social relations, sleep, and enjoyment of life over the past 24 hours[24].

7.2.3 PGI-C

The PGI-C is a simple 1-item self-report outcome measure that assesses a subject's overall treatment satisfaction using a 7-point Likert-type scale. The PGI-C shows good performance and high responsiveness in subjects with chronic pain and is often more responsive than primary measures of pain intensity, possibly because the PGI-C captures additional elements of the analgesic response such as physical and psychological functioning[25].

7.2.4 CGI-I

The CGI-I is a simple 1-item clinician-reported outcome measure, similar to the PGI-C, that assesses a clinician's overall impression of subject improvement in response to treatment using a 7-point Likert-type scale. Although frequently used in clinical trials focused on mental disorders, the CGI has also been evaluated in a context of chronic pain and correlates well with subject responses to the PGI-C[26].

7.2.5 Determination of Opioid Consumption

Physicians will confirm subjects who take an opioid at baseline or who start an opioid during the study, and will be asked to report the opioid type and MME, so that opioid consumption (and any opioid-sparing effect of the ST treatment regimen) can be examined over time.

7.2.6 Other Concomitant Medications

Physicians will confirm subjects who take any non-opioid concomitant medication for pain at baseline, or who start it during the study, and will be asked to report the medication type. The following medication categories have been identified as common medication classes taken by chronic pain patients: Nonsteroidal Anti-inflammatory Drugs (NSAIDs) and Acetaminophen, Antidepressants, Anticonvulsants, Benzodiazepines and Muscle Relaxants. Physicians will be asked to report the medication type and total daily dose, and any changes throughout the study.

7.2.7 AEs/SAEs

All enrolled subjects and site physicians will receive guidance on AE reporting during the investigator training. Spontaneous AE reporting will be entered in *REDCap Cloud* by the subject, during at-home follow-up (subject to verification by physician at physician-verified follow-up). Physicians will classify each AE by seriousness, severity and inferred relation to the study product in the Physician AE form as described below. The GPVD will also review all SAEs with respect to applicable regulatory requirements.

7.2.7.1 AE Definition

An AE is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have a causal relation with treatment. An AE can therefore be any unfavorable and unintended sign, symptom, psychological effect, or disease associated with the use of a medicinal product, whether or not related to the medicinal product.

7.2.7.2 SAE Definition

An AE will be considered serious if it results in 1 or more of the following outcomes:

- Death
- Life-threatening (i.e., at immediate risk of death)
- Subject in-subject hospitalization or prolongation of existing hospitalization
- Persistent or significant disability/incapacity
- Congenital anomaly/birth defect
- Any other AE that the Investigator or company judges to be serious or which is defined as serious by the local regulatory agency.

Important AEs that may not result in death, be life threatening, or that do not require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject or may necessitate medical or surgical intervention to prevent one of the outcomes listed in the definition above. For this registry, the Important Medical Event (IME) list will be used as a reference for the assessment of medically significant adverse events[30].

7.2.7.3 AE Severity

The physician will assess the severity of all AEs reported in eCRFs as mild, moderate, or severe. For consistency, these intensity grades have been defined as follows:

Mild: An event that is usually transient and may require only minimal treatment or therapeutic intervention. The event does not generally interfere with usual activities of daily living.

Moderate: An event that is alleviated with additional specific therapeutic intervention. The event interferes with usual activities of daily living and may cause discomfort but poses no significant or permanent risk of harm to the subject.

Severe: An event that requires intensive therapeutic intervention. The event interrupts usual activities of daily living or significantly affects clinical status.

7.2.7.4 Relationship of AEs to Study Products

The physician will assess the relation of each AE/SAE to the study product after careful consideration and in accordance with the following guidelines:

Definitely related: The AE/SAE is clearly related to the study product (an alternative cause is unlikely).

Probably related: The connection to the study product can be made with a high degree of certainty. This causal relation is assigned when the AE/SAE meets the following criteria:

- Follows a reasonable temporal sequence from administration of the study product.
- Cannot be reasonably explained by the known characteristics of the subject's clinical state, environmental or toxic factors, or other modes of therapy administered to the subject.
- Follows a known pattern of response to the study product.
- Reappears upon subsequent challenge with the study product.

Possibly related: The connection to the study product appears unlikely but cannot be ruled out with certainty. This causal relation is assigned when the AE/SAE meets the following criteria:

- Follows a reasonable temporal sequence from administration of the study product.
- May have been produced by the subject's clinical state, environmental or toxic factors, or other modes of therapy administered to the subject.
- Follows a pattern of response to the study product.

Unlikely related: The AE/SAE is unlikely related to the study product when the AE or SAE meets the following criteria:

- Does not follow a reasonable temporal sequence from administration of the study product.
- May readily have been produced by the subject's clinical state, environmental or toxic factors, or other modes of therapy administered to the subject.
- Does not follow a known pattern of response to the study product.
- Does not reappear or worsen when the study product is re-administered.

Not related: The AE/SAE is judged to be clearly and incontrovertibly due only to a cause other than the study product (e.g., disease, environment, etc.) and does not meet the criteria for a relation with the study product.

8. DATA HANDLING AND RECORD KEEPING

8.1 Data Collection

Data collection will be achieved through a combination of subject and physician reporting with the aid of automated reminders and MSL contact. All data and study-specific forms (including eICF and eCRF forms), will be centralized electronically via *REDCap* (Research Electronic Data Capture Software) *Cloud*. A pdf copy of the ICF will be emailed to subjects for their own records. Access to *REDCap Cloud* will be password-protected and all subjects and physicians will be required to register with a unique username and password.

Physicians will be trained on use of *REDCap Cloud* during Investigator training and ensure that subjects understand and are able to use *REDCap Cloud* software. *REDCap Cloud* is accessible by computer, tablet, or smartphone. Subjects who elect to complete at-home follow-up assessments online will receive an automated email 1 week prior and the day of at-home follow-up with a reminder to complete the questionnaire.

8.2 Data Management

The *REDCap Cloud* system uses a variety of mechanisms for checking data at the time of entry including skip logic, range checks, and data type checks. Upon receipt of new data, the personnel at the Methods Center will query all missing, implausible, or inconsistent data. Study site personnel will be able to conduct a review of open queries in the system and will be trained/required to respond promptly.

8.3 Data Monitoring

Data will be monitored by the Sponsor consistent with International Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines. Source data verification will be performed remotely on 10% of study sites. Continuous, real-time monitoring of data quality and completeness will be performed remotely by the Sponsor. The registry project management team will periodically review site compliance (completion of scheduled visits and questionnaires), send reminders for missed at-home subject follow-up questionnaires, and guarantee that all efforts are made to contact subjects who discontinue the study or ST treatment prior to 1-year follow-up. Issues with data quality or completeness will be addressed on a case-by-case basis and, if necessary, brought to the attention of the Sponsor when requiring remedial action (e.g., retraining of a site).

