Health matters
Legislating for the medical use of cannabis based medicinal products

An examination of the current legislative proposals and the potential health and economic benefits for Ireland.

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The regulation of cannabis in Ireland
Currently cannabis and products extracted from the cannabis plant are controlled under the Misuse of Drugs Acts 1977 to 2016 (the ‘Misuse of Drugs Acts’) and the various ministerial regulations and orders made pursuant to these Acts.

In particular the Misuse of Drugs Regulations 1988 list cannabis as a Schedule 1 controlled substance, which makes it illegal in Ireland to manufacture, produce, prepare, sell, supply, distribute or possess cannabis, save for very limited research purposes.

In 2014 an exception to the above position was introduced to allow a medicine, Nabiximols, which contains an extract from the cannabis plant to be prescribed in Ireland. Nabiximols (also known as Sativex) has been authorised for use in Ireland by the Health Products Regulatory Authority (‘HPRA’) as a prescription only medicine for the treatment of adult patients with moderate to severe spasticity as a result of multiple sclerosis who have not responded adequately to other treatments.

To date this has been the only provision under Irish law allowing for the use of cannabis, or products derived from cannabis, (with psychoactive properties) for medicinal purposes.

However, in late 2016 a private members bill, the Cannabis for Medicinal Use Bill 2016 (the “Medicinal Use Bill”), was introduced to the Dáil and unlike the vast majority of private member bills, the Medicinal Use Bill garnered broad cross party support and the government indicated that they would not oppose its passage through the first stage of the Dáil.

The Bill seeks to decriminalise the use of cannabis for medicinal purposes and also to put in place a regulatory environment which would allow companies to engage in production and research and development activities in Ireland.

On foot of this the Minister for Health, Simon Harris, commissioned a report by HPRA to examine the use of cannabis for medicinal purposes across a number of jurisdictions and the evidence of the efficacy and effectiveness of such medicinal use.

The chemistry behind cannabis
Cannabis as a medicinal product is swiftly moving away from the stereotypical image of a Californian dispensary providing legal highs to those with questionable medical conditions to a pharmaceutical grade product that is capable of providing relief to conditions where existing medicinal products have either proved to be ineffective or have been shown to have limited success.

As our understanding of the medical properties of cannabis develops, the focus has shifted from the plant itself towards the biological agents within the plant that produce the desired medicinal effects.

The cannabis plant produces in excess of 100 biologically active chemical compounds, referred to as cannabinoids. These cannabinoids bind to receptors within the body’s endocannabinoid system, which are located primarily in the brain and throughout the central and peripheral nervous system and play an important role in the body’s general health and in certain disease processes.

The two most prevalent cannabinoids in the cannabis plant are tetrahydrocannabinol (‘THC’) and cannabidiol (‘CBD’) and to date these have been the primary focus of medical research relating to cannabis.

THC is the main psychoactive component within the cannabis plant and is therefore strictly controlled under the Misuse of Drugs Acts. Whereas, CBD does not have a psychoactive effect and therefore products containing only CBD are not regulated under the Misuse of Drugs Acts.
The difficulty with this approach is twofold, in the first instance this rigid approach fails to recognise that there is evidence that certain cannabinoids can counteract the psychoactive effect of THC when combined together, for example it is believed that CBD is capable of counteracting many of the psychoactive effects of THC in products with a high CBD to THC ratio. Similarly, the approach fails to recognise that research to date has shown that the primary medical benefits of cannabinoids are derived from a mixture of cannabinoids interacting with the body’s endocannabinoid system, and therefore an approach which bans specific cannabinoids will limit the overall effectiveness of medicinal products derived from cannabinoids.

**Shortcomings of existing medicinal products**

The primary shortcoming with existing cannabinoid based medicinal products is that they are produced directly from the cannabis plant, which prevents these products from obtaining pharmaceutical levels of consistency of composition.

The clearest comparison to highlight this shortcoming is to opioid based medicinal products, such as oxycodone, hydrocodone and morphine. While these medicinal products have their origin in the poppy plant, in the same way as cannabinoid based medicinal products are based on the cannabis plant, opioid based medicinal products are now synthetically derived from those compounds originally found in the poppy plant.

