Going for Growth

Transforming the UK into the Global Leader in Cannabinoid R&D

Professor Trevor Jones CBE FMed Sci
George Freeman MP
Zack Bellman

Cannabinoid Research & Development Group UK

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CRDG Founding Members

Ananda Developments

Artelo Biosciences

Brains Bioceutical

Curaleaf International

Kingdom Therapeutics

NW Pharmatech

Oxford Cannabinoid Technologies

Phytome Life Sciences

Executive summary

Given its strength in the life sciences, the UK has the potential to become a global leader in cannabinoid R&D, improving patient access to safe, high-quality and effective CBPMs.

To support this, this report makes the following ten recommendations:

1. **The government should transfer the licensing authority for scheduled drugs involved in medical R&D from the Home Office to the DHSC, and in particular the MHRA.**
2. **The Home Office should respond to the ACMD's Barriers to Research report from December 2023, including the implementation of exemptions for companies and universities engaged in cannabinoid R&D in the UK.**
3. **The government should create a medical R&D roadmap for scheduled drugs in the UK over the next decade that includes cannabinoids.**
4. **The government should provide clear guidance that outlines the processes for developing botanical medicines in the UK.**
5. **NICE should continue to engage with up-to-date evidence of CBPMs and update its public-facing communications to reflect this.**
6. **The British Pharmacopoeia and associated regulatory agencies should review monographs for various CBPMs and synthetic cannabinoids.**
7. **The UK's cannabinoid R&D sector should establish an academic research network across the university research ecosystem to foster industry partnerships and develop best practices.**
8. **The Department for Science, Innovation and Technology (DSIT) should encourage institutional and private investors to engage with the cannabinoid R&D sector.**
9. **The biotech investment community should promote collaboration with the UK cannabinoid R&D sector.**
10. **Charities, not-for-profit organisations and scientific societies to engage and promote cannabinoid R&D efforts.**

By implementing these recommendations (covered in more detail in the report), the UK can consolidate its position as a global leader in cannabinoid R&D. This report details the present state of the sector in the UK, the challenges it faces and opportunities for further growth.

Contents

Introduction to Cannabinoid R&D

The UK is global leader in biotechnology. According to the Organisation for Economic Co-operation and Development, the UK's number of biotech firms lags only a little behind the US at just under 28,000 – not bad given that it has only a fifth of the populations of the world leader.

It's therefore little surprise that the UK is also among the top countries for cannabinoid research and development (R&D). As this report reveals, only Canada and US publish more research on the topic, with many leading Russell Group universities having contributed hundreds of scientific papers.

The UK has also proven a pioneer in the application of medical cannabis. In 2018 the Medicines and Healthcare products Regulatory Agency (MHRA) approved the use of cannabis-based products for medicinal use (CBPMs) in specific conditions, based on a review by the Chief Medical Officer Sally Davies, who cited sufficient evidence to reclassify cannabis as a Schedule 2 drug due to its medical value.

Such conditions provide fertile ground for cannabinoid R&D in the UK. But there is more to be done if the seeds of this industry are to bear their full fruit.

First, oversight of medical cannabis should be put under the purview of the MHRA and its parent the Department of Health and Social Care (DHSC). Taking responsibility away from the Home Office will ensure that medical cannabis is regulated as part of the pharmaceutical industry, and not as a criminal matter.

I The Global Context

Cannabinoid R&D is a growing sector with significant potential. It is expected to grow expodentially as new cannabinoid based medicines are approved that treat global unmet medical needs across multiple disease areas. Jazz Pharmaceuticals' $7.2bn purchase of GW Pharmaceuticals in 2021 a sign of the opportunities for companies engaged with scientific and commercial R&D programmes.

The scope of interest for cannabinoid R&D includes the pharmacological targeting of the human endocannabinoid system (ECS), cannabis-based products for medical use (CBPMs), and the discovery and development of synthetic or natural cannabinoid-related compounds for therapeutic purposes, whether derived from the cannabis plant, other botanical sources or novel chemical entities [3-6].
As more detailed scientific mechanisms are still being elucidated, the potential for further innovation and the development of new medicines presents a considerable opportunity within the life science sector.

The ECS is implicated in the aetiology of a plethora of diseases, including multiple sclerosis (MS), epilepsy, Parkinson's, dementia, strokes, traumatic brain injuries, cancer-related disorders, neuropathic pain, substance misuse, and a range of psychiatric conditions. For example, cannabinoids act on many of the 'standard' inflammatory pathways (IL-1 etc). Indeed, much of the scientific research on the ECS is related to fundamental cellular biology and neuroscience, including the roles of endogenous cannabinoids, rather than the cannabis plant [7-9]. For a timeline of notable cannabinoid R&D see appendix i.

Therapeutic applications

As noted, cannabinoid R&D has a range of potential applications across many conditions. What follows is a non-exhaustive list of promising research areas. Other potential use cases for medical cannabinoids include oncology, autism, addiction, PTSD and antimicrobials [11-18].

Beyond cannabinoids, there is scope for research into compounds that act upon the ECS, as well as other medicinal constituents found in the cannabis plant such as terpenes, alkaloids and other novel compounds [11, 19, 20].

Epilepsy

Characterised by seizures of varying type, intensity and nature, epilepsy is a complex disease with various causes that are often poorly understood. It affects millions of patients worldwide, with anti-epileptic drugs (AEDs) and alternative treatments varying in their effectiveness and safety profile – particularly for those with treatment-resistant epilepsy – while current treatments incur unwanted side effects.

Patients with drug-resistant epilepsy are therefore exploring other treatment options. Already CBPMs have been used to treat epilepsy, by reducing seizure frequency and intensity, as one of the most significant research areas for cannabinoid R&D focused on pharmaceuticals [21-23].