8.4 Record Retention

Research data in electronic form will be stored and managed in a secure manner in accordance with applicable federal regulations and guidelines and according to institutional policies and practices. Further, any hard copy documents containing subject data will be stored in secure document containers (file cabinets, lockers, drawers, etc.) in accordance with standard document management practices. At all times, only listed key personnel specifically designated and authorized by the Sponsor shall have access to any research related documents, including electronic data. All such personnel will be properly trained and supervised regarding the management and handling of confidential materials. The Sponsor assumes full responsibility for such training. Site physicians will only have authorization to access data from their respective sites.

8.5 Database Access

The database resulting from this registry is the sole property of Canopy Growth and will only be used for research purposes. During the study, the *REDCap Cloud* database will be accessible to the Sponsor by username and password for the sole purpose of generating summary reports. All forms of data

dissemination will require prior approval from the Sponsor as specified in the Scientific Committee agreement. Site physicians will only have access to their subject's data during the study, but are not permitted to analyze their data or disseminate the results publicly. Site physicians will not have access to the full database; however, a formal request for specific analyses of the entire database can be submitted to the Scientific Committee. Not all requests will be approved.

9. STATISTICAL METHODS

9.1 Statistical overview

The Sponsor will perform statistical analyses. The Sponsor or designee will extract and analyze descriptive data every 6 months. This will be done to keep sites apprised of study progress. A de-identified summary report will be generated and delivered to all registered site physicians.

The report will indicate:

- The number of physician-collaborators stratified by country.
- The number of subjects enrolled stratified by country.
- Subject demographics, chronic pain classification, and treatment goal.
- Subject concomitant medication use.
- Subject ST treatment regimens.
- Incidence of AEs per individual ST product.

Upon database lock a series of analysis will be conducted to address study objectives. For each analysis, the normality of the data distributions will be ascertained using the Shapiro-Wilk test of normality and Levene's test of equality of error variance. Descriptive statistics (frequencies, means, and standard deviations for normally distributed parametric data; medians and interquartile ranges for nonparametric data) will be used to characterize the sample. Outcome analyses will include a change in ST regimen; a change in reported opioid consumption in MME/day; change in daily dose of other medications, including analgesics, sedatives, and benzodiazepines; change in responses to BPI-SF items and EQ-5DL items; initial PGI-C and changes over time; and initial CGI-I and changes over time. For the safety endpoint, AEs will be tabulated descriptively. Detailed analyses are outlined in the Statistical Analysis Plan.

9.2 Sample Size

This study will include as many eligible subjects as are willing to participate; however, site criteria must be met.

Given a continuous enrollment design, the study will include two enrollment milestones over the 2-year study period. Milestone 1, at the end of year 1 will be to recruit 750 subjects. Milestone 2, at the end of year 2, will be recruit 750 subjects. Together, recruitment milestones result in enrolling a total of up to 1500 subjects.

The number of subjects may vary based on the real-life use of ST products. Sites will be recruited from countries where ST products are available: Canada, United Kingdom, Germany, and Australia. Sites from additional countries may be included as ST products become available in those countries.

The present study has an observational design that poses low-burden for subjects, as the number and frequency of in-clinic (telemedicine) visits represent those necessary for adequate monitoring of treatment for chronic pain and at-home follow-ups will be completed using a simple online app and take no longer than 15 minutes to complete. On this premise, we did not restrict the sample size based on an estimated minimum required sample. Furthermore, the observational nature of the primary endpoint (daily average dose [in mg] of THC and CBD and mode of administration [inhaled or ingested]), did not permit a statistical calculation of a sample size. A sample size of up to 1500 subjects is consistent with similar previous observational registry studies.

9.3 Handling of Dropouts, Missing Data

For descriptive summaries of data, there will be no imputation for missing data, unless otherwise stated. All data collected prior to a subject withdrawing will be listed and included in data summaries.

For analyses involving linear mixed effects modeling, data points that are missing due to participant dropout will be handled assuming that data are missing at random (MAR) conditional on observed information, which is less restrictive than missing completely at random assumed in fixed effects analyses such as ANCOVA. In this procedure, all available cases, including those with missing information, will be included in the analyses using full information maximum likelihood estimation. This procedure increases power and reduces bias in parameter estimation.

9.4 Statistical Software

Data manipulation, tabulation of descriptive statistics, calculation of inferential statistics, and graphical representations will be performed using R (version 4.0 or higher)[31] or the SuperMix statistical software. Mixed effects models of continuous outcomes will be conducted using the nlme[32] and/or lme4[33] packages, mixed effects models of ordinal outcomes with the mixor[34] or ordinal[35] package, mixed effects models of binomial outcomes using the lme4 package[33], and mixed effects hurdle regression models with the GLMMadaptive package[36].

If the use of other software is warranted, the final clinical study report will detail what software was used and for what purposes.

10. ETHICS

10.1 Ethical Conduct of the Study

The study will be conducted consistent with consensus ethics principles derived from international ethics guidelines including the ICH GCP, the Declaration of Helsinki, and applicable local regulatory requirements and laws. The registry will only launch after receiving ethical approval from the Canadian SHIELD ethics review board and approval will be renewed on a yearly basis.

Any site that joins the registry will provide additional ethics approval as required by their local regulatory bodies as part of the feasibility evaluation. Canopy Growth will review all outside ethics approvals and only sites with ethical approval will receive a contract and invitation to the investigator training.

10.2 Subject Information and Consent

Informed consent will be obtained prior to the subject participation in any study activities. Prior to obtaining consent, the site physician will ensure that:

- The potential subject has had a discussion with an individual knowledgeable about the research, including the nature and objectives of the study and possible risks associated with participation.
- The potential subject is given a copy of written material (e.g., consent documents, Spectrum Therapeutics leaflet) that has received prior approval by the appropriate ethics committee(s) and meets local regulatory and legal requirements.
- The potential subject has ample opportunity to ask questions about the study.
- An assessment of capacity has taken place. For consent to be ethical and lawfully valid, subjects in this study must be capable of providing informed consent for their participation. A capable person will:
    - Understand the purpose and nature of the research.
    - Understand what the research involves, its benefits (or lack of benefits), risks, and burdens.
    - Understand how their interests and privacy are protected.
    - Understand the alternatives to participation.
    - Be able to retain the information long enough to make an effective decision.
    - Be able to make a free choice.
    - Be capable of making this particular decision at the time it needs to be made.

