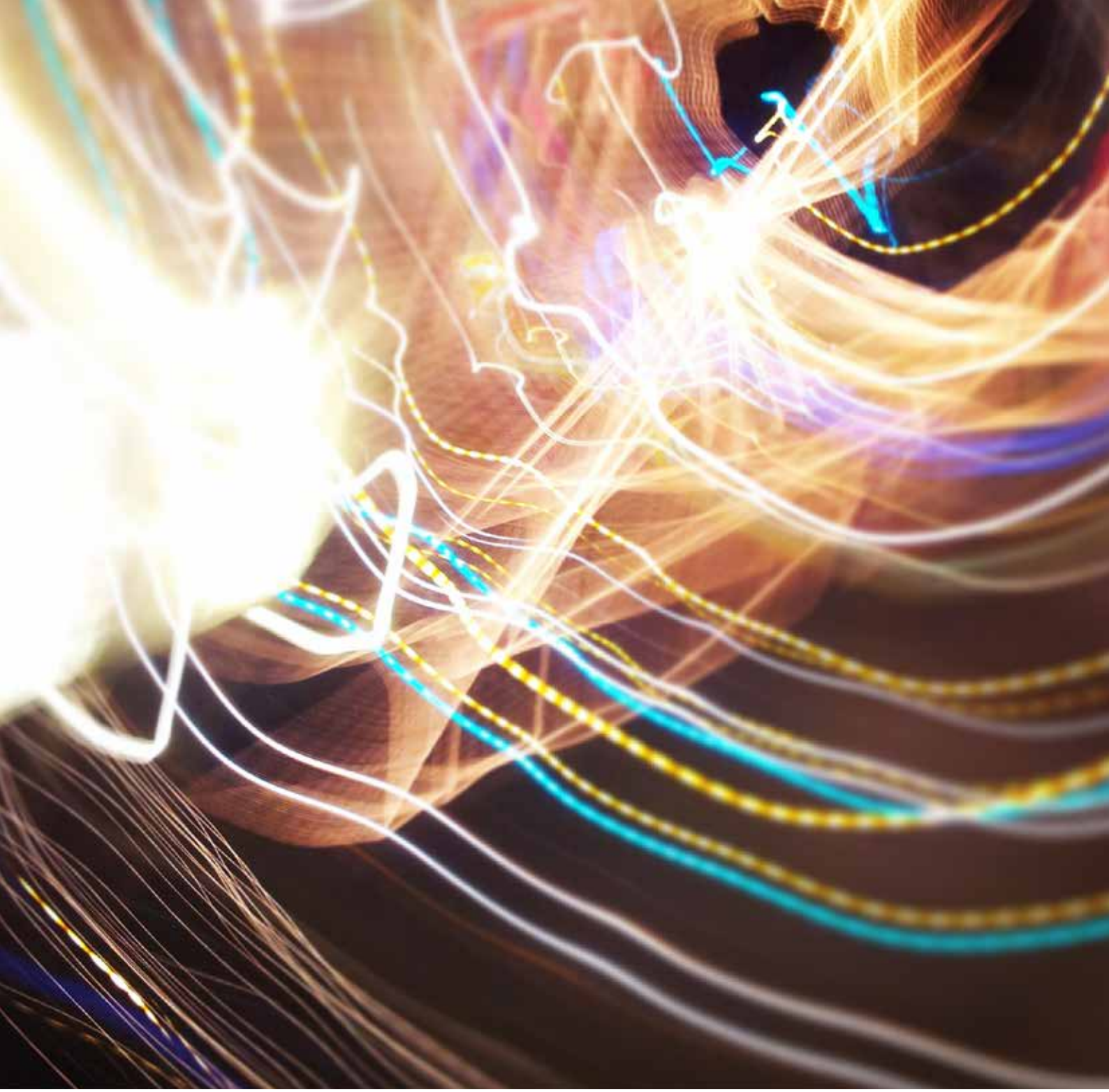

DECALOGUE

IDEAS TO ACCELERATE PATIENT ACCESS & THERAPEUTIC UNDERSTANDING OF MEDICINAL CANNABIS

The Centre For Medicinal Cannabis

CONTENTS

PREFACE

As we pass the third anniversary of the rescheduling of medical cannabis for therapeutic use in the UK, it is prudent to reflect on the positive changes that have ensued.

For a small number of patients medical cannabis treatments are now available on the NHS and access outside of the NHS is effectively expanding with costs falling for patients. The general population, including the medical profession, are supportive of cannabis-based medicines and we have publicly seen some of the life-changing effects these treatments can have on children with intractable epilepsy.

Whilst we should celebrate these successes, we should also acknowledge that there is much work to be done. If we want to accelerate NHS access for all patients who may benefit from these treatments, we need to think outside the box. This requires direct engagement and inter-disciplinary collaboration between policy-makers, regulators, industry, scientists, healthcare workers and patients.

Learning from COVID-19, I sense that there is great support from all relevant stakeholders to redefine and modernise processes of drug development and medical cannabis could be the poster-boy of this new normal as we emerge from the pandemic. The issues, ideas, concepts, and proposals outlined in these essays represent the first step of this journey and signal a bright future for this growing sector.

On that note I would like to warmly welcome you to the Great Hall at Imperial College London and the official launch of Decalogue. I hope it will be an inspiring day and I would like to thank the team at the Centre for Medicinal Cannabis for putting together this exciting pamphlet and congratulate them on their ongoing efforts to innovate and break down barriers in this emerging area of medical therapeutics.

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PRIORITISING CLINICAL STUDIES AND REGULATORY REVIEWS OF CBPMs

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In the UK currently, in addition to a few medical cannabis products that have been approved for prescription use, many unapproved cannabis-based products for medicinal use (CBPMs) are being purchased by patients and their parents/carers to treat a range of medical conditions. It is important for the health and wellbeing of such a population that these treatments are based on the use of products with proven quality and reproducibility and that there is sound evidence of both their safety and efficacy.

In the UK currently, in addition to a few medical cannabis products that have been approved for prescription use, many unapproved cannabis-based products for medicinal use (CBPMs) are being purchased by patients and their parents/carers to treat a range of medical conditions. It is important for the health and wellbeing of such a population that these treatments are based on the use of products with proven quality and reproducibility and that there is sound evidence of both their safety and efficacy.

The literature, especially the popular press, abounds with many anecdotal reports of possible therapeutic efficacy but there remains the need for well-designed clinical studies to establish their true value. In 2018, recognising the potential therapeutic value of some CBPMs, the UK National Institute for Health Research (NIHR) initiated a "themed call" to look at the use of such products for "difficult-to-treat epilepsy or other disorders unresponsive to existing treatments". Unfortunately, there was a poor response to the call.

Meanwhile, the UK Government has continued to prioritise the need for such studies and special arrangements have been established in the NHS for the prescribing of CBPMs by clinicians on the Specialist Register of the General Medical Council.

The considerable growth of research on CBPMs in recent years now forms the scientific basis for selecting areas of unmet medical need that should be the focus of prioritised, well designed, properly conducted, clinical studies.

The literature, especially the popular press, abounds with many anecdotal reports of possible therapeutic efficacy but there remains the need for well-designed clinical studies to establish their true value.

Early in 2021 the UK Government's Taskforce on Innovation, Growth and Regulatory Reform (TIGRR) made key recommendations that, if implemented, could see the licensing of certain aspects of the UK's medicinal cannabis industry moved away from Home Office control to the Department of Health and Social Care or the regulator, the MHRA.

The MHRA is recognised internationally for both its competency in reviewing applications for Product Licences and its speed of review. Importantly, in addition to safety and efficacy it ensures that medicines imported into or manufactured in the UK are sourced from reputable suppliers and manufacturers and are inspected for compliance with Good Manufacturing Practice standards, including confirmation of reproducible quality and stability.

For some years, the MHRA has operated an Early Access to Medicines Scheme (EAMS)and more recently established a new process – the Innovative Licensing and Access Pathway (ILAP) – to improve patient access via the acceleration of the clinical evaluation of medicines; especially those for high unmet need.

Many of the conditions for which a CBPM might be appropriate are likely to be rare disorders. Fortunately, the UK's rare disease framework has established four key priorities viz:

1) helping patients get a final diagnosis faster
2) Increase awareness of rare diseases among healthcare professionals
3) Better coordination of care
4) Improving access to specialist care, treatments, and drugs.

So, processes and procedures are in place to perform these clinical studies and to obtain rapid regulatory review but, given the experience of the NIHR initiative, a different approach is now required.

The path to more UK clinical trials

What is needed is a new mechanism whereby such trials can be prioritised by an expert group skilled in the field and that the trials are conducted at optimal pace so as to ensure the earliest possible benefit to patients. In that respect we should consider what lessons we have learned from the COVID-19 pandemic and how they may be applied to CBMPs

The establishment in the UK of the RECOVERY trial by the UKRI's Medical Research Council and the NIHR proved to be an efficient and effective process resulting in the identification and validation of key COVID-19 therapeutic agents; in months rather than the more usual time frame of

several years.

What is needed is a new mechanism whereby such trials can be prioritised by an expert group skilled in the field and that the trials are conducted at optimal pace so as to ensure the earliest possible benefit to patients.

A similar initiative could be established for identifying CBMPs that could be rapidly evaluated in selected conditions of high unmet need.

It should be noted that CBMPs cover a range of products from single, highly purified, individual cannabinoids e.g., Cannabidiol (CBD) (whether extracted and purified from Hemp or Marijuana plants or chemically synthesized) to extracts containing a number of cannabinoids together with plant constituents such as terpenes and flavonoids. It will be important that companies applying to participate in the prioritised trials demonstrate that such extracts are consistent chemically from batch to batch and have acceptable shelf lives for transport, storage and use.

The steps to the formation of such a Centrally Coordinated initiative would be as follows. First, a working group of clinicians with knowledge of medicinal cannabis (probably selected from the Specialist Register of the GMC) should be convened to identify a short-list of (probably rare/ Orphan) conditions. To this group should be added several scientists / researchers with expert knowledge of the current research on Cannabinoids / CBMPs to match and prioritise candidate CBMPs to the short-listed therapeutic areas.

The MHRA would then need too agree a modus vivendi which will probably include establishing a specialised review group within MHRA, agreeing protocols* for each therapeutic indication and a prioritised pathway for review of the clinical trial data.
These model protocols should be discussed with a group of selected experts from the pharmaceutical and biotech industry so that they are codesigned with respect to their scientific and commercial feasibility. Such a group could include members of a consortium drawn from the Association for the Cannabinoid Industry CMC / ACI.

Patient groups in each therapeutic area should be consulted to ensure that the protocols are realistic for the patients and carers and to raise awareness of the initiative with their respective memberships.

Due to the unique nature of the selected therapeutic areas, it is envisaged that these protocols will be sufficient to determine whether it is acceptable to grant Product License approvals on limited data to be followed by the continued acquisition and reporting of “Real World” data both from the subjects involved in the trials and a wider population. This might also include data from carefully designed observational studies.

Then the Department for Health & Social Care should establish a register of clinical centres (and their specialist clinicians) where clinical trials into CBPMs to full GCP standards can be conducted in the selected therapeutic areas. (This may re-

quire further capacity, building on the specialist centres on the GMC list).

Then the NIHR should issue a call to companies involved in CBMP R&D requesting proposals for consideration; importantly, including evidence that the product to be clinically evaluated is prepared to GMP standards and is of reproducible quality using adequately validated analytical methodology.

Finally, the programme would prioritise the number of products and therapeutic areas that should be the subject of the initial programmes and provide some seed-funding.

Whilst the cost of conducting the trials, the supply of clinical trial material and the construction and submission of dossiers for regulatory review will be borne by the individual companies participating, given that many of these companies could be relatively small enterprises, it is probable that some other form of financial funding will be required. This could be from one or more of new UK Government Life Science initiatives announced during 2021. In that context, companies that submit proposals and the source of the products could be from within the UK or from other countries. It may be necessary to establish what economic incentives are available to companies depending on their geographical base.

Further, before a trial begins and as data emerge, discussion should be held with the National Institute for Health and Care Excellence (N.I.C.E.) to agree what parameters will be required for an appropriate Health Technology Assessment. It is encouraging to note the recent announcement that N.I.C.E. is ambitious in the scope and breadth of its review and that it will continue to welcome contributions from all stakeholders.

Some of the CBMPs that emerge from this initiative may face challenges in the context of supply due to a variety of factors, including their legal status / scheduling. These aspects should be thoroughly reviewed as the clinical trials progress to establish whether current requirements may need modification to ensure ease of access by the patients whilst safeguarding the general public. Equally, patient access might be assisted by applying items from the Accelerated Access Collaboration (AAC) and the expansion of the Innovative Medicines Fund .

In conclusion, given the potential therapeutic benefit to patients that recent research has identified for selected medicinal cannabis products, the UK should take the initiative to identify priorities, streamline clinical and regulatory pathways and patient access schemes, ensuring that the quality and reproducibility of the products is ensured.