The scientific understanding of how cannabinoids can treat epilepsy has partly been elucidated by GW Pharmaceuticals (see page 10), with the company's research revealing complex mechanisms about the interactions between various phytocannabinoids and the role of the ECS and neuronal signalling in epilepsy.

Neurodegenerative disease

In neurodegenerative disease there is a massive unmet need for treatments of a wide variety of symptoms. One example is in Parkinson's Disease, a neurodegenerative disease that often presents itself in patients with motor symptoms such as tremors and bradykinesia, as well as psychological ailments including sleep issues, cognitive impairments, mood disorders and sometimes psychosis [24]. Patients with Parkinson's disease often struggle to treat the wide variety of symptoms and treatments often focus on the management of symptoms.

The ECS and cannabinoids are known to impact on the biological causes of Parkinson's, with proposed mechanisms of actions that include the mood and neuroprotective effects of various endocannabinoid signalling pathways related to dopamine. Treatments are often administered to help alleviate motor and psychological symptoms, such as cognitive impairment or psychosis. Researchers at King's College London are investigating the potential role of CBPMs, in particular CBD, in psychological symptom management of the disease, with Epidiolex being studied adjuvant to current therapeutic treatments [25].

Any potential application of CBPMs in the treatment of Parkinson's disease could also lead to other medical applications in managing neurodegenerative diseases, including dementia, which alongside the category of neurodegenerative diseases are becoming an increasing burden to healthcare systems, especially in countries with ageing populations [26-28, 75-77].

Psychosis

As demonstrated through preclinical models and animal research, the ECS is implicated in the expression of psychotic symptoms, for example in patients with schizophrenia or anxiety [29, 30].

Non-intoxicating CBD-dominant drugs may therefore have a role in the treatment of psychosis [30, 31].

Research conducted in animal models and humans supports the hypothesis that non-intoxicating CBD can act as an antipsychotic [32-34]. There have been active medical R&D efforts exploring CBD as a potential treatment for psychosis, especially at the earlier phases of psychotic symptom expression [35].

Such treatments offer an attractive alternative to conventional psychiatric medications. With SSRIs often causing adverse effects in patients, there is a massive demand for newer and safer alternatives or adjuvant treatments for psychological symptoms in a variety of psychiatric conditions [36].

Pain

Current pain management focuses on steroidal anti-inflammatory drugs (NSAIDs) such as Ibuprofen, as well as opiates, benzodiazepines and other analgesic medicines that often possess undesirable side effects. These can include unwanted liver toxicity associated with Ibuprofen and other NSAIDs, as well as potential addiction to opiates or benzodiazepines [37, 38].

Most clinical research on pain management has related to neuropathic pain in MS patients, as well as other areas including peripheral neuropathic pain, oncology related pain and trigeminal nerve pain [39, 40].

Pain is therefore a hugely promising area for CBPMs and medical cannabinoids. The ECS and cannabinoids are fundamental to regulating the nervous system, with key areas of the brain linked to pain perception and ECS receptors located throughout the nervous system critical for naturally-occurring and drug-induced analgesia [38, 41-43].

Cannabinoid R&D could reveal new ways of targeting the ECS as a method of pain management, either alone or alongside current pain management techniques. Potential applications range from treating mild discomfort to extreme chronic pain, spanning from specific injuries to more complex nerve and tissue damage that may be related to cancer or other neurological disorders [44-46].

The use of cannabinoids as analgesics may serve as a safer alternative to other treatment options and presents an opportunity for pharmaceutical companies to explore different analgesics, or adjuvant treatments, with a better safety profile. While some have begun to explore this area, further studies need to take place on larger patient cohorts across different pain categories and CBPMs in order to establish the efficacy of these potential treatments [38, 46].

Main physiological systems whose regulation is influenced by the endocannabinoid system – sourced from Barrales-Cureño etl. al. 2020 [47].

System	Effect
Respiratory	Bronchial relaxation
Physiological	Endo cannabinoids function
Cardiovascular	Arterial pressure
Gastrointestinal	Gastric emptying
Skeletal	Bone formation
Reproductive	Spermatic implantation and motility
Immune	Cytokine inflammation and release
Peripheral nervous	Neurogenic inflammation and nociception
Hypothalamus-hypophysis-adrenal axis	Corticosteroid release and stress response
Central nervous	Learning and memory, emotion, neuronal excitability, intake, locomotion, motivation, nociception, and synaptic plasticity

IP considerations

Patent protection for cannabinoids follows various normal IP pathways pursued by the pharmaceutical industry. This means that pharma and biotech investors can engage with cannabinoid R&D through a value creation model that they are already familiar with, opening huge opportunities for the commercialisation of cannabinoid R&D with the support of robust legal protections.

The main classes of relevant IP rights are patents, trademarks, and copyrights, sitting alongside supplementary protections focusing on plant breeding and variety rights, which remain relevant to pharmaceutical and medical developments. These protections are granted by designated regulatory bodies in relevant jurisdictions such as the UK, the US and the EU.

Examples of different areas of innovations for cannabis and cannabinoids are listed below [48]

1. Plant breeder rights (or similar plant variety rights), especially in the US
2. Analysis methods
3. Extractions and methods
4. Formulation compositions
5. Devices for medicines delivery and consumption
6. Specific therapeutic treatments
7. Auxiliary methods around cultivation or processing

Similarly, Wyse and Luria (2021) categorise inventions into three main categories, ‘upstream’ agritech, ‘midstream’ chemistry and analytics, and ‘downstream’ medical and biological innovations [49].