11. STUDY TERMINATION

The Sponsor reserves the right to terminate the participation of either an individual site or the study at any time, for any reason, including, but not limited to, the following:

- The information on the product leads to doubt as to the benefit/risk ratio.
- Recommendation of the Scientific Committee.
- Subject enrollment is unsatisfactory.
- Noncompliance of the site physician, delegated staff with any provision of the study protocol, and breach of the applicable laws and regulations.

As directed by the Sponsor, site physicians will be notified and required to inform local ethics committees and all study subjects of study termination.

Local ethics committees or regulatory authorities may also decide to stop the study, part of the study, or a study site at any time.

12. PUBLICATION POLICY

The information obtained during the conduct of this study is considered confidential. It may be used by, or on behalf of the Sponsor for regulatory purposes as well as for the general development of ST medical cannabis products. All information supplied by the Sponsor in connection with this study shall remain the sole property of the Sponsor and is to be considered confidential information.

The site physicians will not disseminate any publication or release pertaining to the study and/or results of the study without the Sponsor's express written consent; the Sponsor will not unreasonably withhold its approval. For example, withholding approval for publication will be deemed unreasonable if such a decision is based exclusively on the fact that the results of the study are negative or equivocal. In contrast, withholding approval will be deemed reasonable if the validity of the study methodology or results are in question. Different parts of the study may be published separately.

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14. APPENDICES

Appendix 1- PHYSICIAN-VERIFIED BASELINE ASSESSMENT

Baseline Interview

Invite Confirmation

Before continuing with this form, please ensure you have invited the patient to create their own account with RedCapCloud.

As a reminder, this is done by clicking the three horizontal lines beside their 'Subject Number' in the table found in the 'Consent' section of 'Subjects'.

Please use an email address the patient has access to.

Has an invite already been sent to the patient's email?

- ◯ Yes
- ◯ No

Demographics

Date of clinic visit (enrollment into registry)

_____
(YYYY-MM-DD)

Country of residence

- ◯ Australia
- ◯ Canada
- ◯ Germany
- ◯ United Kingdom

Province or Territory of residence

- ◯ Alberta
- ◯ British Columbia
- ◯ Manitoba
- ◯ New Brunswick
- ◯ Newfoundland & Labrador
- ◯ Northwest Territories
- ◯ Nova Scotia
- ◯ Nunavut
- ◯ Ontario
- ◯ Prince Edward Island
- ◯ Quebec
- ◯ Saskatchewan
- ◯ Yukon

State of residence

- ◯ Baden-Württemberg
- ◯ Bavaria
- ◯ Berlin
- ◯ Brandenburg
- ◯ Bremen
- ◯ Hamburg
- ◯ Hesse
- ◯ Lower Saxony
- ◯ Mecklenburg-Vorpommern
- ◯ North Rhine- Westphalia
- ◯ Rhineland-Palatinate
- ◯ Saarland
- ◯ Saxony
- ◯ Saxony-Anhalt
- ◯ Schleswig-Holstein
- ◯ Thuringia

State of residence

- ◯ New South Wales
- ◯ Queensland
- ◯ South Australia
- ◯ Tasmania
- ◯ Victoria
- ◯ Western Australia

Age at date of enrollment _____

Sex assigned at birth

- ◯ Female
- ◯ Male
- ◯ Prefer not to answer

Gender identity

- ◯ Female
- ◯ Male
- ◯ Transgender
- ◯ Gender non-conforming
- ◯ Prefer not to answer

Racial identity

- ◯ Aboriginal (e.g. Inuit)
- ◯ Arab / West Asian (e.g. Armenian)
- ◯ Black (e.g. African)
- ◯ East Asian (e.g. Chinese)
- ◯ Latin American (e.g. Brazilian)
- ◯ South Asian (e.g. Indian)
- ◯ Southeast Asian (e.g. Burmese)
- ◯ White (e.g. Caucasian)
- ◯ Prefer not to answer

Current employment status

- ◯ Full-time
- ◯ Part-time (unrelated to medical status)
- ◯ Part-time / Reduced Hours (due to medical status)
- ◯ Student
- ◯ Short-term disability (3 months or less)
- ◯ Long-term disability (more than 3 months)
- ◯ Retired
- ◯ Unemployed (unrelated to medical status)
- ◯ Unemployed (due to medical status)

Length of short-term disability (in months) _____

Length of long-term disability (in months) _____

BMI

Patient's current height (cm) _____

Patient's current weight (kg) _____

Patient's calculated BMI _____

Chronic Pain Classification

Patients classification of chronic pain (Top Level diagnosis)	◯ Chronic Primary Pain ◯ Chronic Post-surgical / Post-traumatic Pain ◯ Chronic Neuropathic Pain ◯ Chronic Secondary Headache/Orofacial Pain (e.g. sinusitis, dental abscess, temporomandibular myofascial pain syndrome)) ◯ Chronic Secondary Visceral Pain (e.g. renal colic, biliary colic) ◯ Chronic Secondary Musculoskeletal Pain (e. g. arthritis, osteoporosis, scoliosis, etc) ◯ Chronic Cancer-Related Pain
Chronic primary pain (1st Level diagnosis)	◯ Chronic Widespread Pain ◯ Complex Regional Pain Syndrome ◯ Chronic Primary Headache or Orofacial Pain ◯ Chronic Primary Visceral Pain ◯ Chronic Primary Musculoskeletal Pain
Chronic neuropathic pain (1st Level diagnosis)	◯ Chronic Central Neuropathic Pain (i.e. nociplastic pain) ◯ Chronic Peripheral Neuropathic Pain
Type of chronic peripheral neuropathic pain (2nd Level diagnosis)	◯ Trigeminal Neuralgia ◯ Peripheral Nerve Injury (e.g. trauma, stroke) ◯ Painful Polyneuropathy (e.g. diabetic or chemotherapy-induced) ◯ Postherpetic Neuralgia (e.g. shingles)
Chronic Cancer Treatment Pain (1st Level)	◯ Post-Radiotherapy Pain ◯ Post-Cancer Medicine Pain
Pain duration in years	_____

Cannabis Experience

Cannabis Experience

Has your patient ever used any form of cannabis? (e.g. smoked or vaped cannabis, synthetic prescribed cannabinoids like *Dronabinol, Nabilone, Sativex*, or *Hemp/CBD*)

- ◯ Yes
- ◯ No

Was it for medical or recreational purposes or both?

- ◯ Medical
- ◯ Recreational
- ◯ Both

Did they use: inhaled, ingestible or topical? (select all that apply)

- ☐ Inhaled
- ☐ Ingestible
- ☐ Topical

Does the patient know the content or ratio of (THC:CBD) in the product they used?