To date cannabinoids have not been synthetically produced in the same manner and therefore it has not been possible to produce cannabinoid based medicinal products with the same compositional consistency as those found in opioid based medicinal products.

This has also posed a significant difficulty when it comes to conducting clinical trials of cannabinoid based medicinal products and compiling data on their efficacy and effectiveness. As cannabinoid consistency can vary significantly between the different dosages of the same drug administered to patients in a clinical trial, it is difficult to say with any degree of certainty whether a patient failing to respond to the treatment is as a result of the drug itself not being effective or whether it is as a result of the drug not containing sufficient levels of the intended cannabinoid to produce the desired effect.

While this difficult is one which has plagued the development of cannabinoid based medicinal products to date, it is a shortcoming which is expected to be addressed in the near future. With the development of new technologies to artificially synthesise cannabinoids it will shortly become possible to produce pharmaceutical grade cannabinoid products.

This will greatly improve the ability to gather robust clinical evidence in relation to the medical benefits of cannabinoid based medicinal products and their effectiveness in relation to certain conditions.

While this technology is still being developed it is important to view the discussions surrounding the use of cannabinoid medicinal products in the light of where the industry is going rather than looking at a snapshot of the present moment in time.

**The HPRA Report**

On 10 February 2017 the Minister for Health published the HPRA Report (Cannabis for Medical Use – A Scientific Review) and announced that he would work with HPRA to provide for a system which would allow access to cannabis-based treatments for certain medical conditions.

The HPRA report has been seen as an important milestone in the development of future policy and legislation in relation to the medical use of cannabis in Ireland, however, in order to interpret and understand the HPRA report it is important to understand the role of HPRA and the scope of the report itself.

HPRA is the regulatory body in Ireland charged with ensuring that medicines on the Irish market are safe, effective and of an appropriate quality based on existing clinical and scientific data. HPRA are therefore not concerned with impact of future development and emerging technologies but rather are concerned with the efficacy and effectiveness of existing medicinal products.

While broadly endorsing the use of cannabinoid based medicinal products, the report correctly identifies the two primary concerns in relation to the current form of medicinal products available on the market, those being the lack of robust scientific evidence supporting their efficacy and effectiveness and secondly the concerns surrounding the potential impact which psychoactive cannabinoids, such as THC, may have on adolescents.

The report discusses the potential risks which psychoactive cannabinoids can have on brain development, particularly during the adolescent years and notes that adolescents may be particularly susceptible to the psychiatric and neurocognitive effects of such cannabinoids, which could disrupt normal brain development.
While highlighting the current shortcomings within the industry and ringing a sensible note of caution in relation to the use of such medicinal products to treat adolescents and young children, the report broadly endorses the use of cannabinoid based medicinal products to treat the following conditions:

- spasticity associated with multiple sclerosis;
- uncontrollable nausea and vomiting associated with the use of chemotherapy; and
- severe treatment resistant epilepsy.

The report recommends the introduction of a monitored cannabinoid based treatment programme for these medical conditions, for a period of five years, with a view to creating a centralised data collection point for evidence in relation to the efficacy and effectiveness of these medicinal products.

While the report goes on to examine the legislative regimes in other jurisdictions in relation to access to cannabinoid based medicinal products, it does not examine the impact of these regulatory regimes on the conduct of research and development activity in relation to these medicinal products or its impact on the production and manufacturing of these products within the relevant jurisdictions.

A developing market

While cannabinoid based medicinal products remain dogged by the stereotypical image of a Californian dispensary, this image is rapidly fading as cannabinoid medicinal products transition into pharmaceutical grade medicinal products.

With this transition comes an opportunity for the Irish economy to place itself at the forefront for research and development activities related to these products and to position itself as a natural environment for the manufacture and production of these products.

Over the past number of years Ireland has successfully developed itself into a market leading economy for the pharmaceutical industry, with eighteen of the world’s top 20 pharmaceutical companies having operations in Ireland and six out of 10 of the world’s best-selling drugs being manufactured in Ireland.