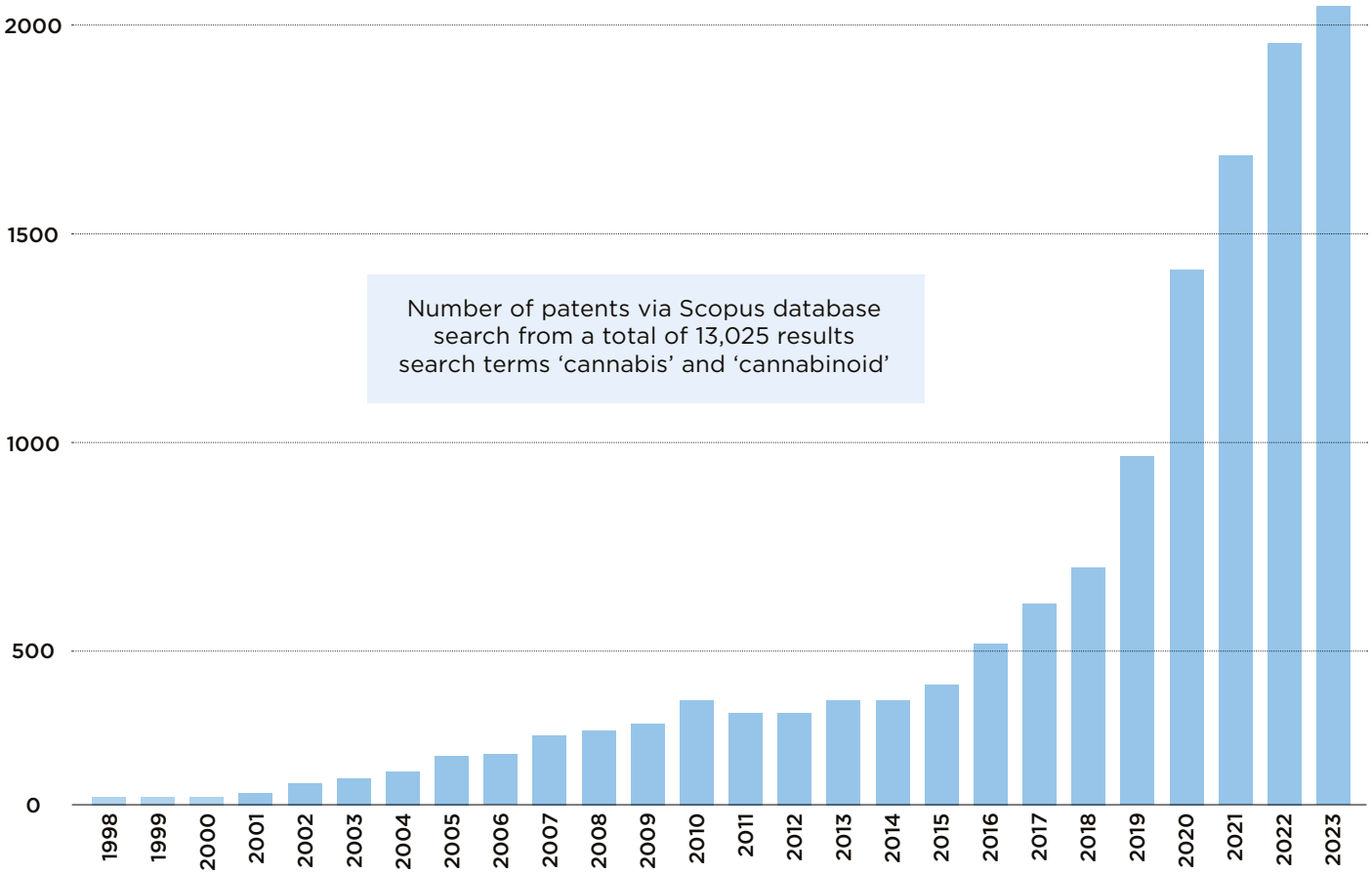
Patent information using keyword searches from Espacenet shows that the main class of patents related to cannabinoids fall under the ‘medical or veterinary science’ category.

It is however worth noting that patents related to cannabinoid R&D cover a wide range of non-medical topics including agricultural, industrial, forensic and other applications.

The complexity around patents makes it difficult to assign an exact number of patents related to cannabinoid R&D. Some estimates using keyword search, whilst having limitations put it between 10,000 and 17,500, while other sources such as Google Patents, Scopus and Espacenet put the number at 20,000 or more, depending on how the patents are classified [50, 51].

Even with the above caveats, the overall trend is positive in terms of patents being registered and the field of cannabinoid R&D is growing in size and interest. For more specific reviews focusing on particular areas of patents, please refer to the references section [49, 52-54].

Estimated number of patents using keyword search illustrating positive growth for the sector.



GW Pharmaceuticals and Acquisition by Jazz Pharmaceuticals

As a British success story in the life sciences space, GW Pharmaceuticals serves as a salutary example of how other companies can boost the relevance of cannabinoid R&D in global healthcare research. Having been set up in 1998 by doctors Geoffrey Guy and Brian Whittle in the UK to develop CBPMs for a mass market, in 2021 the company was acquired by the US pharmaceutical giant Jazz Pharmaceuticals for $7.2bn [55-57].

GW was able to raise and invest money to fund a large network of academics working on a wide variety of topics from historical, fundamental mechanistic R&D through to pre-clinical and clinical work [58]. The company conducted some of the earliest pre-clinical and clinical research trials for cannabinoids in the UK, leading to market authorisation of two CBPMs, Sativex (a formulation based on THC and CBD) and Epidiolex (a formulation based on CBD).

Sativex is an oromucosal spray containing a specially formulated cannabis sativa extract containing THC and CBD. The drug has been approved in the UK, Europe, the US and other countries for treatment of spasticity in multiple sclerosis (MS), as well as various other indications related to the disease and its use in other therapeutic areas is also being investigated [59-61].