- ◯ Yes
- ◯ No

Please select all that apply

- ☐ THC-dominant (i.e.>2:1)
- ☐ CBD-dominant (i.e. 1: >2)
- ☐ Balanced (i.e. 1:1)

Is your patient currently using cannabis for medical purposes?

- ◯ Yes
- ◯ No

Which of the following best captures when you patient used cannabis last?

- ◯ Over a year ago
- ◯ 6-12 months ago
- ◯ 1-6 months ago
- ◯ Less than 1 month ago

What best describes the frequency of use during that time?

- ◯ Every few months
- ◯ Monthly
- ◯ Weekly
- ◯ Daily

Treatment Goals

Which symptom category have you, and your patient identified as the **primary** treatment goal?

- ◯ Pain
- ◯ Mood
- ◯ Sleep
- ◯ Function

Please indicate the type of pain that best describes that which is the primary focus of the patient's primary treatment goal

- ◯ Burning
- ◯ Itching
- ◯ Throbbing
- ◯ Tingling or prickling

Please indicate the type of mood disruption that best describes that which is the primary focus of the patient's primary treatment goal

- ◯ Anxiety
- ◯ Concentration
- ◯ Depression
- ◯ Irritability
- ◯ Stress

Please indicate the type of sleep disruption that best describes that which is the primary focus of the patient's primary treatment goal

- ◯ Increase daytime alertness
- ◯ Increase sleep quality or quantity

Please indicate the type of function that best describes that which is the primary focus of the patient's primary treatment goal

- ◯ Activities unrelated to employment (e.g. leisure activities)
- ◯ Employment related activities (e.g. return to work full time)
- ◯ Improve relationships

Concomitant medication

Is your patient currently taking an of the following classes of prescription medication (select all that apply)

- ☐ Nonsteroidal Anti-inflammatory Drugs (NSAIDs) and Acetaminophen
- ☐ Antidepressants (TCA, SNRI, SSRI)
- ☐ Anticonvulsants (gabapentin, pregabalin)
- ☐ Muscle Relaxants
- ☐ Benzodiazepines
- ☐ Opioids
- ☐ Other
- ☐ Medical Cannabis from a Licensed Producer other than Spectrum

NSAIDs and Acetaminophen Dosing Information

Name of drug _____

Daily dose of [baseline_visit][nsaid1_name] (total mg per day) _____

☐ Check to add additional NSAID /Acetaminophen medications

Name of drug _____

Daily dose of [baseline_visit][nsaid2_name] (total mg per day) _____

☐ Check to add additional NSAID /Acetaminophen medications

Name of drug _____

Daily dose of [baseline_visit][nsaid3_name] (total mg per day) _____

Antidepressants Dosing Information

Name of drug _____

Daily dose of [baseline_visit][antidep1_name](total mg per day) _____

☐ Check to add additional Antidepressant medications

Name of drug _____

Daily dose of [baseline_visit][antidep2_name] (total mg per day) _____

☐ Check to add additional Antidepressant medications

Name of drug _____

Daily dose of [baseline_visit][antidep3_name] (total mg per day) _____

Anticonvulsants Dosing Information

Name of drug _____

Daily dose of [baseline_visit][anticon1_name] (total mg per day) _____

☐ Check to add additional anticonvulsant medications

Name of drug _____

Daily dose of [baseline_visit][anticon2_name] (total mg per day) _____

☐ Check to add additional anticonvulsant medications

Name of drug _____

Daily dose of [baseline_visit][anticonvu3_name] (total mg per day) _____

Muscle Relaxants Dosing Information

Name of drug _____

Daily dose of [baseline_visit][musrel1_name] (total mg per day) _____

☐ Check to add additional muscle relaxant medications

Name of drug _____

Daily dose of [baseline_visit][musrel2_name] (total mg per day) _____

☐ Check to add additional muscle relaxant medications

Name of drug _____

Daily dose of [baseline_visit][musrel3_name] (total mg per day) _____

Benzodiazepines Dosing Information

Name of drug _____

Daily dose of [baseline_visit][benzo1_name](total mg per day) _____

☐ Check to add additional benzodiazepine medications

Name of drug _____

Daily dose of [baseline_visit][benzo2_name] (total mg per day) _____

☐ Check to add additional benzodiazepine medications

Name of drug _____

Daily dose of [baseline_visit][benzo3_name] (total mg per day) _____

Opioid Dosing Information

Please enter MME (total daily morphine equilvalent dose in mg) _____

Other Medication Information

Please indicate name of other drugs not included in the above classes _____

Daily dose (total mg per day), if available _____

ST Regimen Canada

Please enter in the table below total daily amount of Spectrum Therapeutics products consumed. Please be conscious of the units provided:

Inhaled cannabis = total number of inhalations per day

Ingested oils = total mL per day

Spray format = total number of sprays per day

Capsules & edibles = total number of capsules or total number of chocolate bar squares per day

	Inhaled Formats (dried flower, extract vaporizers) -- report daily total number of inhalations	Ingested Oil Formats - report daily total number of mLs	Spray Formats - report daily total number of sprays	Low Potency Capsule & Edible Formats - report daily total number of low-potency capsules (i.e. 2.5 mg), number of chocolate bar squares, etc.	High Potency Capsule Formats - report daily total number of high-potency capsules
Red (examples include Spectrum #1-4; Tweed Bakerstreet, Highlands, Houdstooth, Donegal; LBS Sunset)	inhalations	mL	sprays	capsules	capsules
Orange	inhalations		sprays		
Purple (examples include LBS Ocean View)	inhalations		sprays		
Blue (examples include Tweed Penelope)	inhalations	mL	sprays	capsules	capsules
Green (examples include Tweed Argyle)	inhalations	mL	sprays	capsules	capsules
Yellow (examples include Tweed CBD Softgels)	inhalations	mL	sprays	capsules	capsules
Spectrum Clear (or White)		mL			

You indicated that your patient has been recommended an inhaled format. Please identify their most common method of administration. *(inhal_admin)* *[Branching logic exists]*	○ Smoked ○ Dried flower vaporizer (e.g. Stroz and Bickel, PAX) ○ Extract vaporizer (e.g. vape pen cartridge)
Do you or your patient know the temperature set point of the vaporizer (in °C) *(inhal_vape_Y/N)* *[Branching logic exists]*	○ Yes ○ No
If known, please provide the temperature set point of your patient's vaporizer (in °C) _____ *(inhal_vape_temp)* *(125 / 300)* *[Branching logic exists]*	

Calculated, approximated total daily dose of THC and CBD (in mgs)

	THC	CBD
Inhaled	*(inhal_THC)* View Equation	*(inhal_CBD)* View Equation
Ingested	*(ingest_THC)* View Equation	*(ingest_CBD)* View Equation