1) Epidyolex and Sativex. GW Pharmaceuticals

2) TIGRR https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/994125/FINAL_TIGRR_REPORT__1_.pdf

3) EAMS https://www.gov.uk/guidance/apply-for-the-early-access-to-medicines-scheme-eams

4) UK Government Life Science Initiatives https://www.gov.uk/government/news/bold-new-life-sciences-vision-sets-path-for-uk-to-build-on-pandemic-response-and-deliver-life-changing-innovations-to-patients

5) Accelerated Access collaborative https://www.england.nhs.uk/aac/

6) Innovative Medicines Fund https://www.england.nhs.uk/2021/07/nhs-england-announces-new-innovative-medicines-fund-to-fast-track-promising-new-drugs/

DEVELOPING CANNABINOID SCIENCE IN THE UK: MOVING FROM THE SECURITY TO THE HEALTH DOMAIN

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The UK has a strong history of pharmaceutical Research & Development (R&D) leading to the approval of significant medicines from antibiotics to monoclonal antibodies. More recently, it has been the home for the world's first biotech focused on developing cannabinoid medicines (GW Pharma acquired by Jazz Pharmaceuticals for $7B in February 2021). Against this backdrop, current interest in the benefits of cannabinoid medicines and the new regulatory freedoms afforded by Brexit should make the UK a "go-to" global hub for cannabinoid R&D and first major market regulatory approval.

Globally respected institutions such as Medical Research Council, NIHR, NHS and the MHRA as well as leading academic cannabinoid research institutions located at the University of Aberdeen, Aberystwyth University, Kings College London, Imperial College London, Manchester Metropolitan University and University of Nottingham make the UK an ideal research environment for the development of cannabinoid based medicines.

Real-life experience by the authors of this paper has shown the difficulties of developing controlled drugs such as cannabinoids as licensing of activities across the R&D supply chain is exclusively controlled by the Home Office and not the MHRA. We make the case that for cannabinoids being developed in an already highly regulated clinical trials environment that the licensing authority should shift from the Home Office to the Department of Health and Social Care (DHSC)/MHRA which will speed development, reduce cost and red-tape and lead to increased R&D expenditure and innovation within the UK.

The current barriers

A perspective from a UK-based full service clinical contract research organisation specialising in the design, set-up and delivery of early phase patient studies in oncology, seeking to attract global companies to conduct their early trials in the UK, is useful in highlighting the challenges in working with Schedule 1 controlled Investigational Medicinal Products (IMP) in the UK.

In recent years, the MHRA (responsible for regulatory approvals), the HRA (responsible for ethical approvals) and NIHR (responsible for clinical research within the NHS) have worked closely together to streamline their processes to support faster trial set-up timelines.

As a result, in our experience, a typical timeline from availability of a final protocol to clinical site initiation (i.e. ready to recruit patients) is 4-6 months for a UK site, which places the UK clinical research ecosystem in a strong competitive position globally. However, our operational experience to date is that securing a Schedule 1 licence from the Home Office is adding at least an additional 3 months to the set-up timeline for each UK site compared to a non-cannabinoid oncology clinical trial.

Reasons for these delays were as follows:

Rescheduling changes in 2018 do not cover all research targets. Despite the 2018 Misuse of Drugs Regulations (MDR) moving Cannabis Based Medicinal Products (CBMP) containing tetrahydrocannabinol (THC) to Schedule 2 when being used in clinical trials it does not cover novel synthetic derivatives of THC (so called 2nd and 3rd generation cannabinoids) which remain Schedule 1.

Lack of experience of NHS staff in the requirements for securing Schedule 1 licence approvals and few licensed sites. This is understandable given that opioids such as fentanyl, morphine and diamorphine, regularly used in hospitals, are only classified as Schedule 2 Controlled Drugs. Of the 10 NHS sites approached for this study, including several globally renowned centres of excellence for early phase oncology research, no centre had an active Schedule 1 licence.

Schedule 1 licensing process is operationally complex. There is a complicated on-line form with little/no guidance available and no published assessment criteria. Application requires named individuals at the site (Investigator, Pharmacists etc), who must have an enhanced Criminal Records Check before the application can be processed.

Confirmed payment of £3,000 fee before a Home Office inspection visit can be arranged.

In the experience of this one company, these factors were further exacerbated by resourcing constraints at both the sites and at the Home Office.

The additional complexity, cost and timeline delays directly resulting from the Home Office approvals process has necessitated us to divert some of our trial set-up activities to new sites in Europe and Australia. By way of comparison, the same company achieved set-up of a site in one European country in 5 months. The operational "log jam" caused by the Home Office approval step needs to be addressed if the UK research ecosystem is serious in its stated aim of being a global destination of choice for cannabinoid clinical research.

Current licensing requirements for Schedule 1 agents such as cannabinoids impose almost insurmountable restrictions on the pharmaceutical development activities required to reach the clinical development phase. The ability to identify Contract Research Organisations (CRO)/Contract Development and Manufacturing Organisations (CDMO) with appropriate technical capabilities and quality standards required for project delivery is severely compromised when the additional requirement that each of them is licensed for the possession of controlled drugs is overlaid.

The operational "log jam" caused by the Home Office approval step needs to be addressed if the UK research ecosystem is serious in its stated aim of being a global destination of choice for cannabinoid clinical research.

Pharmaceutical development takes place to convert the active pharmaceutical ingredient into a drug product suitable for its intended use. In the early stages of drug development, this will include design and optimisation of the formulation composition, analysis of the drug substance and drug product and stability testing, process development, scale up and manufacture for preclinical and clinical study supply. It is rare that a single CRO/CDMO could perform the diverse range of processes/analytics required. It is common for aspects such as microbiological testing to be performed by a third-party specialist.

Additionally, in these early phases of development, there is a relatively limited understanding of the compound or product and unexpected results may be observed. To understand the cause of these observations and whether they present risk to patients, investigations using state of the art equipment at specialist CROs (who are even less common) may be required.

Drug substance properties (such as low solubility, poor permeability, or instability within the digestive tract) may necessitate application of advanced formulation techniques. Specialist manufacturing technology may be required, which severely restricts the pool of appropriate CROs/CDMOs suitably equipped to perform formulation, process development and manufacturing activities.

It should be noted that the important phase of pharmaceutical development of cannabinoids (often taking 1-3 years to conduct) is not helped by the 2018 MDR changes which reschedule CBMPs to schedule 2 as they are only rescheduled from schedule 1 to 2 when they are being used for clinical trials (which is not the case in early research as its this research which ultimately leads to clinical trials) and does not cover novel synthetic derivatives of THC or other non-cannabinoid based controlled drugs.

When overlaid with the licensing requirements and controls for the production, possession, storage, supply, and import/export of Schedule 1 agents such as cannabinoids, the challenges are clear. A recent vendor selection exercise to identify a GMP CDMO with a schedule 1 controlled drugs license and the required technical manufacturing capability, lead to a pool of one. While this at least gave us a single way forward, this is a high risk and highly undesirable position to be in. In addition, identifying suitable third-party specialist service providers who also possessed appropriate licences added significant time delays to the project plan. It is our view that under the current licensing requirements, pharmaceutical development of schedule 1 drugs such as cannabinoids is disproportionately challenging.





Two previous reviews conducted in 20171 and 20192 of these difficulties have been conducted by the Advisory Council for the Misuse of Drugs (ACMD) which made a number of extremely useful recommendations which were never adopted by the Home Office. Of particular note is the concept of rescheduling a compound to a temporary "research schedule" with reduced requirements for the purpose of clinical evaluation. If clinical research continues, this status can be maintained but if trials fail then the compound would revert to Schedule 1. Should a compound get as far as product registration then the legal status of the resulting marketed medicine would be determined in the usual manner.

In the light of our new regulatory environment post-Brexit and our proposal for the MHRA to undertake controlled drug licensing decisions for products with medicinal use we strongly urge that the ACMD recommendations are reviewed again alongside industry consultation and implemented as soon as possible.

Under the current licensing requirements, pharmaceutical development of schedule 1 drugs such as cannabinoids is disproportionately challenging.

A better way

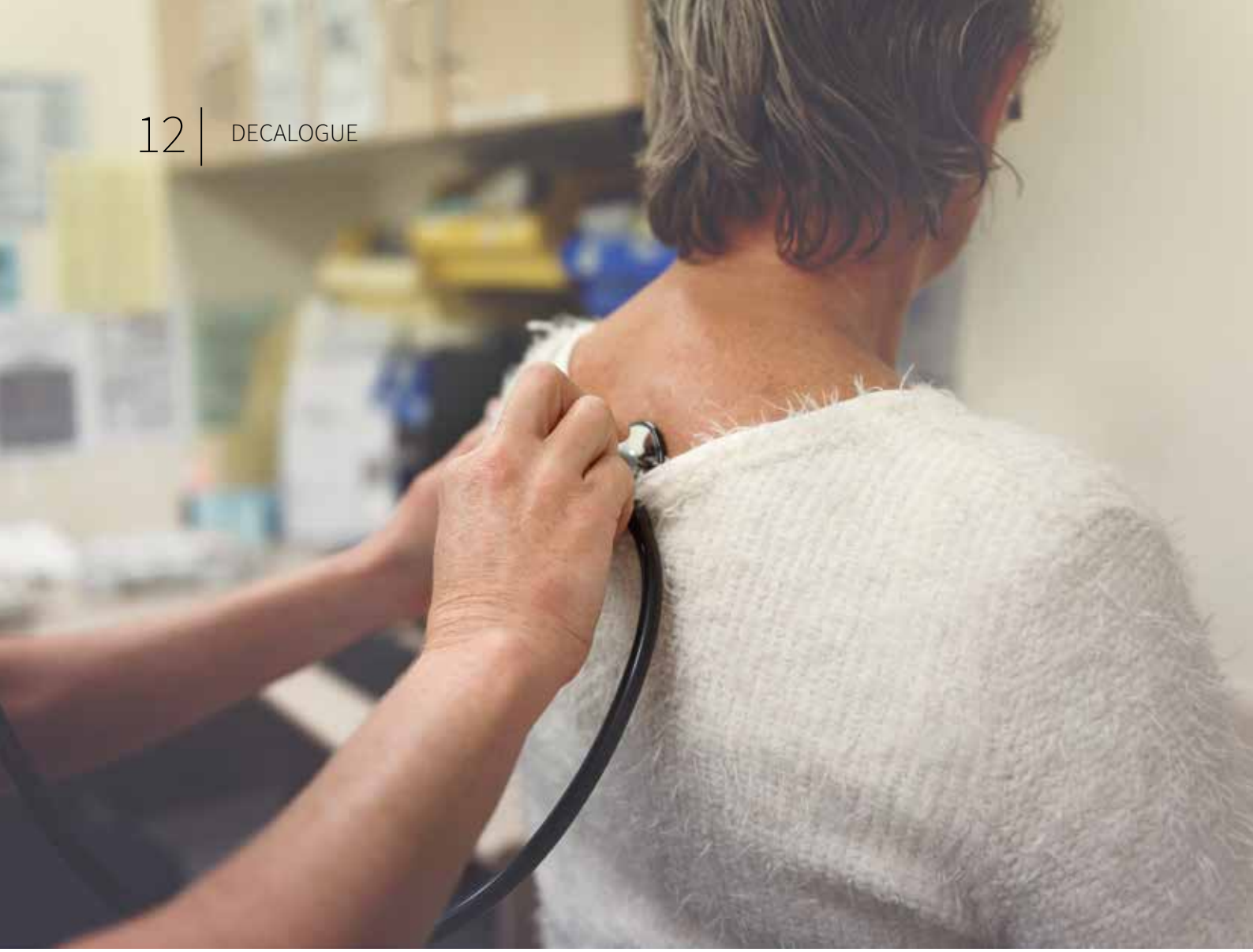
In our proposal, we suggest that the MHRA is well placed to take over the licensing of controlled substances with potential medicinal use for the following reasons.
The MHRA's mission statement is to provide a leading role in protecting and improving public health and supports innovation through scientific research and development. They are a world-renowned and respected regulatory authority which has previously been a "go-to" lead agency (rapporteur) within Europe to oversee the evaluation of medicine applications; a now defunct role since Brexit.

Furthermore, the MHRA is already setup to audit, inspect and license within the highly regulated environment of Human Clinical Trials. They have the prerequisite knowledge of the complexity of drug development to be able to grant the appropriate license to the sponsor at the appropriate time point. There are already mechanisms in place such as Scientific Advice in which a sponsor can explain in full their scientific data and development and regulatory approach in which controlled drug licensing decisions can be made.

We believe that with relatively small changes to the legislation and regulatory framework that the UK's already well-established R&D environment can benefit for becoming the "go-to" home for over 100 ongoing clinical studies with cannabinoids and many more clinical studies for other schedule 1 controlled substances (e.g. LSD, MDMA, Psilocybin) which are currently of high scientific and clinical interest.

1. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/670663/ACMD_Letter_-_Legitimate_use_of_controlled_drugs_research_and_healthcare_22_Dec_17.pdf

2. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1008195/Barriers_to_research_using_SCRAs_-_Report.pdf



THE NEXT STEP – SUPPORTING CANNABINOID PRESCRIBING IN PRIMARY CARE

DR. DANIEL COUCH, Medical Lead | The Centre for Medicinal Cannabis

Medical cannabis in the UK is not where we intended it to be. When the law was changed in 2018 to allow the prescribing of medical cannabis as a schedule 2 drug, many patients anticipated that they would be provided a new prescription to control their symptoms. Many expected that the transition from illegally possessed to legitimately prescribed cannabinoids would now be at least a partially open door.

Medical cannabis in the UK is not where we intended it to be. When the law was changed in 2018 to allow the prescribing of medical cannabis as a schedule 2 drug, many patients anticipated that they would be provided a new prescription to control their symptoms. Many expected that the transition from illegally possessed to legitimately prescribed cannabinoids would now be at least a partially open door.

A glance at the rates of prescription since show that this has not been the case. The Advisory Council on The Misuse of Drugs (ACMD) has found that in England between 2019 and 2020, 328 patients were prescribed a cannabis-based medicine in the NHS, with a further 537 prescriptions issued as a special since 2018.1 More recent data demonstrates that in 2021 at least 1,486 prescriptions were issued for a cannabis based medicine in England, although many of these may have been repeat prescriptions.2

But perhaps this should not be a surprise. It was clear from the outset that there are several immovable factors present in the medical and legislative landscape that prevent a novel medicine such as medical cannabis from being quickly adopted. These obstacles are slow and difficult to overcome.

Firstly, the high bar a medicine must pass prior to licensing is a challenge. The regulator – the MHRA – has a strong pedigree of licensing only medicines which have passed rigorous safety and efficacy testing. The hundreds of millions of pounds necessary to obtain this is often out of reach for the fledgling medical cannabis industry, and as such only a handful of licences have been granted. These make up all of the prescriptions issued by the NHS to date, the majority of them being Sativex and Epidyolex.

Without a licence and the necessary clinical evidence, NICE is unlikely to recommend a medical product for a given medical condition, and without this it is extremely unlikely that such a product would be prescribed within the NHS. Only Sativex, Epidyolex and Nabilone are licensed and recommended for spasticity in multiple sclerosis, two paediatric epilepsy syndromes and intractable nausea and vomiting. The majority of patients hopeful for an NHS prescription outside of these indications are very unlikely to receive an NHS prescription for such.

Patients however can be prescribed an unlicensed medical cannabis product as a "special" and when done so, this occurs largely in the private sector. However, this must be prescribed only by a GMC registered specialist, supported by a multidisciplinary team. That clinician must take personal responsibility for the prescription and any adverse events arising from it. Not only are the financial barriers to a regular private prescription beyond the means of most patients, but there are also just not enough specialists in the UK able to write these prescriptions.

As of 2021 there are 62,000 specialists in the country, each with their own clinical workload from which medical cannabis competes for space. Of these specialists, only a fraction will be working in a specialty with patients

that would potentially benefit from a potential treatment. It takes up to ten years to train a specialist doctor.3

A study by the CMC in 2020 estimated there are 1.4m people in the UK who would seek to be considered for a medical cannabis prescription. In the context that the recent BMJ rapid review suggested that medical cannabis could be used also to treat chronic pain, the UK simply does not hold the specialist faculty to assess this many patients within an appropriate clinical time frame.4

We are at an impasse. We are not able to rapidly train more or reduce the workload of existing specialists. We are not able to reduce the demand, and unable to generate the clinical evidence required to obtain the sufficient licensing to allow wider prescribing within an acceptable clinical time frame. Meanwhile patients suffer.

GPs frequently state that increasingly patients attend their practice to enquire about medical cannabis, but they are unable to help. Clinicians in primary care are not able to prescribe this medicine. Even if they could, they currently may not have the prescribing frameworks necessary to safely do so and monitor their patients for adverse events.

We are at an impasse. We are not able to rapidly train more or reduce the workload of existing specialists. We are not able to reduce the demand, and unable to generate the clinical evidence required to obtain the sufficient licencing to allow wider prescribing within an acceptable clinical time frame. Meanwhile patients suffer.

Paradoxically, despite being prohibited from prescribing by the 2018 regulations, primary care clinicians are in an excellent position to be at the helm of cannabis prescribing. For practicing specialists, whilst patients are admitted in hospital, they are reviewed daily. However once discharged from hospital specialists may see their patients less frequently and can go several months or maybe over a year before seeing them again. This is not conducive to the close clinical relationship required to satisfactorily dose a medical cannabis prescription in an unlicensed manner.

Contrast this with primary care. Family doctors and GPs, the first port of call for patients, see their patients much more often and are arguably more accessible. Furthermore, specialists have an in-depth knowledge of their specialism, but perhaps a limited understanding of wider medical issues. Primary care clinicians are trained across the breadth of medicine, and although they may not have the detailed knowledge of the assessment and management of complex conditions, they are better able to appreciate how a new prescription may impact conditions in other areas of medicine.

Patients may travel many miles to see a specialist, whereas GPs are on hand within their local community. This allows them to develop the skills and tender the clinical resources appropriate to their population, the very reason for the creation of local Clinical Commissioning Groups (CCGs).

Since their creation, CCGs have been the focus of innovation in delivery of healthcare. They question how to deliver care in the most efficient and effective way. CCGs therefore may be the best placed groups to decide how to adopt medical cannabis for their patents. They are the financial key holders in the UK, and perhaps they are the right authority to decide economically and clinically how medical cannabis is delivered.

GPs, for these reasons, are best placed with the financial and innovative backing of CCGs to assess and prescribe these medicines. But this will not come about without legislative change. This is the crucial point. Like any other medicine, cannabis has been handled extremely conservatively with a sharp focus on efficacy and safety. To allow GPs to prescribe outside of a clinical study the law would have to change again.

The original change in scheduling came only through immense political pressure to intervene to help save a life.

How best to bring about any further changes? How best to generate adequate research when existing progress has been slowly gained? How best to overcome the frustration many patients feel when they discuss this with their doctor?

There is a vast capability for research in primary care in the NHS. Perhaps within primary care lies the answer to the enigma of medical cannabis in the UK. There is a clear and apparent need for a clinical pilot study in primary care to assess the effects of community prescribing in a supported format. This would allow us to assess the impact of medical cannabis on our patient's quality of life, the economic effects of reduced referral to specialist care, and catalyse further studies and policy decisions.

If we want the landscape of medical cannabis in the UK to change to the benefit of our patients and prevent other jurisdictions from overtaking us we need to act now. Pilot schemes across Europe and beyond are leaving the UK behind in its understanding of how medical cannabis should be used. We have an opportunity to drive forward innovation and research, one of the pillars of the NHS, and drill down to the facts around medical cannabis.

There is a clear and apparent need for a clinical pilot study in primary care to assess the effects of community prescribing in a supported format.

The answer must lie with evidence and this evidence lies, it seems, in primary care. There is an immense capability for research in primary care that is not being used, and it is up to us to unleash it. Supporting the prescribing of medical cannabis within primary care is the obvious step forward the UK must take to widen access and improve the lives of our patients and communities.

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2. Dronabinol/Cannabidiol prescribing by CCG in England. Openprescribing.net https://openprescribing.net/chemical/1002020Y0/ Accessed 24/1/2022.

3. Medical staffing in England: a defining moment for doctors and patients. British Medical Association. July 2021. https://www.bma.org.uk/advice-and-support/nhs-delivery-and-workforce/workforce/medical-staffing-in-england-report

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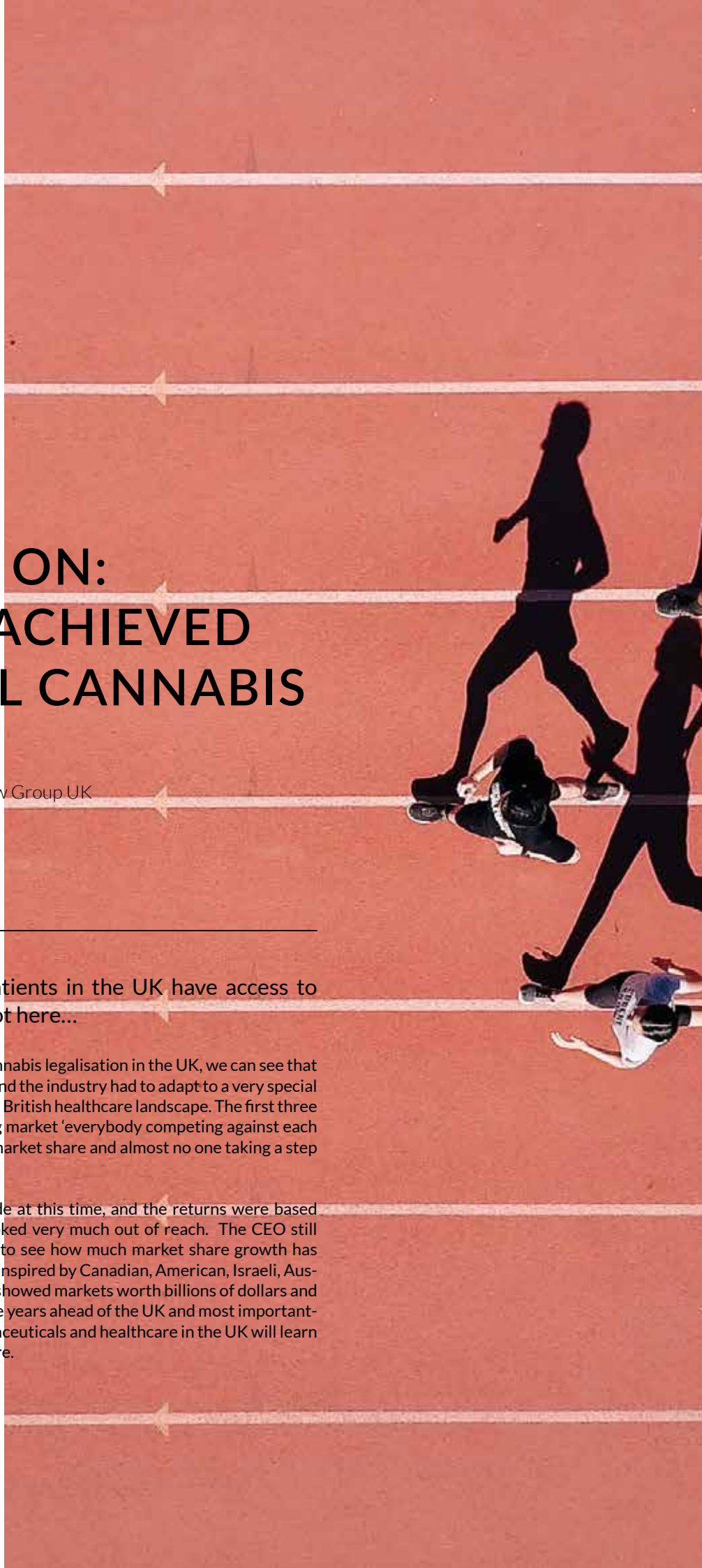

TEN YEARS ON: WHAT WE ACHIEVED IN MEDICAL CANNABIS

PIERRE VAN WERPEN, CEO | Grow Group UK

December 2028, 100,000 patients in the UK have access to medical cannabis – how we got here…

Looking back at ten years of medical cannabis legalisation in the UK, we can see that some important lessons were learned, and the industry had to adapt to a very special context for a new medical frontier in the British healthcare landscape. The first three years (2019-21) was good old emerging market 'everybody competing against each other'. Every supplier competing over market share and almost no one taking a step back and looking at the bigger picture.

Important early investments were made at this time, and the returns were based on growth curves that very quickly looked very much out of reach. The CEO still walking into the room and demanding to see how much market share growth has been achieved over the last quarter. All inspired by Canadian, American, Israeli, Australian and German uptake curves that showed markets worth billions of dollars and pounds. In reality all these markets were years ahead of the UK and most importantly, everybody who ventures into pharmaceuticals and healthcare in the UK will learn very painfully that nothing goes fast here.

Uptake of licensed, very clearly beneficial and sometimes even revolutionary pharmaceutical products is slow, no matter what you do, no matter what you try. The British healthcare machine works at a certain speed, hurdles are there by design to regulate any uptake of new medications and new technologies, even the licensed ones. And there we were, as new companies offering an unlicensed one; a whole raft of unlicensed ones. All lacking randomised controlled evidence, no UK pilot data, no clear dosing advice; flowers, oils, capsules, tinctures, sprays, all very alien to the average clinician, and crucially doctors who were skeptical, not yet trained on the endocannabinoid system, worried about their liability, worried about 'what if it goes wrong?'.