For the cannabinoid R&D of CBPMs, Sativex is a positive example of how a CBPM can be developed and gain marketing authorisation with medicine agencies internationally, treating serious conditions and improving patients' quality of life.

Another medicine, Epidiolex, is the first CBPM to gain market authorisation by the UK MHRA to treat epileptic seizures in Dravet and Lennox-Gastaut syndromes – a positive sign of the innovative medical R&D that can be conducted around cannabinoid science. It has opened up a wave of future opportunities for CBPMs to be investigated for various different clinical conditions and therapeutic areas, especially for conditions that involve seizure treatments.

Such successes have enabled GW to secure key licensing and market authorisation for its products and build unique large-scale development and manufacturing processes to establish safety and efficacy for specific clinical conditions [62, 63]. This allowed the company to scale up, with Epidiolex product sales worth more than $900m in 2023, according to a Jazz financial update in February 2024 [64].

II The UK Context

The UK is a global leader in biotechnology, pharmaceuticals and the life sciences, with unique historical research institutions such as the Royal Societies and a strong base of universities, regulators, healthcare institutions and commercial markets, including startups and venture infrastructure [65, 66]. As such, cannabinoid R&D can leverage many of the key strengths in the UK life sciences sector.

By some estimates, the UK has the fourth largest biotech sector in the world, with the country also featuring among the top five territories for life sciences research. Some of the UK's biotech competitors – namely the US, Germany and Japan – are already conducting large-scale cannabinoid R&D [66, 67].

Several of the UK's leading scientists, most notably John Bell, the president of Ellison Institute of Technology (EIT) Oxford, have argued that the country's dominant position in life sciences will slip without adequate support from the government and investors [65, 68]. Cannabinoid R&D is a strong candidate for such intervention and can help maintain the UKs biosciences leadership.

Outside of the UK, a relaxing of attitudes and the liberalisation of scheduled drug regulations is creating opportunities for R&D and the development of safe and efficacious cannabinoid medicines abroad. The UK must keep pace with these developments, or risk expertise, capital and other resources being diverted to cannabinoid R&D efforts in other countries.

Top 5 countries publishing cannabinoid-related research.

Research process

Cannabinoid R&D in the UK is conducted under the oversight of the MHRA, though any company working in the field must also satisfy the requirements of the Home Office. Cannabinoid R&D encompasses classic drug discovery programmes, with active research across rational drug-design, pre-clinical safety and pharmaceutical quality standards and development programmes.

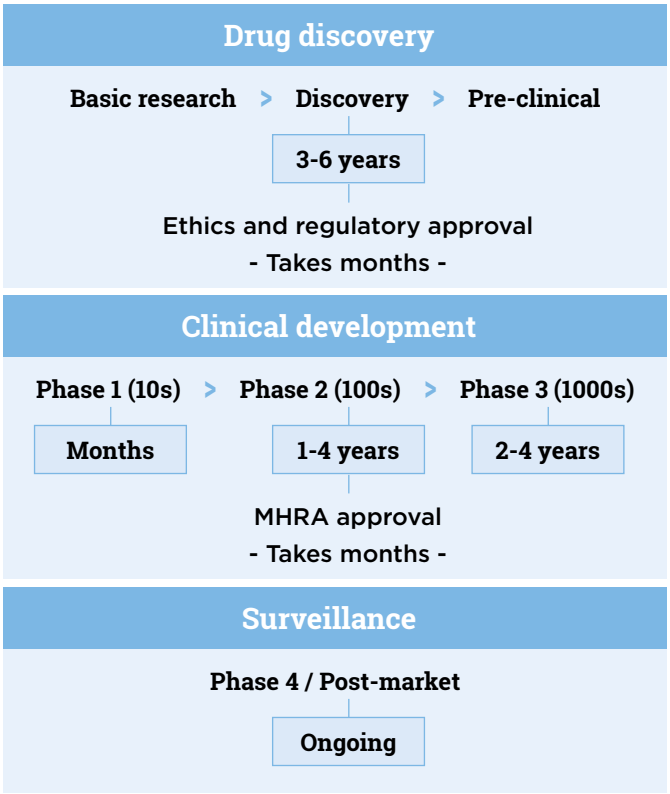
Applicants must demonstrate good quality scientific approaches and the passing of preclinical and clinical phases establishing safety and efficacy of any investigate drug before authorisation by the MHRA for prescription by the NHS or private clinicians.

While the drug development process is comparable to medicine development in other areas, cannabinoid R&D remains at a relatively early stage in the pharmaceutical and medical sector in the UK.

The scientific study of the ECS is largely underrepresented in universities and healthcare training for doctors, pharmacists, nurses and other healthcare providers, with only a small presence in neuroscience courses and medical programmes. While there is a small, strong research community in the UK focusing on cannabinoid R&D, it needs to be integrated into the education infrastructure.

In other countries, most notably the US, there has been an increase in academic degrees and professional training focused solely on the science of cannabis and cannabinoids, including a slow rise of specific degrees related to the emerging markets [69]. This is undoubtedly tied to the development of clearer and more liberal legislation that is facilitating effective cannabinoid R&D and education in such jurisdictions.

Drug development pipeline in the UK
Tony Blair Institute, 4 October 2022 [70].



Five key themes in the UK life sciences vision and potential impact of cannabinoid R&D.

NHS Partnerships	Large scale NHS trials with medical cannabinoids and CBMPs
Commercial Business	National and international medical cannabinoid R& focused businesses boost UK research and economy
Reinforcing UK Life-Science Infrastructure	Promote and enhance UK academic and industry infrastructure well equipped & engaged in cannabinoid R&D
UK Manufacturing & Innovation	Unique opportunity for companies manufacturing and leading innovative cannabinoid R&D in the UK
Global Healthcare Challenges	Cannabinoid R&D focused upon top healthcare challenges: Dementia, Cancer, Obesity & Addiction

University research

Many Russell Group universities in the UK are engaged in cannabinoid research, including King's College London, University College London, the University of Oxford, and the University of Cambridge. These efforts are well supported by the government, with funding provided through agencies such as Innovate UK, the Biotechnology and Biological Sciences Research Council (BBSRC), and the Medical Research Council (MRC). Private companies have relatively limited access to such support.