Patient reported outcomes

BPI

Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

- ◯ Yes
- ◯ No

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes your pain at its worst in the last 24 hours.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes your pain at its least in the last 24 hours.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes your pain on the average.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes how much pain you have right now.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **General Activity**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **Mood**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **Walking ability**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **Normal work (includes both work outside the home and housework)**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how during the past 24 hours, pain has interfered with your: **Relations with other people**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how during the past 24 hours, pain has interfered with your: **Sleep**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how during the past 24 hours, pain has interfered with your: **Enjoyment of life**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

EQ5D

Mobility

- ◯ I have no problems in walking about
- ◯ I have slight problems in walking about
- ◯ I have moderate problems in walking about
- ◯ I have severe problems in walking about
- ◯ I am unable to walk

Self-Care

- ◯ I have no problems washing or dressing myself
- ◯ I have slight problems washing or dressing myself
- ◯ I have moderate problems washing or dressing myself
- ◯ I have severe problems washing or dressing myself
- ◯ I am unable to wash or dress myself

Usual Activities

- ◯ I have no problems doing my usual activities
- ◯ I have slight problems doing my usual activities
- ◯ I have moderate problems doing my usual activities
- ◯ I have severe problems doing my usual activities
- ◯ I am unable to do my usual activities

Pain/Discomfort

- ◯ I have no pain or discomfort
- ◯ I have slight pain or discomfort
- ◯ I have moderate pain or discomfort
- ◯ I have severe pain or discomfort
- ◯ I have extreme pain or discomfort

Anxiety/Depression

- ◯ I am not anxious or depressed
- ◯ I am slightly anxious or depressed
- ◯ I am moderately anxious or depressed
- ◯ I am severely anxious or depressed
- ◯ I am extremely anxious or depressed

We would like to know how good or bad your health is TODAY. Please write a number between 0 and 100.

100 means the best health you can imagine

0 means the worst health you can imagine

_____

Appendix 2 – PHYISICIAN-VERIFED FOLLOW-UP ASSESSMENT

ST Regimen Canada

Please enter in the table below total daily amount of Spectrum Therapeutics products consumed. Please be conscious of the units provided:

Inhaled cannabis = total number of inhalations per day

Ingested oils = total mL per day

Spray format = total number of sprays per day

Capsules & edibles = total number of capsules or total number of chocolate bar squares per day

Physician-recommended Regimen of Spectrum Therapeutics Products

	Inhaled Formats (dried flower, extract vaporizers) -- report daily total number of inhalations	Ingested Oil Formats - report daily total number of mLs	Spray Formats - report daily total number of sprays	Low Potency Capsule & Edible Formats - report daily total number of low-potency capsules (i.e. 2.5 mg), number of chocolate bar squares, etc.	High Potency Capsule Formats - report daily total number of high-potency capsules
Red (examples include Spectrum #1-4; Tweed Bakerstreet, Highlands, Houdstooth, Donegal; LBS Sunset)	inhalations	mL	sprays	capsules	capsules
Orange	inhalations		sprays		
Purple (examples include LBS Ocean View)	inhalations		sprays		
Blue (examples include Tweed Penelope)	inhalations	mL	sprays	capsules	capsules
Green (examples include Tweed Argyle)	inhalations	mL	sprays	capsules	capsules
Yellow (examples include Tweed CBD Softgels)	inhalations	mL	sprays	capsules	capsules
Spectrum Clear (or White)		mL			

You indicated that your patient has been recommended an inhaled format. Please identify their most common method of administration. *(inhal_admin)* *[Branching logic exists]*	○ Smoked ○ Dried flower vaporizer (e.g. Stroz and Bickel, PAX) ○ Extract vaporizer (e.g. vape pen cartridge)
Do you or your patient know the temperature set point of the vaporizer (in °C) *(inhal_vape_Y/N)* *[Branching logic exists]*	○ Yes ○ No
If known, please provide the temperature set point of your patient's vaporizer (in °C) _____ *(inhal_vape_temp)* *(125 / 300)* *[Branching logic exists]*	

Calculated, approximated total daily dose of THC and CBD (in mgs)

	THC	CBD
Inhaled	*(inhal_THC)* View Equation	*(inhal_CBD)* View Equation
Ingested	*(ingest_THC)* View Equation	*(ingest_CBD)* View Equation

Concomitant medication

Concomitant medication - Existing

Existing NSAIDs and Acetaminophen Dosing Information

At last visit, you indicated that your patient was taking [baseline_visit][nsaid1_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

What is their current daily dose of [baseline_visit] [nsaid1_name] (total mg per day)?

_____

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

At last visit, you indicated that your patient was taking [baseline_visit][nsaid2_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [nsaid2_name] (total mg per day)?

_____

At last visit, you indicated that your patient was taking [baseline_visit][nsaid3_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [nsaid3_name] (total mg per day)?

_____

Existing Antidepressants Dosing Information

At last visit, you indicated that your patient was taking [baseline_visit][antidep1_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [antidep1_name] (total mg per day)?

_____

At last visit, you indicated that your patient was taking [baseline_visit][antidep2_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [antidep2_name] (total mg per day)?

_____

At last visit, you indicated that your patient was taking [baseline_visit][antidep3_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [antidep3_name] (total mg per day)?

_____

Existing Anticonvulsants Dosing Information

At last visit, you indicated that your patient was taking [baseline_visit][anticon1_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [anticon1_name] (total mg per day)?

_____

At last visit, you indicated that your patient was taking [baseline_visit][anticon2_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [anticon2_name] (total mg per day)?

_____

At last visit, you indicated that your patient was taking [baseline_visit][anticonvu3_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [anticonvu3_name] (total mg per day)?anticon1_dose_follow1

_____

Existing Muscle Relaxants Dosing Information

At last visit, you indicated that your patient was taking [baseline_visit][musrel1_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [musrel1_name] (total mg per day)?

_____

At last visit, you indicated that your patient was taking [baseline_visit][musrel2_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [musrel2_name] (total mg per day)?

_____

At last visit, you indicated that your patient was taking [baseline_visit][musrel3_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [musrel3_name] (total mg per day)?

_____

Existing Benzodiazepines Dosing Information

At last visit, you indicated that your patient was taking [baseline_visit][benzo1_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [benzo1_name] (total mg per day)?

_____

At last visit, you indicated that your patient was taking [baseline_visit][benzo2_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [benzo2_name] (total mg per day)?

_____

At last visit, you indicated that your patient was taking [baseline_visit][benzo3_name]. Is your patient still taking this medication?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current daily dose of [baseline_visit] [benzo3_name] (total mg per day)?

_____

Existing Opioid Dosing Information

At last visit, you indicated that your patient had an MME of [baseline_visit][opioid_mme]. Is your patient still taking opioids?