After the law changed in 2018 and prescribing became legal, this new industry was glaringly unaware of all the inner workings of the NHS and how prescribing could scale, whilst the NHS lacked understanding of cannabis medicines as a new option for managing symptoms of many diseases. We were supported by a small group of brave parents campaigning for medical cannabis for their epileptic children without structured evidence and constantly emphasising the enormous cost to them - thousands of pounds per month - as an argument for including it on the NHS. Perhaps an unhelpful argument to make; the fact that something is expensive makes NICE and the NHS nervous. And even with the two licensed products on the market, NICE saying yes to a cannabis-based treatment does not mean that the local NHS offers it. Local Clinical Commissioning Groups will create their own pathways and treatment algorithms based on local priorities and financials.

Most of those involved in the early medical cannabis industry had very little if any knowledge of the UK healthcare system, no understanding about how to communicate with healthcare professionals, little recognition of the compliance limitations of marketing in an unlicensed medicine environment and not helped by the fact that the market predominantly consisted of patients who were already taking cannabis for medical purposes supplied by a dealer.
In the early years, most of these patients were not aware that cannabis medicines had been made legal to prescribe, and even those who did were not aware of the obvious advantages of medical oversight, improved quality of products (pharmaceutically grown, not laced or contaminated) and yet the newly licensed industry could not talk to them. And we could not talk to the hundreds of thousands of patients in the NHS or private pain clinics that could benefit from medical cannabis but were unaware of the option, their doctor did not want to speak about it, and if aware they would not know how to get to it.

Most of those involved in the early medical cannabis industry had very little if any knowledge of the UK healthcare system, no understanding about how to communicate with healthcare professionals, little recognition of the compliance limitations of marketing in an unlicensed medicine environment and not helped by the fact that the market predominantly consisted of patients who were already taking cannabis for medical purposes supplied by a dealer.
We saw cheap marketing ploys to lure patients in with the promise of generating evidence via registries that had never been approved or submitted to the MHRA and were lacking in quality to the degree that neither NICE nor the NHS would ever consider their results, so professional doctor associations and societies simply ignored them.

Early 2022 all of that changed. More experienced professionals with experience from the pharmaceutical industry joined the medical cannabis industry: medical advisors and medical directors, trial design and importantly communications and marketing specialists who understood healthcare, the NHS and the private market. The established players in the market started to see reason. The calls for working together became louder and we started to truly collaborate.
Somehow in 2022 we reached a point where we started talking to each other, where the industry started thinking about working together to grow the market, to increase awareness with the general public, to start generating safety and efficacy data through proper MHRA and REC approved protocols with control groups.

It all started with the first ever MHRA and REC approved trial with an unlicensed cannabis medicine, launched in early 2022, from the LVL clinic with their partners Aurora and Grow Pharma (IRAS 304548). The trial was in non-oncological pain and garnered significant media attention. This not only increased general awareness but, with the data that were presented at the end of the trial, also gave clinicians more confidence in the safety and in the benefits of symptom management with cannabis medicines. During 2022 there was also a significant increase in clinics and their marketing activities, suddenly psychiatrists started to see the benefits of CBMPs in areas like PTSD, sleeping disorders and anxiety.

The narrative started to shift from 'the NHS has to do this' towards simply focusing on the patients that could be helped with medical cannabis and how they could get access for example through their GP referring them to a clinic or from their NHS specialist writing a private prescription for them because they too started to see the evidence and rationale behind medical cannabis. The industry was working together, clinics were talking to each other. All finally understanding that the market was big enough for all of them and there would be an upside in bringing in new 'cannabis-naive' patients instead of competing for the pool of existing ones.
As a result of conversations between all parties, acknowledging that the goal was simply to provide a stable and controlled pathway and system for widespread medical cannabis access, we launched new educational initiatives that addressed the actual needs of the market. Doctors wanted the knowledge and security to be confident that what they were doing was safe. Many doctors were wary about the opioid crisis and started to be even more careful with new medications, including cannabis medicines, rather than the opposite. These initiatives created a much more positive environment.

Supported by the data we educated specialists about the endocannabinoid system and how to prescribe CBMPs. We educated GPs and pharmacists to think about medical cannabis and importantly, we found a way to explain to

the public the difference between CBD (bought in health stores and online) and medical cannabis. We also found ways to educate MPs and regulators about the difference.

People also gradually learned about the limitations of CBD. Yes, it improves sleep and anxiety, but for pain relief, MS, Parkinson's, epilepsy, IBD, oncological pain, for end of life support replacing high dose painkillers, you need THC containing cannabis treatments with medical oversight, high quality products, supported by data, prescribed by an appropriate medical professional and dispensed through a licensed pharmacy. We all finally started to see that this was about patients actually getting prescriptions, patients and doctors being educated about the right medicine for the symptoms they were trying to manage. We now knew much more about these medicines, from the second they were grown to how all the different administration forms worked (flower, vapes, oils, inhalers, capsules, patches) to how they were being used by patients day-to-day. We were able to improve the lives of thousands of cannabis naive patients whose symptoms were often much better managed than with conventional high dose and addictive painkillers that would stop working after six months if not stopped sooner due to their side effects.

We got the narrative right, started talking about the benefits in symptom management, started sharing the data and looked at making small, incremental steps. The first step was on-boarding more specialists in more disease areas. The second was NHS doctors accepting the potential benefits and, instead of their patients using a street drug dealer, they would refer them to a clinic. Some began writing private prescriptions for these patients so they could access legal products. The third step saw more GPs referring patients to specialists for CBMPs and importantly being open to having an informed conversation about medical cannabis with their patients and not being dismissive and shrugging their shoulders if asked for advice about it.

We got the narrative right, started talking about the benefits in symptom management, started sharing the data and looked at making small, incremental steps.

Shifting attitudes among clinicians was key. Not sending people to buy retail CBD but actually being able to have a conversation and explain the difference between CBD and medical cannabis. That was a big thing in 2023 when we got to over 25,000 patients. Eventually GPs wanted to start prescribing themselves for certain symptom clusters. They were tired of writing prescriptions for high dose painkillers with significant side effects. By mid 2025 we had reached 70,000 patients in the UK. The evidence was getting increasingly compelling, several proper clinical trials were starting to report data and some private insurers were now including CBMPs in their packages and some even started advertising about it to potential clients looking for private healthcare policies.

By the middle of the decade, the UK had finally fully embraced cannabis medicines as a treatment option for patients with chronic pain, pain related to cancer or other diseases and symptom management in Parkinson's, epilepsy, MS, endometriosis and others. Sleeping disorders, PTSD and other mental health issues were regularly being addressed and treated with cannabis medicines, a significant percentage of illicit market consumers had converted to having medical oversight of their treatment instead of going to their street dealer. Many patients who were cannabis naive and on high dose painkillers and opioids had managed to reduce those and replace them with cannabis medicines, also reducing the number of side effects and deaths related to high dose opioid use. Medical cannabis prescriptions were still private, but the NHS had allowed and endorsed these prescriptions to be written during NHS consultations. The result of all these changes meant that by 2028, ten years after the law was changed, 100,000 patients in the UK are now regularly using cannabis medicines and the evidence from all prescribing is being collected properly in an official national registry supported by the Department of Health and the MHRA. Public awareness and acceptance also with pharmacists, nurses and other healthcare professionals has increased and there are now hundreds of prescribers across the country.

This is how we got here. It happened because we started talking to each other, because we understood how to talk to HCPs and patients. Pharmacists got involved in their medication reviews with patients. Prices have come down for patients to more affordable levels, supply is consistently reliable and many different modes of administration and cannabinoid ratios are available to address different patient needs.

The result of all these changes meant that by 2028, ten years after the law was changed, 100,000 patients in the UK are now regularly using cannabis medicines and the evidence from all prescribing is being collected properly

Unlicensed medical cannabis is not on the NHS yet in 2028, but there has been talk about certain limited indications to run a national pilot and see how it goes. With decreased cost and the positive evidence around it there are already areas where the use of CBMPs as part of the pathway will reduce cost for the system and that is what mobilises the NHS and their commissioners. Importantly for future long-term growth and innovation, training and education about the endocannabinoid system are now part of the curriculum for medical and pharmacy students.

Looking back from 2028 we should be proud of what we achieved together as an industry and how we did it. We focused on the bigger picture. We focused on the patients and on the healthcare professionals who take care of them. We understood we had to focus on the accumulation of evidence to drive and create the right climate for changes to the public system, rather than trying to change the system by force.

TAKING A RISK-BASED APPROACH TO MEDICAL CANNABIS ACCESS

HARI GULIANI, Head | Colombia Care International

A common question amongst cannabis industry professionals in the UK recently has been 'how many patients in the UK have a cannabis prescription?'. But that is the wrong question. We would gain a much better understanding of the success of our sector and the regulatory environment by instead asking 'what percentage of people using cannabis for a diagnosed condition source it from the legal market?'

We lack published data on the volume of unlicensed CBMP prescriptions issued privately in the UK. Whether you think that there are 5,000, 10,000 or even 50,000 patients with a cannabis prescription in the UK in January 2022 – that still means that at least 95% of those using cannabis for medicinal reasons do so from the illicit market, based on opinion poll survey responses.

This shocking reality means there is a much greater ongoing risk of harm than was intended from the 2018 rescheduling regulations, which were designed to provide a safe and legal prescription route for cannabis-based products, and so control the risks that might result in harm to patients.

The risks we run today

The problem with illicitly sourced cannabis is the lack of transparency in the supply chain and any quality management and quality assurance process in place. While medicinal cannabis cultivation and processing includes tests that should systematically eliminate the presence of bacteria, fungus, pesticides and residual solvents in products, illicit market supply chains do not have the same level of oversight. Where there are issues with legally produced medicines, there are reporting systems in place and protocols designed to systematically address these.

According to a 2019 report from the European Monitoring Centre for Drugs and Drug Addiction, the UK produces large quantities of illicit cannabis for the domestic market alongside the quantities originating in Morocco, Albania and other countries. Other recent reports estimate the UK's production at being upwards of 250 tonnes a year, raising concerns about the widespread use of rat and insect poisons in illicit grows with residues present in the products being consumed.

According to these reports, synthetic plant growth regulators commonly being used are banned from food crops given the links to them as a cause of cancer, liver problems and infertility. Illicit grows often occupy unoccupied spaces, with news outlets reporting seizures of illicit cannabis cultivation in locations such as the basement of a commercial building in the City of London, a former Argos store in Liverpool and sites in Welwyn Garden City. Images of these sites often show stained walls and environments that suit mold and other contaminants. The challenge of choosing buildings based on speed of set up and low likelihood of disturbance and detection becomes clear: quality just is not front and centre of mind in these operations.

A quick search of random illicit market cannabis samples submitted to WEDINOS

– an organisation that enables the collection and testing of psychoactive substances aimed at disseminating harm reduction advice – highlights numerous examples of undesirable contaminants including heroin, paracetamol, noscapine, aspirin, ketamine, MDMA and in some cases, synthetic chemicals (the impact of which cannot be separated from the widely reported associations with psychosis).

Can we continue to tolerate this risk of harm to patients, many of whom have been looking to avoid traditional narcotics in the first place? How can doctors manage drug interactions effectively when it is unclear what patients are putting into their bodies? A doctor can only use the information that is available to them to make a decision – but what percentage of patients using cannabis illicitly feel comfortable sharing this with their doctor?

It seems safe to assume that very few patients discuss use of illicitly sourced cannabis compared with medicinal products recommended by a doctor. We have to change this dynamic dramatically and create an environment for patients and their healthcare professionals to work together to access products that have been carefully assessed from a quality perspective, and which make sense for that patient.
So what is the answer? The patient access conversation in the UK to date has focused on NICE and their perspective that the cost-benefit analysis has not been established to support widespread use of medicinal cannabis in the NHS. However, there are alternative approaches to the status quo of all-or-nothing.

Two ideas to widen access and help reduce risks

First – if NHS doctors were allowed to prescribe medicinal cannabis, purchased by the patient themselves in all but the most severe cases, we would materially improve the risk profile noted above. Without adding any cost burden for the NHS and taxpayers, we would stimulate important conversations about patient health within the doctor's surgery. There is precedent for this approach. NHS dental services allow patients to self-pay for additional services. Perhaps more relevant, is the example of Viagra over twenty years ago.

The British Medical Journal noted in 1998 the challenge faced by Viagra: there were real concerns about the cost impact of introducing this for all legitimate patients who wanted access to it. One parallel between Viagra and medicinal cannabis is the fame and media interest in both products, far ahead of the typical route to prescribing for medicinal products. Demand simply far outstripped supply and ran ahead of clinical experience. This culminated in a set of regulations where GPs were permitted to write private prescriptions for patients to purchase Viagra with their own money. Would it not be better if we did the same with medicinal cannabis?

One parallel between Viagra and medicinal cannabis is the fame and media interest in both products, far ahead of the typical route to prescribing for medicinal products. Demand simply far outstripped supply and ran ahead of clinical experience.

What bears more risk: a patient alienated by modern pharmaceuticals, purchasing unknown substances from a street dealer in the unregulated market; or an NHS doctor engaging with a patient about their healthcare and their options, including self-paid medicinal cannabis, sourced from a licensed UK pharmacy?