A sense of the scale of cannabinoid research in UK can be seen through academic databases such as Scopus (Elsevier) or Web of Science. While the number of publications does not account for quality, it provides some sense of comparison.

Top 10 UK universities publishing cannabinoid research in the UK.

University	No. of publications of cannabinoid-related research using 'cannabinoid' and 'cannabis' from Scopus
King's College London	717
University College London	380
Imperial College London	257
Nottingham	214
Aberdeen	196
Oxford	174
Cambridge	133
Bristol	95
Hertfordshire	87
Manchester	76

DEFRA

The Department for Environment, Food & Rural Affairs (DEFRA) is critical to ensuring that the agricultural and environmental aspects around cannabis and cannabinoid production are appropriately regulated. It is also responsible for licensing and regulating plant varieties and ensuring that compliance measures are satisfied across various protocols, such as the UN's Nagoya Protocol which governs fair access to genetic resources.

In its role, DEFRA can provide guidance and support for cannabis cultivators, including for specific plant varieties that may be bred or engineered. The department can also assist companies working with plants and biological resources related to cannabinoids and ensure the supply of safe and good quality plant material for R&D purposes [71].

Department for Science, Innovation and Technology

The Department for Science, Innovation and Technology (DSIT) has an important role in promoting the UK as a global leader in cannabinoid R&D. Much of this is integral to its role in supporting businesses and life sciences more widely through attracting investment, facilitating trade partnerships, and promoting the UK abroad.

The NHS and NICE

As the primary healthcare provider in the UK, the National Health Service (NHS) plays a unique role in the large-scale adoption of proven, safe and effective medicines. Currently the only CBPMs it prescribes are Sativex, Epidiolex and Nabilone, with these applying to certain conditions and in cases where other treatment options have not proven effective [72].

Evidence-based reviews of medicines with potential applications in the NHS are conducted by the National Institute for Health and Care Excellence (NICE).

In 2020, NICE committed to reviewing large-scale trials and recommendations around the use of CBPMs in pain management, though at the time of this report's publication no such trials appear to have been undertaken.

NICE should continue to engage and work closely with industry to conduct timely reviews of new data as it becomes available [73, 74].

UKRI and Research Councils

UK Research and Innovation (UKRI) and its associated research councils are the official funding agencies for research in the UK, being critical to fostering academic and industry collaboration, stimulating medical discoveries and promoting related economic activity. The medical and life sciences councils offer world-leading support to conduct research through grants and different funding initiatives.

The MRC and BBSRC are already funding preclinical research into cannabinoids, but these projects are often limited in scope, consisting of grants of less than £1m [75, 76].

Companies in the UK are in a position to conduct advanced phase 2 and phase 3+ trials for cannabinoid research, with these mid-to-late phase clinical trials supported by university and industry infrastructure. However, progressing to this stage of cannabinoid R&D will require more funding than what is currently available, with the UKRI needing to offer larger scale grants for later stage clinical trials.

The ABPI

The Association of British Pharmaceutical Industry (ABPI) is an industry body that has a pivotal role in representing the interests of its members to the government. It also promotes guidance and industry best practices.

Currently there is limited understanding of how specific CBPMs or cannabinoids available for prescription relate to existing rules established by the pharmaceutical sector. There is therefore a role for the ABPI in establishing the place of CBPMs and cannabinoids alongside other pharmaceutical products. It is also crucial that CBPMs are marketed in line with the Prescription Medicines Code of Practice Authority (PMCPA).

III Challenges and Barriers for UK

While the UK has many strengths as a location for cannabinoid R&D, there are challenges that exist, most notably in the form of legislative barriers.

Misuse of Drugs Act

The most significant legislation underpinning cannabinoid R&D is the Misuse of Drugs Act (MDA), enacted in 1971 and enforced by the Home Office through licensing and permissions. Under this legislation plant and synthetic cannabinoids are classified as controlled substances, meaning that researchers must obtain licenses to possess, produce, distribute or supply these scheduled substances.

Classifying cannabinoids within these controls is complicated due to the large variety and nature of the substances [77]. In both 2001 and 2018 several CBPMs were rescheduled as Schedule 2 substances in recognition of their medical uses [78]. Among those moved in 2001 was Sativex, the medicine developed by GW Pharmaceuticals, which was recategorised to Schedule 4 after being authorised by the MHRA [78].

Many organisations in the sector are familiar with regulatory compliance and applying for the relevant controlled drug licences for R&D. However, the lengthy wait times, often opaque schedules and costs involved all presents barriers to progressing cannabinoid R&D. Those in the sector report that there are delays when dealing with the Home Office.

The uncertainty this causes makes it difficult for cannabinoid R&D companies to conduct standard business operations, in turn incentivising skilled workers within life sciences to focus their attentions elsewhere.

At the same time, it becomes difficult for companies to generate interest from investors, being unable to provide clear timelines as would be expected in other areas of pharmaceutical R&D.

For cannabinoid R&D in the UK to grow it will therefore be necessary for the Home Office to implement new protocols and clarify its processes, while also reflecting these changes in public guidance.

Transferring oversight to the DHSC

In light of these difficulties, this report recommends that licensing responsibility be transferred from the Home Office to the DHSC, benefiting both cannabinoid R&D and the wider life sciences sector.