- ◯ Yes
- ◯ No

Please select the reason why your patient stopped taking this medication.

- ◯ Side effects
- ◯ Cost
- ◯ Lack of benefit
- ◯ No longer needs/ replaced by medical cannabis
- ◯ Unknown

What is their current MME?

_____

Existing Other Medications Dosing Information

At last visit, you indicated that your patient was taking other medications, including [baseline_visit][othmed_name]. Is your patient still taking any of these other prescription medications?

- ◯ Yes
- ◯ No

Please describe any **changes** to their other existing prescription medications since last visit (including changes to total daily dose)

_____

Concomitant Medications - New

Since last visit, has your patient **started** taking any of the following classes of prescription medication (select all that apply)

- ☐ Nonsteroidal Anti-inflammatory Drugs (NSAIDs) and Acetaminophen
- ☐ Antidepressants (TCA, SNRI, SSRI)
- ☐ Anticonvulsants (gabapentin, pregabalin)
- ☐ Muscle Relaxants
- ☐ Benzodiazepines
- ☐ Opioids
- ☐ Other
- ☐ Medical Cannabis from a Licensed Producer other than Spectrum

Name of new NSAID/Acetaminophen medication (started since last visit) _____

Daily dose of [physician_1st_follow][nsaid4_name] (total mg per day) _____

Name of new antidepressant medication (started since last visit) _____

Daily dose of [physician_1st_follow][antidep4_name] (total mg per day) _____

Name of new anticonvulsant medication (started since last visit) _____

Daily dose of [physician_1st_follow][anticon4_name] (total mg per day) _____

Name of new muscle relaxant medication (started since last visit) _____

Daily dose of [physician_1st_follow][musrel4_name] (total mg per day) _____

Name of new benzodiazepine medication (started since last visit) _____

Daily dose of [physician_1st_follow][benzo4_name] (total mg per day) _____

Please enter MME (total daily morphine equilvalent dose in mg) _____

Name of new prescription medication (started since last visit, not covered in above classes) _____

Daily dose of [physician_1st_follow][othmed4_name] (total mg per day) _____

Physician AE form

Product information

Do you have any adverse events to report related to this patient?

- ◯ Yes
- ◯ No

Suspect product(s) name _____

Start date _____ (YYYY-MM-DD)

End date _____ (YYYY-MM-DD)

Route of administration

- ◯ oral - oil
- ◯ oral - softgel
- ◯ oral - spray
- ◯ oral - beverage
- ◯ oral - chocolate
- ◯ oral
- ◯ inhalation - smoked
- ◯ inhalation - vaporized
- ◯ inhalation

Dose (please include amount and unit i.e. mg, ml, #softgels, #inhalations, etc.) _____

Did reaction disappear after reducing the dose or stopping the product ?

- ◯ No
- ◯ Yes
- ◯ Unknown

Did reaction reappear after same product/treatment was restarted?

- ◯ No
- ◯ Yes
- ◯ Unknown

AE description

Onset date of event _____ (YYYY-MM-DD)

End date of event _____ (YYYY-MM-DD)

Select seriousness criteria

- ◯ Non-serious
- ◯ Death
- ◯ Life-Threatening
- ◯ Inpatient/Prolonged Hospitalization
- ◯ Congenital Anomaly/Birth Defect
- ◯ Persistent of Significant Disability /Incapacity
- ◯ Other Medically Important Condition

Admission date _____ (YYYY-MM-DD)

Discharge date _____ (YYYY-MM-DD)

Date of death _____ (YYYY-MM-DD)

Cause of death _____

Was an autopsy performed?

- ◯ Yes
- ◯ No

Please provide autopsy results _____

Select outcome of event(s)

- ◯ Recovered
- ◯ Recovering
- ◯ Ongoing
- ◯ Fatal
- ◯ Unknown

Select severity

- ◯ Mild
- ◯ Moderate
- ◯ Severe

Investigator Causality Assessment:

- ◯ Related
- ◯ Probable
- ◯ Possible
- ◯ Unlikely
- ◯ Not related

Please describe alternate possible causes for the AE? _____

Please provide patients medical history _____

Please provide a summary of the patients course during the time of the event (AE, symptoms, events chronology, treatments, medical history. titration information, outcome per event, etc.). _____

CGI-I

Clinician Global Impression of Improvement

Since the start of Spectrum Therapeutics treatment, my patient's overall symptom status is:

(best describe how your patient's symptom is now, compared with how it was before they began taking medical cannabis)

- ◯ Very Much Improved -nearly all better; good level of functioning; minimal symptoms; represents a very substantial change
- ◯ Much Improved -notably better with significant reduction of symptoms; increase in the level of functioning but some symptoms remain
- ◯ Minimally Improved -slightly better with little or no clinically meaningful reduction of symptoms. Represents very little change in basic clinical status, level of care, or functional capacity
- ◯ No Change -symptoms remain essentially unchanged
- ◯ Minimally Worse -slightly worse but may not be clinically meaningful; may represent very little change in basic clinical status or functional capacity
- ◯ Much Worse -clinically significant increase in symptoms and diminished functioning
- ◯ Very Much Worse -severe exacerbation of symptoms and loss of functioning

Patient reported outcomes

BPI

Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

- ◯ Yes
- ◯ No

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes your pain at its worst in the last 24 hours.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes your pain at its least in the last 24 hours.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes your pain on the average.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes how much pain you have right now.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **General Activity**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **Mood**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **General Activity**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **Mood**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **Walking ability**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **Normal work (includes both work outside the home and housework)**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how during the past 24 hours, pain has interfered with your: **Relations with other people**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how during the past 24 hours, pain has interfered with your: **Sleep**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how during the past 24 hours, pain has interfered with your: **Enjoyment of life**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

EQ5D

Mobility

- ◯ I have no problems in walking about
- ◯ I have slight problems in walking about
- ◯ I have moderate problems in walking about
- ◯ I have severe problems in walking about
- ◯ I am unable to walk

Self-Care

- ◯ I have no problems washing or dressing myself
- ◯ I have slight problems washing or dressing myself
- ◯ I have moderate problems washing or dressing myself
- ◯ I have severe problems washing or dressing myself
- ◯ I am unable to wash or dress myself

Usual Activities

- ◯ I have no problems doing my usual activities
- ◯ I have slight problems doing my usual activities
- ◯ I have moderate problems doing my usual activities
- ◯ I have severe problems doing my usual activities
- ◯ I am unable to do my usual activities

Pain/Discomfort

- ◯ I have no pain or discomfort
- ◯ I have slight pain or discomfort
- ◯ I have moderate pain or discomfort
- ◯ I have severe pain or discomfort
- ◯ I have extreme pain or discomfort

Anxiety/Depression

- ◯ I am not anxious or depressed
- ◯ I am slightly anxious or depressed
- ◯ I am moderately anxious or depressed
- ◯ I am severely anxious or depressed
- ◯ I am extremely anxious or depressed

We would like to know how good or bad your health is TODAY. Please write a number between 0 and 100.