The sector’s success can be attributed to two primary factors, the first being the inherent strengths within the Irish economy (those being a well-educated English speaking workforce, an economy that offers a gateway to the European market and a competitive corporate tax regime) and the second being strong governmental support for the industry.

The Irish government has seen the pharmaceutical sector as one of the pillars of the Irish economy and has supported the sector through the introduction of various incentive schemes, such as the knowledge box to promote and stimulate research and development activity within the Irish economy, together with ensuring that a responsive and engaging regulatory regime is in place for the sector, with HPRA being recognised as one of Europe’s leading regulatory bodies in relation to practical engagement with the companies it regulates.

While this approach has been extremely successful in helping to grow the sector within Ireland, the current legislative regime in Ireland does not offer the same supportive structures for research and development activities or manufacturing activities related to cannabinoid medicinal products.

The rigid treatment of cannabinoid based medicinal products under the Misuse of Drugs Acts will make it difficult for pharmaceutical companies engaging in research and development activities or manufacturing activities to base themselves in Ireland over other jurisdictions such as, Canada, Israel, the Netherlands, Australia and the United States, all of which have more welcoming regulatory regimes in relation to medicinal based cannabinoid products.

Future regulation in Ireland

While the Minister for Health announced on 10 February 2017, in conjunction with the launch of the HPRA report, that he would be proceed with the advice of HPRA and establish an access programme for cannabis-based treatments for certain conditions, where patients have not responded to other treatments and there is some evidence that cannabis may be effective, to date there has been no indication as to the amendments which will be sought to the Medicinal Use Bill.

The HPRA report has now been referred to the Select Committee on Health, who are currently considering amendments to the Medicinal Use Bill. While the HPRA report will be a key component in the Medicinal Use Bill’s development, the report itself only covers certain aspects of the Bill, which goes beyond the availability of these medicinal products to Irish consumers and seeks to comprehensively overhaul the regulatory regime in Ireland.

It is unclear whether the HPRA report will serve to limit the scope of the Medicinal Use Bill when it emerges from the Committee Stage or whether it will instead serve to inform those parts of the Bill which specifically deal with access for Irish consumers.

Pharmaceutical companies who are currently investing in technology to bring cannabinoid based medicinal products into the pharmaceutical grade medicinal product market will undoubtedly be keenly watching to see how the Bill emerges from the Committee Stage, in order to determine whether Ireland is positioning itself to take advantage of this emerging marketplace.
Commentary
Unfortunately, much of the debate about the use of cannabinoid medicinal products is hampered by the stigma associated with recreational cannabis abuse. While opioid based medicinal products are linked to far more severe drug abuse, their value as medicinal products is not linked to the recreational abuse of their sister drugs. This is however, undoubtedly due to the fact that cannabinoid based medicinal products are yet to be produced to the same standards as those of opioid based medicinal products.

While this is currently the case, technologies are currently being developed, and are at an advanced stage, that will ensure that pharmaceutical grade consistency is possible with cannabinoid based medicinal products. That being the case it is essential that when reviewing the existing regulatory regime the Irish government looks towards the future of this industry rather than taking a snapshot of its current status.

When considering amendments to the Medicinal Use Bill, it is essential that the Select Committee is mindful that the HPRA report looks at a certain aspect of a much larger picture and that, when producing this report, HPRA has approached the task from its position as a regulatory body concerned with the efficacy and effectiveness of those medicinal products currently available.

Many other jurisdictions have long viewed cannabinoid based medicinal products as the next generation of medicinal products, offering potential treatments to those conditions which, to date, have proven resistant to existing medicines.

With the Medical Use Bill, Ireland has the opportunity to position itself as a market leading economy for the research and development and manufacturing of these medicinal products, in the same manner as it has with the broader pharmaceutical industry.

In considering the Bill, it is therefore essential that the government not only consider the question of access for Irish consumers, but also consider the broader economic opportunities for Ireland.

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