As indicated above, the experience of many researchers liaising with the Home Office is that the department is not well placed to oversee areas of pharmaceutical development. One oft-cited example is that scheduled drug licenses for R&D are being granted by the same department that deals with firearms licensing. Certainly, the DHSC's focus on health outcomes is a better fit for cannabinoid R&D and associated UK life science companies.

The department's close relationship with the MHRA also provides opportunities to reduce the time taken to obtain necessary scientific guidance and expertise for scheduled drugs in medical R&D. This reflects the MHRA's current expertise, where drugs and medicines may also hold the potential for recreational abuse or misuse (as per MDA legislation) while having medical applications.

Pharmaceutical companies and investors are also more familiar with DHSC and MHRA infrastructure and processes.

Moving the responsibility of cannabinoid R&D oversight away from the Home Office would therefore facilitate access for clinical research, contract research organisations (CROs), university research networks, and other related healthcare specialists. This would likely reduce costs for the sector, with attendant improvements in efficiency for research into the safety and efficacy of this innovative class of medicines.

The ACMD

Alterations to the MDA are influenced by the Advisory Council on the Misuse of Drugs (ACMD), which makes recommendations to the government on controlled substances, including classifications and scheduling. In performing this role it compiles expert reviews and evidence to guide future regulations and enforcement.

In 2001 the ACMD influenced an amendment to the act on the grounds of health research considerations. The government should look to emulate this in following up on the committee's 2023 recommendations to reduce research barriers for all Schedule 1 controlled drugs [79].

In a similar vein, the ACMD should conduct a review that considers moving cannabinoids from Schedule 1 to Schedule 2, or a separate classification that grants special exemptions for research purposes. This would respond to the criticism that the current classification system does not reflect the medical potential or safety profile of cannabinoids and CBPMs in light of the growing evidence base from observational research, clinical trials and other sources about their therapeutic potential.

The relevant ACMD subcommittees should revisit their review and make recommendations specifically related to cannabinoid R&D.

Other potential reforms to the MDA would aim to harmonise regulations with international laws such as the UN and other jurisdictions by focusing on easing cross-border collaborations to facilitate import and export. Given the importance of multi-centre and multi-country clinical trials in R&D, this is pivotal for opening up international markets for UK-based companies and is a vital area of consideration.

New Psychoactive Substances Act

The New Psychoactive Substances (NPS) Act was implemented in 2016 to reduce access to novel psychoactive drugs, sometimes known as 'legal highs', which had become an increasing public health issue. While it has struggled to achieve its chief policy objective, an unintended side effect has been to increase the barriers for cannabinoid R&D.

The act has required that those researching synthetic cannabinoids apply for further licences, synthetic cannabinoids having been caught in the scope of the act due to their public health concerns. But such substances are a broad and complex category, thought to include more than a thousand types, including many that are neither psychoactive or intoxicating. Even those with toxicity are vital for fundamental preclinical research, such as research chemicals for animal studies and molecular probes to understand basic fundamental ECS science [80, 81].

The NPS has thus deterred researchers from focusing on synthetic cannabinoids in favour of botanical sources. This is despite the potential of synthetic cannabinoids as research tools or as medicines in areas that require innovation, including pain relief.

As with the MDA, enforcement of the NPS is influenced by an expert panel subcommittee within the ACMD that focuses on novel psychoactive drugs, drawing on independent scientific opinion on the associated harms.

As with other drugs covered by the MDA, the relevant decision-making lags behind the most recent research on cannabinoids, creating a further challenge for R&D. The ideal would be for new committees specialising in novel psychoactive substances or the effects of drug legislation on R&D to address these issues.

Innovative Licensing and Access Pathway

The Innovative Licensing and Access Pathway (ILAP) is a government initiative designed to accelerate the development and delivery of medicines in the UK, especially in areas that lack adequate therapies. It has been described by government as an "innovation passport", easing the ability of researchers to complete compliance processes with the MHRA, NICE and other regulators.

The pathway's focus on safety and efficiency aligns with the needs of the cannabinoid R&D sector, which as noted faces additional barriers on traditional drug discovery routes. Acquisition of the innovation passport would send a strong signal to investors of the potential for a drug to obtain full market authorisation.

Applicants under ILAP enjoy the following benefits:

1. Phases of using historical and real-world evidence data gathering. For instance, as medical cannabis is being used as unlicensed medicines by patients, a framework could be developed that integrates medical data collection from clinically validated assessment tools alongside quality control data of pharmaceutical products used. In principle, whilst limited in scope now due to the quality of specials medications on the market, if the correct protocols are developed the data can be accessed this data could be validated for specific CBMPs.
2. Adaptive licensing approaches that allow companies easier access to domestic, import or export licensing of any medicines in clinical development. This would not be fixed but applied on a moving scale basis if certain clinical endpoints are met.
3. Novel approaches to assessing any related pharmacology data or medical technologies and pharmacology data. These could include medical data from genetic and clinical tests or the use of new medical devices such as vaporisers.

IV Recommendations for UK Growth

As the role of cannabinoid R&D in life sciences continues to grow, the UK has the opportunity to become a world leader, leveraging its advanced academic and industrial infrastructure to lead medical innovation in the sector.

The government must align its policies and regulatory oversight with this objective. We are therefore proposing **ten main recommendations** across four main categories by which the government, industry and other stakeholders can help promote and foster cannabinoid R&D in the UK.

Five calls to action for government and regulators

Recommendation 1. The government should transfer the licensing authority for scheduled drugs involved in medical R&D from the Home Office to the DHSC, and in particular the MHRA.

The government should transfer responsibility for scheduling of cannabinoids with medical applications to the DHSC, with oversight passed to the MHRA. This could be accomplished through a licensing review focused on improving drug discovery and opening clinical research pathways.