100 means the best health you can imagine

0 means the worst health you can imagine

_____

PGI-C

Global Impression of Change

Since the start of Spectrum Therapeutics treatment, my overall symptom status is:

(best describe how your symptom is now, compared with how it was before you began taking medical cannabis)

- ◯ Very Much Improved
- ◯ Much Improved
- ◯ Minimally Improved
- ◯ No Change
- ◯ Minimally Worse
- ◯ Much Worse
- ◯ Very Much Worse

Appendix 3 – SUBJECT-VERIFIED FOLLOW-UP ASSESSMENT

ST Regimen Canada

Please enter in the table below total daily amount of Spectrum Therapeutics products consumed. Please be conscious of the units provided:

Inhaled cannabis = total number of inhalations per day

Ingested oils = total mL per day

Spray format = total number of sprays per day

Capsules & edibles = total number of capsules or total number of chocolate bar squares per day

Physician-recommended Regimen of Spectrum Therapeutics Products

	Inhaled Formats (dried flower, extract vaporizers) -- report daily total number of inhalations	Ingested Oil Formats - report daily total number of mLs	Spray Formats - report daily total number of sprays	Low Potency Capsule & Edible Formats - report daily total number of low-potency capsules (i.e. 2.5 mg), number of chocolate bar squares, etc.	High Potency Capsule Formats - report daily total number of high-potency capsules
Red (examples include Spectrum #1-4; Tweed Bakerstreet, Highlands, Houdstooth, Donegal; LBS Sunset)	inhalations	mL	sprays	capsules	capsules
Orange	inhalations		sprays		
Purple (examples include LBS Ocean View)	inhalations		sprays		
Blue (examples include Tweed Penelope)	inhalations	mL	sprays	capsules	capsules
Green (examples include Tweed Argyle)	inhalations	mL	sprays	capsules	capsules
Yellow (examples include Tweed CBD Softgels)	inhalations	mL	sprays	capsules	capsules
Spectrum Clear (or White)		mL			

You indicated that your patient has been recommended an inhaled format. Please identify their most common method of administration. *(inhal_admin)* *[Branching logic exists]*	○ Smoked ○ Dried flower vaporizer (e.g. Stroz and Bickel, PAX) ○ Extract vaporizer (e.g. vape pen cartridge)
Do you or your patient know the temperature set point of the vaporizer (in °C) *(inhal_vape_Y/N)* *[Branching logic exists]*	○ Yes ○ No
If known, please provide the temperature set point of your patient's vaporizer (in °C) _____ *(inhal_vape_temp)* *(125 / 300)* *[Branching logic exists]*	

Calculated, approximated total daily dose of THC and CBD (in mgs)

	THC	CBD
Inhaled	*(inhal_THC)* View Equation	*(inhal_CBD)* View Equation
Ingested	*(ingest_THC)* View Equation	*(ingest_CBD)* View Equation

Side Effects

Does your daily dose include any side effects (e.g. nausea, dry mouth, drowsiness, euphoria, etc.)?

- ◯ Yes
- ◯ No

You indicated that you experience side effects from your daily dose. Please indicate which side effects you experience (check all that apply)

- ☐ Nausea
- ☐ Dry Mouth
- ☐ Dizziness
- ☐ Somnolence (i.e. sleepiness/drowsiness)
- ☐ Euphoria
- ☐ Other

Please describe the 'other' side effects that you experienced _____

Subject Adverse Event Reporting

AE diary

Since you have been taking Spectrum Therapeutics medical cannabis products, have you experienced any side effects? Please include any side effects you have experienced, regardless of whether you believe they are related to medical cannabis.

- ◯ Yes
- ◯ No

Please describe in as much detail the adverse event (side effect) that you experienced.

Adverse events, symptoms, start date/end date, event(s) chronology, treatments, outcome. _____

PGI-C

Global Impression of Change

Since the start of Spectrum Therapeutics treatment, my overall symptom status is:

(best describe how your symptom is now, compared with how it was before you began taking medical cannabis)

- ◯ Very Much Improved
- ◯ Much Improved
- ◯ Minimally Improved
- ◯ No Change
- ◯ Minimally Worse
- ◯ Much Worse
- ◯ Very Much Worse

Patient reported outcomes

BPI

Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

- ◯ Yes
- ◯ No

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes your pain at its worst in the last 24 hours.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes your pain at its least in the last 24 hours.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes your pain on the average.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= no pain, 10= pain as bad as you can imagine) that best describes how much pain you have right now.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **General Activity**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **Mood**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **Walking ability**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how, during the past 24 hours, pain has interfered with your: **Normal work (includes both work outside the home and housework)**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how during the past 24 hours, pain has interfered with your: **Relations with other people**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how during the past 24 hours, pain has interfered with your: **Sleep**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

Please select the number (0= does not interfere, 10= completely interferes) that best describes how during the past 24 hours, pain has interfered with your: **Enjoyment of life**

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10

EQ5D

Mobility

- ◯ I have no problems in walking about
- ◯ I have slight problems in walking about
- ◯ I have moderate problems in walking about
- ◯ I have severe problems in walking about
- ◯ I am unable to walk

Self-Care

- ◯ I have no problems washing or dressing myself
- ◯ I have slight problems washing or dressing myself
- ◯ I have moderate problems washing or dressing myself
- ◯ I have severe problems washing or dressing myself
- ◯ I am unable to wash or dress myself

Usual Activities

- ◯ I have no problems doing my usual activities
- ◯ I have slight problems doing my usual activities
- ◯ I have moderate problems doing my usual activities
- ◯ I have severe problems doing my usual activities
- ◯ I am unable to do my usual activities

Pain/Discomfort

- ◯ I have no pain or discomfort
- ◯ I have slight pain or discomfort
- ◯ I have moderate pain or discomfort
- ◯ I have severe pain or discomfort
- ◯ I have extreme pain or discomfort

Anxiety/Depression

- ◯ I am not anxious or depressed
- ◯ I am slightly anxious or depressed
- ◯ I am moderately anxious or depressed
- ◯ I am severely anxious or depressed
- ◯ I am extremely anxious or depressed

We would like to know how good or bad your health is TODAY. Please write a number between 0 and 100.