We know that patients would welcome this option. In October 2021, Columbia Care International asked over 3,000 people living in the UK if they would like to be made aware of privately-paid medications not paid for by the NHS when visiting their NHS doctor. A large majority, 82%, said yes. This demonstrates a clear appetite among the British public for alternative treatments and an openness to pay privately for them.

Was the Viagra story a success? According to an article in The Times in 2007, Alex Gourlay, then Boots health-care director was reported to estimate that

10% of the three million men suffering erectile dysfunction were being treated. The article in question was reporting the announcement of a pilot scheme to improve access. Boots started a Patient Group Direction pilot in Manchester. Such was the success of this programme that by 2010, Tesco could do the same from its 300 pharmacies.

GPs were permitted to write private prescriptions for patients to purchase Viagra with their own money. Would it not be better if we did the same with medicinal cannabis?

By 2017, the MHRA allowed an over-the-counter version to be sold, called Viagra Connect, and patient uptake further expanded. Risk management remains front and centre of the Viagra story today, with a pharmacist reviewing answers to a set of questions about the patient's health and medication to determine whether there is an acceptable risk profile for the use of the drug. The product's website contains a prominent link to the MHRA's yellow card scheme for reporting side effects, enabling centralised oversight of the ongoing risks associated with that product. The end result is that the concerns flagged initially by the BMJ have been appropriately addressed: the financial burden does not sit with the state, but risk is being appropriately managed by healthcare professionals.

Furthermore, since 2017, and perhaps more importantly since the COVID-19 pandemic, there has been a material improvement for patients in the ease to consult a GP, with the move to video consultations. It does not seem far-fetched to expect that we might see a higher number of people using GP-led services now than was possible a decade or more ago, especially given the stigma or embarrassment of speaking to your village GP about sensitive subjects. Second – for some patients, the time and effort involved in accessing the private market does not always make sense, such as patients in a palliative care environment. Often family members will do anything to help their loved ones, including turning to the illicit market for cannabis, which can be a quicker and even less daunting route to pursue. How can this make any sense? Most patients say it does not. Eight out of ten people who took part in Columbia Care International's survey thought it was wrong to restrict healthcare professionals' use of the cannabis plant as a medicine because of old fashioned views of cannabis as a recreational drug. This restriction means patients are left with no choice.

In defined circumstances, where healthcare professionals and carers are deeply knowledgeable about an individual patient's care, Patient Group Directions (PGDs) have been used to improve overall care to patients. A PGD for medicinal cannabis might allow healthcare professionals providing palliative care another option for their patients, when they consider it appropriate, based on individual patient needs including quality of life.

The current guidance makes clear that PGDs are intended for use with drugs that have achieved marketing authorisation and that unlicensed and special manufactured medicines should not be included. Changes would need to be made for this framework to improve access to medicinal cannabis, initially for particular types of patients. Further, to meet the guidance issued by NICE, a protocol would need to be developed with specialist clinicians who could determine appropriate parameters and flag where further clinical assessment would be required, but given increasing adoption by leading clinicians this is not unrealistic.

Any healthcare professional who has worked in a palliative setting knows the material impact of opioids on these patients. When you compare the risk profile of opioids and medicinal cannabis side-by-side, our current approach of driving people to the illicit market while making opioids readily available looks misguided.

In conclusion, the question we really should ask ourselves is whether the current framework does the right thing for patients with real unmet healthcare needs. By making patient access so difficult, in a country where so many claim to be accessing cannabis for medical reasons, this status quo creates more risk than we should accept by driving patients to the illicit market.

The question we really should ask ourselves is whether the current framework does the right thing for patients with real unmet healthcare needs

The answer is not to blame the NHS or direct our weight of expectation to NICE, who are both playing very important roles. However, we do need to change the theatre of conversation from the street corner to the surgery and to allow patients to purchase, from their own pocket, the medicines that help them, both legally and safely in the knowledge that they are getting what they expect.

What should give us hope is that the British healthcare system has previously created mechanisms that balance the needs of patients, the needs of the nation's finances and the need to ensure risk is managed by the appropriate healthcare professionals. What excites me is that there are specialist doctors who are advocating for the use of medicinal cannabis for some patients.

We need to change the theatre of conversation from the street corner to the doctor's surgery

Now it is on industry to engage constructively with government and regulators to find a pragmatic way forward to improve legal access. The two proposals in this paper should stimulate this conversation and, ultimately, drive better access for patients to a medicinal product that continues to change lives daily.

1)EU Drug Markets Report 2019, European Monitoring Centre for Drugs and Drug Addiction

2) https://www.vice.com/en/article/3aqak8/illegal-cannabis-farms-are-making-the-climate-crisis-worse

3) https://www.wedinos.org/

4) BMJ 1998;317:824

5) The impact of Covid-19 on the use of digital technology in the NHS, Rachel Hutchings

6) https://www.nice.org.uk/guidance/mpg2

EXPORT-LED GROWTH FOR THE UK MEDICAL CANNABIS INDUSTRY

JONATHAN HODGSON, CEO | Rokshaw Laboratories
PIERRE VAN WEPEREN, Managing Director | Grow Group UK

The unlicensed Medical Cannabis market in Europe is forecasted to grow to between £3bn and £5bn. Although different estimates vary, none of them come in below £3bn by 2025. Towards the lower end estimate, the German market alone will be worth close to £1bn with France, the UK, Italy, Poland and potentially Spain contributing to the total.

Over the past 12 months, countries all over the world have begun to liberalise medical cannabis. During 2021, trial access to medical cannabis began in France and the first pharmaceutical cannabis medications became available in Ukraine. It is expected that governments around the world will continue to legalise medical cannabis for patients who need it, and it is important that the UK is setting a standard and maximising the economic value of this emerging healthcare industry.

The UK industry today

Despite being several years behind Germany and with different regulations, the UK has already a quite established internal medical cannabis industry that imports finished products and also manufactures for the local market from imported extracts and concentrates. In the UK, all manufacturing activity is performed by specials manufacturers license holders and wholesalers need a so-called WDA license for the distribution of medicinal products for human use.

The main companies involved in medical cannabis are Rokshaw Ltd (part of EMMAC Life Sciences Group), and IPS Ltd (part of Grow Pharma Ltd) as importers, wholesalers and distributors. The main foreign companies currently exporting into the UK include Althea (Australia), Spectrum (Canada), Aurora and Tilray (Canada).

We estimate the current value of the internal UK unlicensed medical cannabis market to be approximately £15m+ per annum with employment for several hundred people. This excludes the licensed pharmaceutical market with products like Epidyolex from GW Pharma and their global reach. It also does not take into account the jobs in academia involved in medical cannabis research and the research money that is put into this area. It also excludes the value to the conference and events industry, consulting, law firms or PR and other agencies that work in this area.

The Volteface report entitled 'The new leaf: beyond Brexit, countering COVID', estimates that the UK's medical cannabis market could reach up to £1.2bn, creating 41,000 direct jobs and a further 17,000 supporting jobs. With Brexit in place, it creates the perfect opportunity for the UK to become the centre of European cannabis and add tens of thousands of jobs to that number. Another report by Maple Tree consultants and Mackrell solicitors from April 2021 stated: "There is a potentially huge job market for cannabis related industries, which require farmers, researchers, production workers, accountants, lawyers, IT specialists, financial experts, researchers, and lab technicians to name a few."

The European market as a whole has the potential to be very significant, given the growth of legal access schemes in many European countries. In the literature, the 1% rule about the share of the population that would benefit from medical cannabis seems to be quite accepted and is being borne out – Israel with a population of around 9 million had 108,013 registered medical cannabis users in November 2021 according to the Israeli Ministry of Health. The legal frameworks across Europe differ per country. That said, there is significant opportunity in current and soon to be legalised medical cannabis countries to explore as export targets for the UK industry. With a population of 448 million in the EU27 (excluding the UK), there could be 45 million people using cannabis in Europe for medical purposes if access was enabled everywhere.

Whilst the UK has seen a significant increase in patient access from a few hundred patients in early 2020 to an estimated 7,000 by the end of 2021 (authors' data), we are still at the start of this industry. The economic growth potential for the UK and the rising demand in the European market in the coming years, is what should make the UK government keen to support the industry. One of the most important early supporting measures would be to permit the domestic industry to export.

Scaling the UK's nascent cannabinoid industry

Presently, export of unlicensed cannabinoid medicines is not permitted in the UK. Domestic patients receive finished products from UK-based companies, but the source material is imported – mostly from Denmark, Portugal, Canada or Australia. These other legal markets can reap the benefit of exporting quality cannabis to the UK, but the British industry is prevented from doing the same.

The current restrictions on importing would need to be adjusted to allow the import of material in larger quantities for export at a later date. It would not be an issue to track this and continue with the current system for import for local UK patients. The latter currently requires a justification for the quantity such as a clinical need letter, when exporting this would not be possible as it is unlikely we would know the exact clinic or country even requiring the product.

Denmark, Portugal, Canada or Australia [and] other legal markets can reap the benefit of exporting quality cannabis to the UK, but the British industry is prevented from doing the same.

If exporting of CBPMs were allowed there is potential for economies of scale in the production of these medicines whereby average production costs would fall as outputs increased. Currently, the production of oils is in very small batches and unautomated, like with all specials they are labour intensive in paperwork and production, checks, release, etc due to the small batch sizes. Exact efficiencies would depend on batch size which will also be reliant on having extended shelf life.

With export permitted, between companies we would certainly invest in the equipment and stability studies to upscale this product. Quite quickly we could scale up to 50L, then 100L and 200L batch sizes and we would estimate a 70% saving in production costs. That in return would also make local production for the domestic market more efficient and affordable, recouping profits that are now being made by foreign companies exporting their finished oils to the UK.

If the regulations were to change to allow export of product (requiring MHRA and Home Office consent), the current UK-based medical cannabis industry – and by extension patients – would benefit significantly. If exports were permitted and over time, the UK could secure just 5% of the European market – a conservative estimate – then exports could be worth over £150million annually. If import, export and scale-up is feasible, the majority of the savings would be passed on to help lower prices for patients and the remainder would be reinvested as this market grows and will need further development.

There seems to be no clear reason for the two tier treatment where CBMPs are prevented from being exported from the UK today when other specials can. This seems unfair and unjustified. Speculations point towards the fear that product might be diverted to the illegal market but processes can be put in place to monitor that and the UK medical cannabis industry would be well aware of its responsibility.

If import, export and scale-up is feasible, the majority of the savings would be passed on to help lower prices for patients

The UK as a medical cannabis leader

As the global cannabis sector expands in the decades ahead, the UK is unlikely to become a leading centre of cannabis cultivation. However, where it can win market share is in developing high quality finished products, and cutting-edge research to support clinical practice. The UK has the research and innovation clout to become a leader in the development of cannabinoid treatments.

New medicines developed in the UK should not just benefit British patients. By allowing the export of finished products, the UK's medical cannabis industry could easily expand into the European market and become a major player in that larger market, thereby generating significant additional revenue for the UK and creating tens of thousands of extra jobs in the process.

The UK has the research and innovation clout to become a leader in the development of cannabinoid treatments – and new ones developed in the UK should not just benefit British patients.

As well as attracting local and foreign investments into the industry, the UK should aspire to become Europe's medical cannabis knowledge hub that would also attract substantial investment in conducting clinical trials from the UK and thereby also drive IP and academic knowledge that in turn can be exported or used to attract investment. There is thus a strong case for allowing export of unlicensed medical cannabis products from the UK, in a move that would support the domestic industry to scale and achieve greater efficiencies, tap into important overseas markets where patient demand is rising, and help to build the UK as a hub of medical cannabis knowledge and innovation.


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MEDICAL CANNABIS AFTER THE PANDEMIC: ADDRESSING LONG-STANDING INJUSTICES AND HEALTH INEQUALITIES

DR. AYESHA MIAN, Medical Advisor | The Centre for Medicinal Cannabis

The cannabis plant is among the most versatile in the world. For millennia, it has been used across cultures as a way to socialise, provide food, textiles, shelter and as medicine. The endocannabinoid system that the plant interacts with is so essential to life that it can be found in every vertebrate. And yet in the last century we have erased the history of cannabis and demonised its use.

It has been weaponised against the poor, people of colour, women, children, and those who are 'different'. A plant has become a tool of oppression. By driving it underground, prohibition has caused untold harm in society and we have lost decades worth of scientific discovery. It is an injustice on many levels.

The pandemic has worsened pre-existing health inequalities. In the UK, Black and minority ethnic groups (BAME) consistently had higher rates of mortality compared to white counterparts. The recent Build Back Fairer report concluded: "[The] most damaging impacts have been for young people, low paid workers, BAME groups, disabled workers, women, part time workers, and the self employed." The North, the Midlands and coastal towns in the South of England host the areas of most deprivation. These regions and communities struggled before the pandemic, but COVID-19 exacerbated their challenges, a result of a decade of disproportionately higher cuts to local services in areas of greatest need.