The research licensing transfer proposal should contain guidance and details on the transfer of current licence holders and related data to the DHSC, the training of relevant personnel within the MHRA to grant licenses, and an update of current government communications in the form of new documentation and online guidance.

A licensing review could also develop guidance for companies working with non-intoxicating cannabinoids, notably CBD, with the potential for clarifying clear conditions so that these may not be considered scheduled drugs.

The licensing proposal should also include clear decision-making timeframes for R&D applications across scheduled drugs covered under the MDA, the NPS and relevant future legislation. This is to help promote efficient business practices and to allocate resources appropriately to clinical development and research activities.

Recommendation 2. The Home Office should respond to the ACMD's Barriers to Research report from December 2023, including the implementation of exemptions for companies and universities engaged in cannabinoid R&D in the UK.

The government must respond to the ACMD Barriers to Research review, published in December 2023 and proposing changes to licensing decisions for scheduled drugs for well-established research organisations and businesses conducting cannabinoid R&D.

These changes will need to be made in accordance with regulations and advisory committees associated with the MDA 1971, 2001, NPS 2016, Human Medicines Regulations (2012) and other legislation concerning clinical trials. The government must ensure it communicates clearly with any working groups involved in the relevant legislation and regulations.

Recommendation 3. The government should create a medical R&D roadmap for scheduled drugs in the UK over the next decade that includes cannabinoids.

The government must create a detailed medical R&D roadmap for the next decade that provides guidance on scientific research for cannabinoids and other psychoactive substances in the UK. It should outline clear routes for funding from the government and UK research councils – including the DHSC and NIHR – and incorporate the UK's academic and pharmaceutical infrastructure.

One option is to create three dedicated funds for cannabinoid R&D:

Fund one: £10m which is non-dilutive and not needing to be matched that is available for academic and industry applications conducting fundamental and pre-clinical science.

Fund two: £20m-30m for well-established academic R&D centres working with cannabinoids to carry out clinical trials.

Fund three: £20m+ for matched funding with industry and biotech partners with incentives to invest in later stage cannabinoid R&D and clinical trials.

The roadmap and associated funds will help UK biotech companies traverse the gap between pre-clinical and clinical research in the UK, discouraging investment in other territories.

Recommendation 4. The government should provide clear guidance that outlines the processes for developing botanical medicines in the UK.

The government should conduct a review on botanical medicine development in the UK in collaboration with the MHRA, Defra and the DBT, highlighting key points around IP protection, trade of biological material and establishing guidelines for botanical medicines using existing medical regulatory requirements.

The review must clarify the impact of the Nagoya Protocol and protections for biological diversity, which will help de-risk investment in botanical related R&D.

Recommendation 5. NICE should continue to engage with up-to-date evidence of CBPMs and update its public-facing communications to reflect this.

Following the rescheduling of medical cannabis in 2018, NICE should continue to monitor the clinical evidence for cannabinoids, including CBPMs, to reflect the evolving evidence base.

Call to action for the scientific and research community

Recommendation 6. The British Pharmacopoeia and associated regulatory agencies should review monographs for various CBPMs and synthetic cannabinoids.

In partnership with the British Pharmacopoeia, regulators, academic and industry bodies should establish good quality monographs, alongside the relevant experts to review the pharmacopeial monographs for cannabinoids in a timely manner.

Recommendation 7. The UK's cannabinoid R&D sector should establish an academic research network across the university research ecosystem to foster industry partnerships and develop best practices.

UK universities engaged in cannabinoid R&D should come together with commercial businesses and the wider biotech and pharma industry, including industry groups such as the ABPI, to set out clear guidelines that establish best practices and ethics for CBPMs and medical cannabinoids. Further to help create guidelines and processes for the commercialisation of research conducted from government funded projects at universities that may lead to the development of new medicines from cannabinoid R&D.

Call to action for investment

Recommendation 8. The DBT should encourage institutional and private investors to engage with the cannabinoid R&D sector.

The DBT should explore options to provide tax benefits or other incentives, such as matched funding, to promote institutional and private investment into cannabinoid R&D.

Recommendation 9. The biotech community should promote collaboration with the UK cannabinoid R&D sector.

The UK's biotech industry should create an annual cannabinoid R&D conference to engage with peers, investors and the wider life sciences industry on the topic of investment. This would highlight key investment opportunities and strategies that promote cannabinoid innovation.

As part of this effort, it is imperative that the industry engages with venture capital, public stock exchanges and industry associations. Guidance should be created to assist financial analysts in covering the sector for private and institutional investors.

Call to action for charities and not-for-profit organisations

Recommendation 10. Charities, not-for-profit organisations and scientific societies to engage and promote cannabinoid R&D efforts

Charities should be encouraged to collaborate with industry on campaigns, research projects, fundraising and public communication around the science of the ECS and cannabinoids, including CBPMs, in line with their charities' key objectives. Well-established medical and scientific charities in the UK can help promote good quality science, reduce stigma, and increase public understanding.

Conclusion

This report provides a comprehensive analysis of the current landscape and future potential of cannabinoid R&D in the UK. Our findings underscore the sector's potential to advance life sciences and public health in this country, as well as the associated economic benefits.

As outlined above, the UK is a global leader in industries that are relevant to cannabinoid R&D, namely biotech, pharma and life sciences. Its historical strength in scientific research through the Royal Societies, leading universities and regulatory institutions is matched by the strength of the financial sector.

To fully tap into these strengths, the UK requires some changes to how the sector is regulated. Our key recommendation is that regulatory oversight of cannabinoid R&D be transferred from the Home Office to the DHSC and the MHRA. This would mark a profound change in government thinking, treating the sector as medical rather than criminal.