100 means the best health you can imagine

0 means the worst health you can imagine

_____

Appendix 4 ST Discontinuation Assessment

ST Discontinuation

Date of Spectrum Therapeutics treatment discontinuation

_____
(YYYY-MM-DD)

Why did your patient discontinue Spectrum Therapeutics treatment?

- ◯ Adverse Event
- ◯ Didn't like/uncomfortable (not associated with an AE) with cannabis
- ◯ Lack of patient overall treatment satisfaction
- ◯ Lack of physician overall treatment satisfaction
- ◯ Patient switched to prescription cannabinoids (nabilone, dronabinol, nabiximols)
- ◯ Patient is obtaining cannabis for medical purposes from a different licensed producer
- ◯ Patient is obtaining cannabis for medical purposes from a non-licensed source
- ◯ Symptom(s) no longer present
- ◯ Unable to afford Spectrum Therapeutics cannabis/no coverage
- ◯ No longer wanted to participate in the registry
- ◯ Difficulties accessing medical cannabis (regulatory or logistics barriers)
- ◯ Patient is deceased
- ◯ Other

Is your patient still taking cannabis for medical purposes?

- ◯ Yes
- ◯ No

Please describe "other" or include further comments regarding treatment discontinuation

_____

Is your patient obtaining cannabis for medical purposes from an alternative source?

- ◯ Yes
- ◯ No

Given the response provided for "Why your patient discontinued Spectrum Therapeutics treatment?", they are still eligible for participation in the registry. Does your patient wish to continue to participate in the registry?

- ◯ Yes
- ◯ No

Please indicate which medical cannabis company _____

Please indicate why (select all that apply)

- ☐ More product variety within categories offered by Spectrum Therapeutics (e.g. more strains of dried flower)
- ☐ More product categories not offered by Spectrum Therapeutics (e.g. edible formats)
- ☐ Pricing
- ☐ Insurance coverage
- ☐ Product quality
- ☐ Product availability
- ☐ Other

Please describe other _____

Based on the response provided for "Why your patient discontinued Spectrum Therapeutics treatment?", they no longer meet the requirements for participation in the registry. Please confirm their withdrawal from the study using the 'Exit Assessment' form.

Based on the response provided for "Does your patient wish to continue to participate in the registry?", we kindly request that you confirm their withdrawal from the study using the 'Exit Assessment' form.

Thank you for your on-going participation in the study. Please continue to follow the protocol and complete scheduled follow-ups. With respect to the tables requesting information on the "Regimen of Spectrum Therapeutics Products", simply reply "No" to the question "Is your patient still taking Spectrum Therapeutics products" and submit.

Appendix 5 Exit Assessment

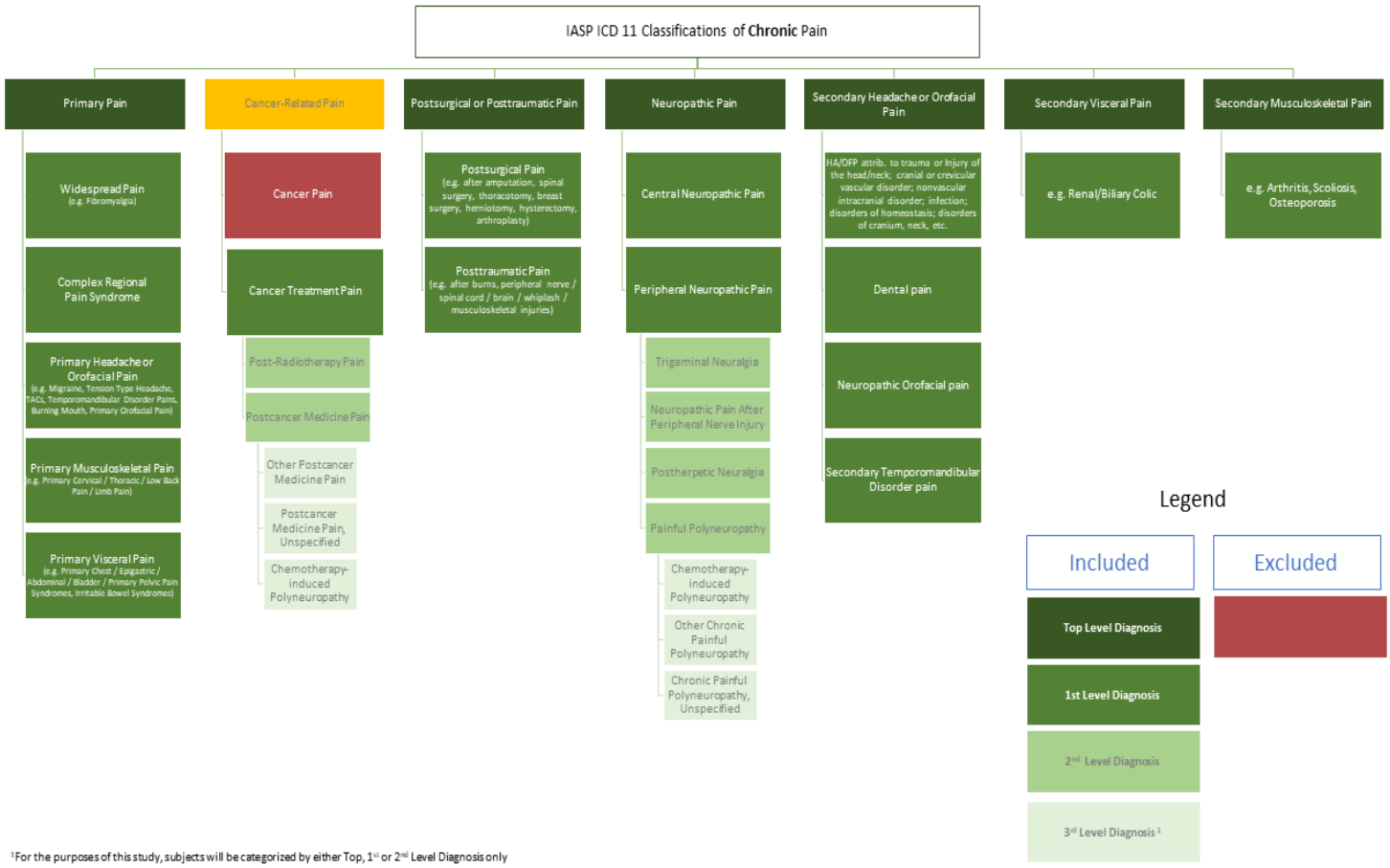
Exit Assessment

Confirm Study Exit

Please check the box to confirm the withdrawal of this patient from the study.

☐ EXIT the Study

Appendix 6 IASP ICD 11 Classifications of Chronic Pain



[1]For the purposes of this study, subjects will be categorized by either Top, 1st or 2nd Level Diagnosis only