The pandemic created a syndemic which "exists when risk factors or comorbidities are intertwined, interactive and cumulative—adversely exacerbating the disease burden and additively increasing its negative effects." Addressing the complexity of these associations are now better recognised by many healthcare agencies. Focusing on the Social Determinants of Health (SDH) (see box 1), cross-sectoral integrated approaches to reducing inequalities, have become core priorities in several national agendas, including the NHS's new Long Term Strategy.

Without understanding the impact of drug policies on SDH, the newly emerging UK medical cannabis industry will continue to exacerbate the inequalities we are trying to overcome. Areas and people most affected by the pandemic are also most easily targeted by violent gangs related to drugs crime. They are being deprived of the opportunities, educational, social and economic, to develop the resources and skills needed to thrive in a technologically advancing world. Practicing in the field of medical cannabis requires a high skill set and patients require access to medicine. With expensive private clinics, many people most impacted by drug control are excluded from accessing cannabis's therapeutic benefit and left unprotected from its illicit market harms.

Without understanding the impact of drug policies on social determinants of

health, the newly emerging UK medical cannabis industry will continue to exacerbate the inequalities we are trying to overcome.

Globally, import of medical cannabis from developing countries where production costs are cheaper poses risks of exploitation of local communities and economies. Even in the UK, Vietnamese people, especially children, are trafficked into slave labour on illegal cannabis farms. Young people across the country are easily recruited into county lines drug trafficking networks when faced with dwindling educational and economic opportunities.

Dame Carol Black's recommendations of her independent review informing the recent Ten Year Drug Strategy acknowledged the need for a 'whole systems approach' tackling the profit-driven harms of illicit drugs trade through prevention. However, it does not recognise that many people who engage with the illicit market for cannabis use may be among the estimated 1.4 million patients caught in the middle of the drugs trade. These people put their health and safety at risk while engaging with the illicit market to access their medicine, because private clinic options are too expensive and hard to access. This is unacceptable.

Black, Asian and Minority Ethnic (BAME) people who are four times more likely to encounter law enforcement in terms of being stopped and searched for drugs. According to the pressure group Release: "Low level cannabis possession offences drive this disparity, with an estimated one in three of all police searches for cannabis possession alone." There is almost no research into the effect of drug policy on medical cannabis access for BAME and other groups disproportionately affected by prohibition.
Lord Simon Wooley argues for more advocacy from doctors on this issue, writing in the British Medical Journal: "In its implementation, prohibition has provided the opportunity and alibi for decades of harassment and over-policing of black communities. It provides one of the very sharpest tools in the box of systemic racism: enabling police to use the flimsiest of pretexts to search and arrest black people, thus allowing wider society to associate black people with all the violence and exploitation that prohibition creates in the drug supply chain. It also intersects with poverty, exclusion, and health inequalities, creating cycles of harm that become hard to break."

The reawakened interest in cannabis as medicine is failing to develop an industry aware of its past and the urgency to incorporate equity and fairness. There is almost no attempt to address the British historical narrative in shaping the inequalities we see today (see box 2). If this is analysed and incorporated into regulation and industry development, we will avoid past mistakes and can create solutions for equitable progress. The medical cannabis industry in the UK struggles to platform diverse communities, including patients and advocates, most affected by prohibition. There is an asymmetry of knowledge between patients who have researched and utilised cannabis medicinally from illicit sources, and medical and industry professionals relatively new to the space.

To rapidly advance progress in the industry, it is imperative to support patients and incorporate the knowledge they have into research for better therapeutics. They should not be at risk of criminalisation and instead integrated into an equitable reform of regulation. Human rights lawyer and key proponent of the knowledge equity movement Baljeet Sandhu states "If we don't think about the knowledge that is present in all our communities we will continue to privilege the few as knowledge producers and see them as having a larger stake in how we design the future."

The complexity of studying endocannabinoids lies in their interaction with every system in the body. Difficulty translating this complexity has led to widespread misinformation on purported benefits and risks. Many medical cannabis companies have tried to fill the knowledge gaps among medical professionals. Unfortunately, this encourages cynicism against undue private influence over prescribing. It also complicates access to knowledge for health professionals who may be time and money restricted, hesitant to invest in costly unregulated information. The companies have good knowledge of their products but there is a need for a regulatory body that can impartially assess how this knowledge is integrated into medical learning. It is vital to develop a standardised, professionally accredited curriculum that consolidates global knowledge and best clinical practice.

The UK is also at risk of missing out on health innovations based on plant therapeutics. Plant based medicines such as cannabis provide an opportunity to pilot innovations in integrated, personalised healthcare. Progress comes through experimentation, and we must dare to explore new avenues to maximise health and wellbeing. We must be allowed to fail safely.

It is vital to develop a standardised, professionally accredited curriculum that consolidates global knowledge and best clinical practice.

In terms of production and supply, diverse participation in the knowledge and policy making process is the goal and should be encouraged through an Institute of Pharmacognosy. This institute can issue guidance for the fair production, development and distribution of medical cannabis among other plant-based medicines. Knowledge networks based on diverse collaboration can support oversight into technologies utilised in drug development, such as ethical Artificial Intelligence. It can provide additional support for new treatments, and improving accessibility into the industry, supporting skills development and technical assistance. 18.

Through equity-based internships and mentorships at medical cannabis companies and research groups it is possible to solidify an industry pipeline. Support for local enterprise is also key. Leveling the playing field for small and medium businesses in the UK should include extra support for people who face disproportionately higher barriers to access in the context of enabling social and economic equity.

Developing processes to ensure minimal environmental impact from production and distribution will ensure a fair chance for British based businesses to

compete locally and internationally, for example by enabling more domestic cultivation. Communities most affected by drugs should also have priority in shaping the industry. To reduce the harms and maximise the benefits around cannabis, all stakeholders should be involved in developing regulation.

The UK has a unique advantage to establish an industry based on the wisdom of lessons learned from past mistakes. It can once again lead in scientific discovery around plant-based therapeutics. Emerging markets around the world lack reconciliation between past and present, licit and illicit. Now the UK has an opportunity to become a global leader in modeling equity-based cannabis regulation. We should establish a legacy that future generations can be proud of. This is our chance to build back fairer.

Box 1: What are the Social Determinants of Health?

The social determinants of health (SDH) are the environmental, social and economic factors that influence the health of populations. The WHO outlines the SDH and their impact as "the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life. These forces and systems include economic policies and systems, development agendas, social norms, social policies and political systems. The SDH have an important influence on health inequities - the unfair and avoidable differences in health status seen within and between countries. In countries at all levels of income, health and illness follow a social gradient: the lower the socioeconomic position, the worse the health." See: https://www.who.int/health-topics/social-determinants-of-health

Box 2. The British Empire had a major role in controlling cannabis trade and shaping modern day views on cannabis.

In the 1800s, among colonialist adventurers seeking to bring back treasures and knowledge from the Empire, doctors were first introduced to its medicinal properties while in India. They had observed its longstanding cultural use in both social ceremonies and as a medicine. The Lancet and other medical journals published on its therapeutic applications, while recognising issues with inconsistencies of preparation, since the late 1800s. It was found in different preparations utilised for a number of diseases from tetanus and epilepsy to gastrointestinal disorders and menstrual cramps. The British originally imposed taxes to profit from a well-established cannabis trade, eventually moving to take full control over its production and supply. Overregulation and policies disinterested in the wellbeing of the community it governed created a black market and the birth of an ill-conceived association between cannabis consumption and mental health issues. The lunatic asylums in India, where clerical deficiencies led to miscategorising of patients, inflated the association of cannabis and burden of mental health disease on the local Indian populations. Arguably, this could be seen as the foundations of the modern-day misconceptions of cannabis use as a definitive cause for psychosis. As western medicine moved away from plant-based therapeutics there was a lack of further scientific inquiry for many decades. Ongoing racism towards people who continued to use cannabis came after the war. Many Immigrants from former colonies brought back cannabis which became an indirect way to marginalise and target these communities. See: J. Mills, 2005. Cannabis Britannica: Empire, trade and Prohibition 1800-1928)

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THE THIN BLUE LINE OF POLICING CANNABIS

CARLY BARTON, Founder | Cancard

The general attitude of law enforcement in the UK around the consumption of cannabis has significantly changed in the past two years. Despite there being a lack of Home Office or police guidance around the law change in 2018 that brought about a clinical access route for medicinal cannabis, policing approaches are evolving. Cancard – a policing tool that aids use of discretion for cases of simple cannabis possession for medicinal consumers – has seen a dramatic uptake in engagement from police forces who have felt the pressure of criminalising bona fide patients for whom the current lawful access route is not adequate.

Carly Barton, Cancard

The illicit market itself has also adapted since the 2018 law change and in many ways is providing a service that many medical consumers are choosing, over an expensive, private clinic pathway. However, criminalisation of cannabis patients continues, and will persist unless changes are made to accommodate existing users who are outside of the present legal access pathway.

Patient demand and current access challenges

The latest and most in-depth data we have available with regards to medicinal consumption was conducted via a YouGov survey in 2018. This research showed that 1.4 million people in Britain report consuming illicit market cannabis to treat a medically diagnosed condition. If we compare the condition lists that are currently being covered by private clinics in the UK against the list of reported conditions surveyed patients are using cannabis for, we can safely estimate that a little over 1.1 million of these people would likely already qualify for a private prescription based on their diagnosis

General cannabis consumption may be on the rise. This could be due to laws changing in other countries and also due to a better understanding of its medicinal properties. Policing this is becoming problematic. In fact it could be argued that ongoing prohibition and the current tight legal regulations around prescribing cannabis medicines has generated a perfect space for organised crime to thrive, by doing little to provide adequate legal access but managing to legitimise the medicinal benefit of the plant, thus actually encouraging illicit suppliers and giving more confidence to users.
The current state of the illicit cannabis market is fraught with contradiction. Demand is currently being met by two very different types of supplier: those involved in organised crime and those who would be considered to be specialist caregivers in many other countries.

Organised crime in the illicit cannabis market is something that negatively impacts all our communities. This comes with rising levels of violence, friction for control of territory, child and human trafficking, theft of electricity, anti-social behaviour in housing areas, a pathway for organised European (mainly Albanian) gangs. Patients are very aware that this is an issue and generally would much rather not engage with any market that is causing harm.

On the other hand, particularly since international law changes, access to educational courses, better research and international patient advocacy, the illicit market has an army of experienced suppliers who are nothing short of specialists in this area. Many of these suppliers charge little in the way of fees for their service. They will often provide clean, safe cannabis that has been grown organically, extracted, and blended to a ratio to suit the condition that is being treated. These caregivers are forging a path to an underground market that is often much more sophisticated than products available in dispensaries in legal countries.

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In terms of ease of access within this market, patients will often request a 'menu' of available products via smartphone messages. These products will be a mix of flower, concentrates, oils, topicals, capsules and edibles and will often contain information about genetics, how the plant was grown, terpene profiles, likely effects, and occasionally lab test results. They will often receive a same or next day service to their front door, ongoing support, advice and a range of other products available to try.

Estimates suggest more than 10,000 private prescriptions have been written in the UK since 2018, which is far below the number of patients using cannabis obtained from the illicit market to self-medicate. But all of these patients are putting themselves at the risk of prosecution, which is where Cancard plays a role.

Why Cancard is needed

In polling and through patient disclosures, we know that medicinal consumers in 2018 were still frequently being enforced against – either charged, fined or issued a cannabis warning which impacted their ability to travel to certain countries and to pass CRB checks for employment or volunteering roles. In data from 2021 we have found that the vast majority (98%) of stops and searches of patients carrying their Cancard ID not facing a criminal record nor having their medicine confiscated. It is important to note that while discretion has always been an option for officers on the street, historically we have never seen a tool of this kind being utilised at such a high rate.

Cancard, a medical ID that records that a patient has a condition for which they are using cannabis medicinally, has seen 50,000 patient registrations in a little over 12 months. All of those patients have been medically qualified and undergone passport style ID checks in order to be part of the scheme. All Cancard holders are given support in the event that their consumption has an impact on their lives or if they are investigated criminally. The scheme is supported by the National Police Chiefs' Council, the Police Federation, the Police Foundation and many other policing organisations. Every force in the UK has received a briefing and the project is now available nationally.

The main drug offence recorded in the recent national statistics Drug Crime: Statistics for England and Wales 2020/2021 report was possession of cannabis. This amounted to 63% of all drug offences in the year. This is an increase of 20% from the previous year. After cases of drunk and disorderly, possession of cannabis was the second most common offence for which the offender received a monetary sanction. Many also received a criminal record, despite only consuming cannabis in order to treat a legitimate medical condition for which cannabis provides them relief.

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There is also an economic imperative to justify more discretion in police enforce-

ment of cannabis possession. A recent research paper by the Taxpayers' Alliance demonstrates that approximately 200 million pounds per year is spent on policing cannabis alone. When looking at the wider context of cost saving and based on cost savings to the NHS, police and courts, legal aid funds, etc the estimated savings amount to £892 million annually. This is not taking into consideration any generated income that would come with a regulated market, which has been estimated in a report by Health Poverty Action to be worth between £1bn-£3.5bn to the treasury in tax revenue per year.