Ideally this would be accompanied by changes to the scheduling of cannabinoids under the MDA, at least for the purposes of medical research. The timelines for licensing approvals should also be reduced whichever department has oversight of the sector.

Alongside regulatory reforms, cannabinoid R&D would benefit from a changed approach in government funding of the sector. Better funding would allow researchers and companies to bridge the gap between pre-clinical and clinical research, the latter being underdeveloped at this stage.

More investment will also come as a result of better co-ordination within the industry. We are calling on the sector to establish an annual conference to share knowledge and educate potential investors about the opportunities for cannabinoids in the UK.

By implementing the recommendations outlined in this report, the UK can solidify its position as a global hub for cannabinoid research. While it will cement the country's position in life sciences and generate significant economic benefits, the most important beneficiaries will be the patients enjoying a better quality of life as a result of the sector flourishing.

Contributors

Zack Bellman

Prof. Sagnik Bhattacharyya

Barinder S. Bhullar

Paul Birch

Dr Grace Blest-Hopley

Jake Elms

George Freeman MP

Bill Griffin

Professor Trevor Jones

Damian Mitchell

Steve Moore

Dr Ado Hadejia Muhammad

Jimmy Nicholls

Dr Elisabeth Philipps

Dr Mikael Sodergren

Clarissa Sowemimo-Coker

Jeremy Sturgess-Smith

Dr Sebastian Vaughan

Dr Andy Yates

Zehra Zahir

Abbreviations

ABPI Association of the British Pharmaceutical Industry

CB1 Cannabinoid receptor type 1

CB2 Cannabinoid receptor type 2

CBD Cannabidiol

CBG Cannabigerol

CBMPs Cannabis-Based Medicinal Products

Defra Department for Environment, Food & Rural Affairs

DSIT Department for Science, Innovation and Technology

DHSC Department of Health and Social Care

ECS Endocannabinoid System

HO Home Office

IP Intellectual Property

MHRA Medicines and Healthcare products Regulatory Agency

MS Multiple Sclerosis

NHS National Health Service

NICE National Institute for Health and Care Excellence

NIHR National Institute for Health Research

R&D Research and Development

THC Tetrahydrocannabinol

UKRI UK Research and Innovation

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Appendix i

Timeline of notable cannabinoid R&D until 2012 to illustrate notable research. In the UK medical cannabis was rescheduled in 2018. Adapted and sourced from Pertwee, R. G. (Ed.). (2014). Handbook of cannabis – see [10] for more detail.

1998	GW Pharmaceuticals begins cultivation, UK	*Guy and Stott*
	"Endocannabinoids" described: "relax, eat, sleep, forget, and protect"	*Di Marzo*
	Endocannabinoid "entourage effect"	*Ben-Shabat et al. Mechoulam and Ben-Shabat 1999*
	THC, CBD, neuroprotective antioxidants	*Hampson et al.*
	THC produces apoptosis in glioma	*Sanchez et al.*
2000	CBD antagonizes tumor necrosis factor-alpha in rheumatoid model	*Malfait et al.*
2001	CBD is a TRPV1 agonist, fatty acid amide hydrolase-inhibitor, stimulator of AEA synthesis	*Bisogno et al.*
	Clinical endocannabinoid deficiency syndrome hypothesized	*Russo*
2002	CBD antinausea effects	*Parker et al.*
2003	First trial of Sativex in multiple sclerosis symptoms	*Wade et al.*
	THC, cannabis extract benefit mobility, subjective spasticity in MS	*Zajicek et al.*
	THC improves Tourette symptoms without neuropsychological sequelae	*Muller-Vahl et al.*
2004	Sativex benefits pain	*Notcutt et al.*
	Cannabis extracts reduce urological symptoms in MS	*Brady et al.*
	Sativex, high-THC extracts effective in brachial plexus avulsion pain	*Berman et al.*
	THC reduces MS pain	*Svendsen et al.*
	CBD increases wakefulness, counteracts THC sedation	*Nicholson et al.*
2005	Sativex approved in Canada for neuropathic pain in MS	*Rog et al.*
	THCV CB1 antagonist	*Thomas et al.*
	CBD agonist at serotonin-1A	*Russo et al.*
2006	CBD, other phytocannabinoids cytotoxic in breast cancer	*Ligresti et al.*
	Sativex reduces pain, disease activity in rheumatoid arthritis	*Blake et al.*
2007	Sativex in peripheral neuropathic pain	*Nurmikko et al.*
	Sativex approved in Canada in opioid-resistant cancer pain	*Johnson et al.*
	CBD antagonizes CB1 in presence of THC	*Thomas et al.*
	CBD reduces prions, toxicity	*Dirikoc et al.*
2008	Benefit in short-term study of HIV neuropathy	*Ellis et al.*
	CBD, CBG antibiotic for methicillin-resistant *Staphylococcus aureus*	*Appendino et al.*
	Cannabis effective in brief neuropathic pain trial	*Wilsey et al.*
2010	Sativex approved UK, Spain for intractable spasticity in MS	*Novotna et al.*
	Sativex reduces pain in opioid-resistant cancer	*Johnson et al.*
	THCV anticonvulsant	*Hill et al.*
	Sativex benefits urological MS symptoms	*Kavia et al.*
	Cannabigerol a potent TRPM8 antagonist for prostate cancer	*De Petrocellis and Di Marzo*
	Cannabidivarin, THCV anticonvulsant	*Hill et al. 2010; Jones et al.*
	Sativex improves intractable nausea of chemotherapy	*Duran et al.*
	THC attenuates breast cancer	*Caffarel et al.*
	Cannabis genome published	*Medicinal Genomics; Van Bakel et al.*
2011	THC, CBD synergize with temozolomide reducing glioma growth	*Torres et al.*
2012	CBD equals standard antipsychotic	*Leweke et al.*

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