Law enforcement are not immune to balance sheets and common sense approaches. The vast majority of cannabis cases that are dealt with are 'offenders' who are non violent, not involved in any other crimes and hold cannabis for personal use only. Continuing to criminalise these people does not add up financially or morally: this is the current attitude of law enforcement in the UK. Cancard has given officers on the beat an appropriately regulated tool with which to justify use of discretion in cases where no harm is being caused, at least initially for those who have a medical condition.

Cancard has given officers on the beat an appropriately regulated tool with which to justify use of discretion in cases where no harm is being caused

The scheme has been met with enthusiasm by the police and positive input generating policing partnerships, training programmes and greater visibility of potentially vulnerable medicinal cannabis patients.

Uptake of Cancard

Cancard has published the following results (as of December 2021):
The police have been supported this year (2021) to opt for discretion over criminalisation for 1,400 people with health conditions who are consuming cannabis medicinally;
Social workers and families have been supported in almost 300 cases that have resulted in keeping families together in all such cases;
Interventions in social housing eviction cases have resulted in 103 families retaining their houses through community resolution, education and equipment donation;
98.8% of stops and searches have resulted in Cancard patients not facing a criminal record nor having their medicine confiscated.

The implications of this de facto decriminalisation against Home Office legislation governing clinical access could be significant. It suggests that those in uniform who have first hand experience of policing in this area feel that the time is right for change.

Moving forward
There have been many suggestions for pilot schemes, regulation changes and access improvements made by various organisations in the past year. To conclude, below is a summary of one route which may be a viable opportunity to follow the lead of the police and make sensible and appropriate moves towards a more acceptable market for cannabis consumers in the UK.

Access:
In order to improve access and accountability of suppliers, a first step towards evidence gathering and reducing harm for marginalised groups would be to initiate a national trial for those patients who are already benefiting from illicit market cannabinoids. This could be introduced via an online pharmacy which could hold a formulary of expanded products and offer full traceability and sales tracking. Patients could opt in via self-certification/medical evidence of diagnosis similar to registration for Cancard. This would provide lower cost for patients, stable genetics and dependable product. It would also allow real world evidence generation and access to advice and support via a buddy system of caregivers. Such a scheme would need an official ID card for the benefit of police and other third parties. Together it would contribute to harm reduction by helping to move 1.4 million people away from the illicit market.

Supply:
With imported products that are currently on the private market it is clear

that both the pricing and the quality of these products is not acceptable to every cannabis consumer. In order to develop a quality range of official products that could feed into this trial cultivation, the UK needs more domestic cultivation and licenses to cultivate cannabis must be more accessible. A cooperative community owned cultivation model at a number of smaller sites across the UK could generate employment, and better quality products with room for research and development and less dependence on imports. It would also mean less dependence on the illicit market, specialist knowledge sharing and the beginning of a UK-wide industry (to also include hemp). This industry could spawn educational centres and more university partnerships, as well as small scale trials into practical issues like wattage limits on a grow your own model.

Better legal regulations that widened access and regulated domestic supply could see our knowledgeable experts recognised as such and given the opportunity to create small businesses. This is a far cry from being considered to be drug dealers and could lead to sharing and expanding knowledge for the benefit of millions of patients.

While there are hundreds of possible avenues to expand access and increase research it would seem that the best route would be to 'on-board' existing medicinal consumers – many of whom are Cancard users – and provide them with trial products to generate required evidence for confidence building among clinicians. With the recent MHRA draft guidance on randomised real-world evidence to support regulatory decisions - it would seem that the time is certainly right to explore options to apply these protocols to a medicine that cannot readily fit within a randomised controlled trial model.

While there are hundreds of possible avenues to expand access and increase research it would seem that the best route would be to 'on-board' existing medicinal consumers – many of whom are Cancard users – and provide them with trial products

The time has also come to stop criminalising patients, caregivers, specialists and experienced cultivators and instead provide a framework for them to be legitimated, so they can generate an industry that will contribute towards the health of the whole country and the individuals that live within it.

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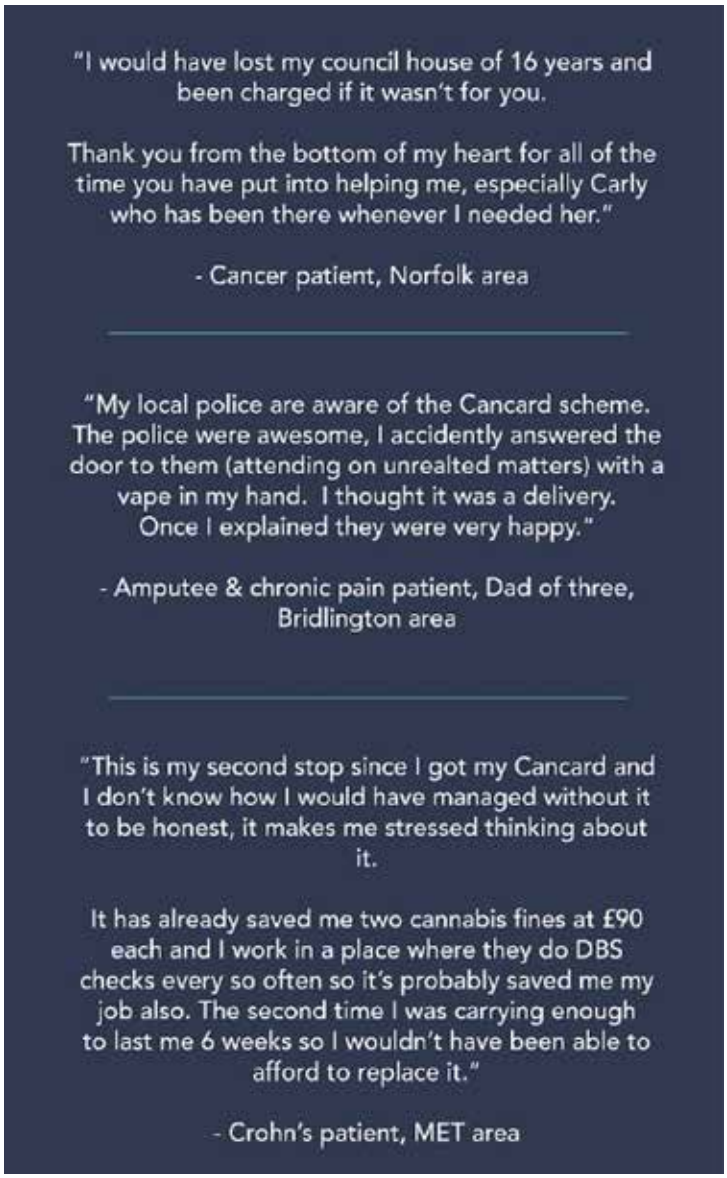

DRIVERS OF PATIENT GROWTH IN GERMANY

ALFREDO PASCUAL, Investment Analyst | Seed Innovations

Many European countries have legalised medical cannabis in some form or at least implemented medical cannabis programs or pilots in recent years, but Germany has drawn the most attention as it has quickly become the largest market in Europe after its 2017 law change that expanded access to medical cannabis.

The November 2018 medical cannabis reform in the UK could be loosely compared to the March 2017 German law change. But markets in these two countries evolved quite differently during their first years after the new regulations were adopted.

The 2017 German medical cannabis reform led to a statutory health insurance (SHI) covered market that in 2018 already totaled €74 million, subsequently growing 66% in 2019 to €123 million, and a further 34% in 2020 to €165 million. Almost 90% of the population in Germany is covered by SHI. Some of the pillars of the system include that it is financed based on the solidarity principle and that those who are covered by it "receive medical treatment without having to outlay the costs themselves". This also applies to cannabis prescriptions, even to cannabis products without marketing authorization – loosely equivalent to UK's unlicensed cannabis-based products for medicinal use (CBPMs) – provided certain circumstances are fulfilled, including that the treatment needs to be for a severe condition and normally not as first line of treatment. However, for any cannabis product without marketing authorization an individual application for coverage needs to be done in Germany, many of which end up being rejected.

With €130 million reimbursed using 262,996 prescriptions in the first nine months of 2021 reimbursement of medical cannabis will likely continue growing in 2021, albeit at a slower pace. And this is only a partial picture of the German medical cannabis market. Total sales are actually significantly higher because statutory health insurance reimbursement does not include so-called private prescription sales, for which there is no reliable, publicly available data but which are widely believed to be an increasingly significant part of the market, particularly in the flower category.

The German private market includes not only the c.10% of the population with private health insurance. It also includes a significant patient population with SHI but that was either rejected by their SHI for cannabis coverage or that could not find a doctor willing to write the coverage application, but could find a doctor willing to write a cannabis prescription for the patient to buy out of pocket.

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Although the UK market for unlicensed cannabis-based products for medicinal use (CBPMs) has been growing, total sales in the UK as of 2021 have paled in comparison to Germany, even when accounting for the later November 2018 reform in the UK versus March 2017 in Germany. Rather than a specific, single factor explaining Germany's faster market growth, the reasons can likely be found in the broader context of the German regulations and the history of medical cannabis in Germany.

Pillars of the German medical cannabis market

The German medical cannabis market has several pillars that when combined explain its comparative success – at

least on a European level – providing broader access to medical cannabis:

Statutory health insurance coverage;
Any doctor – other than dentists and veterinarians – can prescribe;

A history of prescriptions preceding the 2017 reform;

Pharmacies play a central role; In-country cultivation;

Magistral preparations – compounding – allowed including for flower; and

No limited list of medical conditions for which cannabis can be prescribed.

When looking at the seven pillars from a UK perspective, it becomes evident that the UK shares a comparable situation when it comes to the regulations not restricting the therapeutic indications for which unlicensed CBPMs may be prescribed. In the UK, patients also have access to a range of cannabis products – including flower. However, the stark differences in all the other pillars may explain Germany's broader access to medical cannabis.

Rather than a specific, single factor explaining Germany's faster market growth, the reasons can likely be found in the broader context of the German regulations and the history of medical cannabis in Germany.

Although German statutory health insurers reject about a third of the applications for cannabis reimbursement, the German law reform from 2017 mandated that provided certain conditions are fulfilled, seriously ill medical cannabis patients should have their cannabis prescriptions covered by the public health system.

During the first nine months of 2021, 262,966 medical cannabis prescriptions were covered by the German public health system, and 77% of which were for products that in the UK would be considered unlicensed CBPMs. This marks a stark difference with the almost purely private UK market for unlicensed CBPMs.

Finding doctors willing to prescribe medical cannabis products that do not have clinical trials to support their efficacy is complicated in any country. But in the UK – where prescribing is something limited to specialists – the situation is more restrictive than in Germany, where cannabis prescriptions can be written by general practitioners, effectively expanding the pool of doctors that can consider cannabis as a therapy option.

Before the regulatory changes in recent years in both countries, Germany had a more meaningful history of limited cannabis prescriptions, with a relatively small group of German doctors – though highly educated in cannabinoid science – who had been able to prescribe medical cannabis long before the 2017 reform.

Dronabinol has been used for magistral preparations since 1998. Sativex – the first cannabis-derived drug to obtain marketing authorization – became available in 2011 and about a thousand patients were accessing cannabis on an exceptional basis (including imported flower) before the 2017 reform, paying for it out of pocket through a complicated process of case-by-case approvals.
Finding doctors willing to prescribe medical cannabis products that do not have clinical trials to support their efficacy is complicated in any country. But it is probably somewhat easier than in the UK because in Germany cannabis prescriptions can be written by general practitioners.

The March 2017 change of rules expanded the toolbox of these physicians and drastically expanded that market so that it is estimated to be about 100 times larger in terms of number of patients as of the end of 2021.

The role of pharmacies is also somewhat different in Germany than in the UK, with Germany possibly providing

broader access. Both in the UK and in Germany, a small number of pharmacies are believed to be responsible for most cannabis prescriptions. However, the situation is more decentralized in Germany, where the magistral preparation characteristic of unlicensed CBPMs mean pharmacies play a central role. This role goes beyond the compounding and dispensing of a cannabis prescription, with pharmacists also involved in developing quality standards.

Another difference between the 2017 German and 2018 UK reforms was the emphasis Germany's lawmakers placed on in-country cultivation to supply the domestic market. The first German harvests became available to patients in July 2021, longer than originally expected and in volumes that only represent a fraction of the total market. However, the €4.30 price per gram at which the domestic cannabis flower is sold to pharmacies likely contributed to downward pressure on the prices of imported products as well, thus reducing prices overall and making cannabis therapy more affordable to those patients paying out of pocket.

Like in the UK, a range of unlicensed – or also called unapproved – medical cannabis products are available to patients in Germany. This virtue of both Germany and the UK is not always shared by other European countries with a medical cannabis program, with for instance Austria not offering to patients the possibility of cannabis flower as one of the options. Finally, while some countries, such as Portugal, restrict the therapeutic indications for which cannabis is considered appropriate, there is no such restriction in Germany as well as in the UK.

What the UK can do beyond more research

The need for more research is often touted as the key to broaden access to medical cannabis. It has been so for decades, with German pharma news in 1998 already emphasizing the need for more research when dronabinol first became available to patients.

Without minimizing the importance of research – which would be beneficial to expand access anywhere in the world – stakeholders in the UK interested in broadening access to medical cannabis should also look at the structural differences between the German and UK medical cannabis programs.

The need for more research is often touted as the key to broaden access to medical cannabis. It has been so for decades, with German news in 1998 already emphasizing the need for more research when dronabinol first became available to patients.

More research is needed both in the UK and in Germany, but it is not the volume or quality of scientific research or clinical trial results that explains why Germany has a much larger population of medical cannabis patients than the UK five years after the law changed. While more research continues to be done, stakeholders in the UK interested in broadening access to medical cannabis could focus on the differences in most of the pillars described above and see what would be applicable in the UK context. The most important of these pillars being public health insurance coverage; that any doctor – not just specialists – be allowed to prescribe unlicensed CBPMs; and a policy emphasis on authorised in-country cultivation to limit the dependency on imported products, possibly making cannabis-based end-products more affordable.

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THE PROCEEDS OF CRIME ACT 2002 AND ITS IMPACT ON CANNABIS INVESTMENTS

DYLAN KENNETT, Senior Associate | DLA Piper

London is the largest public equity market in Europe and remains one of the leading venues globally. In particular, it has liquid markets in small-cap companies, including the ability to raise money on public capital markets for companies valued up to €100mn. Whilst competing jurisdictions offer some public markets at this size, it is our experience that such markets are, in general, less attractive, with London also providing the opportunity for companies to migrate and 'up list' onto other, larger UK capital markets as they grow.

In short, London is a functioning and well-trodden path for capital raising from startup, through scaleup, to publicly listed. Despite these advantages, and the concentration of expertise in the cannabis industry in the UK, there have been remarkably few listings for the industry in London.

To date, this author is aware of around a half-dozen listings, with the majority pursuing purely cannabidiol (CBD) related strategies for consumer products, and a large minority – one-third – pursuing a medical-first approach whereby cannabis is supplied to patients by a medical practitioner, or pharmaceutical development businesses.

Currently, the UK has relatively strict laws relating to cannabis compared to other major European and North American centres. In particular, and in contrast to Canada, Germany, Switzerland, and a rapidly growing number of US states, the sale of tetrahydrocannabinol (THC) containing substances is restricted solely to medicinal products. The relative legality of activities is usually a minor issue for capital markets, as companies are generally assumed to be compliant with relevant law in order to operate freely.

In fact, London has routinely hosted companies pursuing businesses where the legality of some operations has been contentious, with investors taking account of legal uncertainty with little formal regulatory intervention, pricing in any such risk into the share price. One well-known example is the London-listed global gaming industry. In contrast, for the cannabis industry, there has been a surprising and, this paper argues, unresolved dispute regarding one particular piece of UK legislation.

Proceeds of Crime

The principal cause of difficulties today is the application of the Proceeds of Crime Act 2002 (POCA). This statute has been much debated, especially as it relates to the cannabis industry. Originally drafted as broad legislation to combat money laundering and terrorist financing, POCA has also captured the nascent cannabis industry in the UK. Within it lies a concept of 'criminal conduct' which captures offences taking place in the UK, but also conduct outside of the UK which would be criminal in the UK if carried out here.

Given the possession or supply of cannabis for recreational use carries a significant criminal sanction in the UK under the 1971 Misuse of Drugs Act, and does not fall within the 'Spanish Bullfighter' defence under the legislation (which covers those activities which are lawful abroad and carry less than a maximum sentence of 12 months in the UK), POCA would then apply to proceeds generated from businesses who participate (even tangentially) in adult-use sales. Therefore, dealing with such proceeds or property (including dealing in shares, receipt of dividends from such a company, even the uplift in the value of shares) could constitute an offence of money laundering under POCA.

For some time, the market operated without explicit confirmation of this, although it soon became critical amongst all the deal making, coming from the excitement of those in the UK wanting to make investments in high-growth Canadian cannabis opportunities in 2018-19. The Financial Conduct Authority (FCA) issued guidance in September 2020 and a subsequent technical note on that guidance in the summer of 2021. In short, the FCA confirmed that overseas recreational activities, conducted entirely lawfully, would nonetheless be considered as generating proceeds of crime in the UK, and therefore unable to list their securities on the Official List.

In order to do so, overseas cannabis companies would need to satisfy the FCA that POCA would not apply to their business and that the company's

overseas activities would also be legal in the UK if they were to take place here; a rub to the technical guidance that many companies fail to realise when approaching a listing. UK-only companies have a marginally easier path, since their regulatory regime is clear and the activities they can undertake are limited to those conducted under licence from the Home Office, or with the appropriate authorisations in relation to CBD focused companies. UK companies who have or have had dealings with adult-use companies may still find themselves in difficulties if the overseas company's money is potentially considered 'tainted'.

Overall, the application of POCA continues to cause material difficulties for the industry and has acted as a substantial gating item to navigate in order to achieve a listing, which is already a significant mountain to climb.

UK companies who have or have had dealings with adult-use companies may still find themselves in difficulties if the overseas company's money is potentially considered 'tainted'

As such, I believe the resultant listing regime in London is now unattractive for the cannabis industry, for five main reasons: (i) lack of certainty; (ii) apparent discrimination against the industry; (iii) elevated transaction costs; (iv) competing listing venues taking a different approach and (v) doubts over whether in this instance POCA is being applied as Parliament intended.

Lack of certainty

The current regime makes it highly uncertain whether companies are able to access the London capital markets. This uncertainty arises from whether the relevant combination of the FCA, AIM and/or the LSE will accept proposed listings, the longer timeline for any such approval and because of the unclear timelines and incremental costs, the ability to engage and sustain investor interest.

Discriminatory

The requirement imposed appears to be unique to companies active in the cannabis industry that are seeking a new listing. No equivalent requirement is imposed on companies in other industries, and this is in contrast with companies with existing listings, who are able to pursue cannabis investments or commercial relationships without any apparent listing-related hurdle. There are multiple examples where UK-listed entities have invested in, or created commercial partnerships with, overseas companies who derive their revenues partially or wholly from adult-use cannabis sales. External lawyers are now well equipped to mitigate potential issues by making relevant filings with the appropriate UK regulatory agencies indicating that such a transaction is forthcoming. As such, there is an asymmetry in how companies are being treated across the market, creating an unjustified competitive market advantage for existing listed entities.

It is difficult to see the public policy objective that is met by preventing London capital markets from fulfilling their function of providing capital to one specific industry, but only for potential new issuers. Given its broad applicability, POCA captures a very wide range of stakeholders, including those – both retail and institutional investors - holding shares in UK and overseas listed entities that already have cannabis investments or commercial partnerships. As pursuing this would clearly lead to untenable outcomes, no regulatory action has so far been evident, illustrating that the application of POCA already has practical limits.

Transaction costs

The FCA's Summer 2021 guidance specifically requests legal opinions for every country that an issuer is active in, identifying that the activities being undertaken at local level are within the parameters of the local regulation. In addition to this, an overarching legal opinion is then provided by UK counsel identifying that the issuer, given the local activities, would comply with the provisions of POCA, as well as ensuring that its activities are for purposes which are lawful in the UK. Practically speaking, this means a doubling of already significant legal fees.

Out of step with other jurisdictions

No other potential competitive listing jurisdiction imposes this level of requirement on potential listings. In fact, very close to home, other jurisdictions like Guernsey and Jersey, for example, have taken alternative paths, clarifying or amending their existing anti-money laundering legislation to make clear that overseas adult-use cannabis activities will taint neither their markets nor participants, provided they are derived in legal frameworks overseas. Even in a country which has legalised adult-use cannabis, the Canadian Securities Administrators apply a permissive, disclosure-based approach to an issuer's entrance to and participation in Canadian capital markets. If an issuer operates in various jurisdictions, it must confirm to the applicable exchange (in the listing agreement or, as applicable, a director's statement) that the issuer is in compliance with the laws of those countries. London's standard is highly onerous compared with other comparable jurisdictions like Canada.

The impact of POCA also has a bearing on the ability of the UK to receive investment from allied countries that have significant domestic regulated cannabis industries. Whilst there are various countries pursuing cannabis reform, the two most prominent are Canada, where adult-use has been legalised, and Germany, where it has been widely reported that adult-use is planned to be imminently legalised under its new government. These two countries are amongst the most reputable partners for the UK globally, and both are recognised as some of the least corrupt, lawful and best policed societies in the world. Furthermore, adult-use in both countries is (and, in the case of Germany, undoubtedly will be) subject to strict formal controls. The requirement in UK law to seek active confirmation of the UK legality of activities in these countries, for

activities that are carried out by regulated corporate entities, is, on the face of it, unnecessary and onerous.

Interpretation of the law

Under the Misuse of Drugs Act 1971 cannabis and certain associated substances are considered controlled drugs; the production and supply of controlled drugs (including cannabis plants) gives rise to a criminal offence. This is subject to any regulations made pursuant to that statute, which authorises the Home Secretary to make other provisions as they see fit. The Secretary of State has indeed made such further regulations under the Misuse of Drugs Regulations 2001. Within those regulations the Secretary of State has the legal authority to issue a licence for the production and supply of a controlled drug, including cannabis. Although to date, Government policy has not allowed for adult-use cannabis to be produced and supplied to the wider UK, Parliament has given the Secretary of State the unencumbered facilities to do so. It then follows that the production of adult-use cannabis within the UK could be done without any further Parliamentary authorisation, as the legal basis already is in place.

Therefore, many in the legal community, including prominent Queen's Counsel, have concluded there are no grounds to find criminal conduct under POCA for activities pursued under a licence that is issued in an analogous jurisdiction to the UK overseas (i.e. Canada and Germany), when such a licence could readily be transposed to the UK. It is conceded that this is a matter subject to legal uncertainty (which is part of the point), but the broader issue is that in such an instance, it is unusual for regulators to impose a specific interpretation in formal guidance.

Challenges for the sector

All of the foregoing combined, present an onerous barrier to listing, and for such a narrow and contentious point this seems prima facie, strange.

The result of these foregoing challenges are two-fold. First, investors are being actively discouraged from participating in cannabis listings because of the legal challenges and the uncertain timing of any potential listing. This, in turn, has created a chilling effect on institutional interest in the sector. Secondly, potential issuers are equally discouraged, and it takes unusually sustained commitment from issuers to successfully list a cannabis-linked company in London.

Conclusion

The Government's 'Global Britain' agenda to boost trade and inward investment post-Brexit depends on the health and growth of capital markets in the UK, including the continued promotion of the UK's role as a regional capital market for Europe as well as an important global financial centre. The following changes would significantly improve the current situation:

Confirmation that new issuers are subject to the same rules as existing issuers, to the effect that POCA risks can be extinguished through appropriate use of the disclosure and consent regime with the National Crime Agency. Many listed companies are already using this legal process to participate in the industry.

Revision to legislation or new guidance to clarify that POCA does not apply in relation to overseas activities which are legal in the jurisdiction in question; given that the current legal basis is in dispute, perhaps modelled on similar legislation already in place in the Channel Islands. This could potentially be restricted to certain highly reputable jurisdictions which meet a set of predetermined criteria.

Government and regulators continue to facilitate growth in the medicinal cannabis industry in the UK, thereby normalising the prescription of cannabis, increasing R&D in the sector and helping to reduce perceived risks which inform old tropes around its use. It is noted that the legality of adult-use cannabis is a political decision for each country.

The UK public equity markets are globally respected and currently hold a competitive advantage to their peers. By amending and/or clarifying the POCA legislation as it relates to cannabis, this strength and standing can be extended to support the growth of the legal cannabis industry, as seen across multiple jurisdictions around the world, to the benefit of the UK Treasury, investors, issuers and patients alike.

*The foregoing analysis and recommendations relate purely to the funding of lawfully pursued businesses out of the London capital markets, or for investors in overseas cannabis companies operating legally in their respective markets.

1) https://www.legislation.gov.uk/ukpga/2002/29/contents

2) https://www.legislation.gov.uk/ukpga/1971/38/contents

3) https://www.fca.org.uk/news/statements/listings-cannabis-related-businesses

4) https://www.fca.org.uk/publication/ukla/fca-tn-104.1.pdf

5) See Carey Olsen for Guernsey: https://www.careyolsen.com/sites/default/files/Information%20Notice%20on%20Cannabis%20Cultivation%20and%20Production%20in%20Other%20Jurisdictions.pdf

6) See: 1(1)(b) of the Proceeds of Crime (Jersey) Law 1999 https://www.jerseylaw.je/laws/current/Pages/08.780.aspx and the list of applicable exempted jurisdictions in the Proceeds of Crime (Cannabis Exemption – List of Jurisdictions) (Jersey) Order 2021 https://www.jerseylaw.je/laws/enacted/Pages/RO-087-2021.aspx

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