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# Note of Meeting – Cross- Party Group on Epilepsy, 26 April 2018

## In Attendance:

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| Dr Swaraj Alkanti, NHS Fife | Raymond Hussain, Epilepsy Connections |
| Jane Anderson, NHS Fife | Chris Jeans, SUDEP Action |
| Mary Antczak, Epilepsy Connections | Sylvia Lawrie, Observer |
| Rebecca Bell, Media Officer & Parliamentary Researcher for Alex Cole-Hamilton MSP | Dr Pamela Martis, Observer |
| Karen Berry, NHS Tayside | Shirley Maxwell, Epilepsy Connections |
| Lyndsay Bews, Journalist | Barbara McCulloch, Observer |
| Andrew Boyle, NHS Fife | Michael McCulloch, Observer |
| Celia Brand, ESN NHS Lothian | Dr Ailsa McLellan, NHS Lothian |
| John Bruce, Epilepsy Connections | Hilary Mounfield, Observer |
| Aileen Bryson, Royal Pharmaceutical Society | Ann-Marie Nelson, Muir Maxwell Trust |
| Susanne Cameron-Neilson, Royal Pharmaceutical Society | Ronnie Prentice, West Dunbartonshire Support Group (WDSG)/ observer |
| Jane Cassidy, Observer | James Riddick, WDSG/observer |
| Dianne Carroll, NHS Greater Glasgow & Clyde | Kelly Robertson, WDSG/observer |
| Dr Richard Chin, Muir Maxwell Epilepsy Centre | Brian Rocks, WDSG/observer |
| Eugine Chizooma, Eisai Ltd | Jillian Rose, Observer |
| Alex Cole-Hamilton MSP | Dr Eleonora Saturno, NHS Fife |
| Steven Connolly, Epilepsy Connections | Anna Smaill, Muir Maxwell Trust |
| Magnus Corkish, NHS Forth Valley | Michelle Small, NHS Lothian |
| Dr Susan Duncan, NHS Lothian | Dr Jane Stuart, NHS Lothian |
| Ian Forbes, UCB Pharma | Elaine Tait, WDSG/observer |
| Kenneth Gibson MSP | Sharon Thinn, NHS Fife |
| Paul Gillon, Veriton | John Thomson, Eisai Ltd |
| Tracey Goodfellow, NHS Lothian | Anissa Tonberg, Epilepsy Scotland |
| Ann Gray, West Dunbartonshire Support Grp | David Torrance MSP |
| Karen Gray, Observer | Sam Whitmore, Epilepsy Connections |
| Ann Greenall, NHS Fife | Grant Wright, Epilepsy Scotland |
| Joanne Hill, Quarriers | Kim Workman, Observer |
| Andrena Hughes, Observer | Lesslie Young, Epilepsy Scotland |

## Apologies:

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| Declan Aherne, NHS Lothian & ESNA | Ann Maxwell OBE, Muir Maxwell Trust |
| Dr Jean Barclay, Observer | Lorraine MacKenzie, Observer |
| Jane Cassidy, Observer | Mary-Anne McCafferty, Lanarkshire Epilepsy |
| Lynne Dignon, Share Scotland | Kevin McKay, Lanarkshire Epilepsy |
| James Dornan MSP | Caroline McKenna, WDSG/Observer |
| Bridget Fordham, WDSG | Dr Aline Russell, Quarriers |
| Tom Fordham, WDSG | Margaret Walker, WDSG/Observer |
| Jane Holmes, Observer | Darren Wilkinson, NHS Forth Valley |
| Jennifer Irvine, NHS Lanarkshire | Margaret Wilson, NHS Greater Glasgow & Clyde |

1. Convener Kenneth Gibson MSP welcomed attendees to today's meeting.

2. The draft note of the January 2018 meeting was approved. An update was given on activities:

- Kenneth Gibson MSP submitted a Parliamentary Members' Motion about improving the health and wellbeing of children and young people with epilepsy in Scotland, hoping to secure a members' debate on the issue during National Epilepsy week. The motion has achieved cross party support.
- Kenneth has received written answers to three recent parliamentary questions on sodium valproate, epilepsy and pregnancy and specialist nursing; these have been circulated by the Secretariat.

- Following our CPG meeting on “Epilepsy and Pregnancy” in January, a company has now agreed to support the Scotland-wide roll out of a scheme for pharmacists to give information cards on epilepsy and pregnancy to women with their epilepsy medication prescriptions. The Secretariat is working towards convening a Scottish working group on epilepsy and pregnancy
- It was announced yesterday that sodium valproate should no longer be prescribed for women and girls of childbearing age unless they are on a pregnancy prevention plan and are fully informed of the risks.
- An application by Quarriers Scottish Epilepsy Centre to the NHS’s National Services Division to become a Nationally Designated Service has been declined. The epilepsy clinical community is preparing a letter to Cabinet Secretary Shona Robinson.
- Kenneth welcomed Jeremy Balfour MSP as the newest CPG on Epilepsy member.
- In September we will have a joint CPG meeting with the Cross Party Group on Multiple Sclerosis. The Minister for Public Health will attend to talk about the government’s Neurological Action Plan and will take questions about epilepsy and government policy.

3. Kenneth welcomed guest speaker Dr Richard Chin to talk about epilepsy and medical cannabis, and his involvement in recent trials of a new treatment. The presentation included the following points:

- Dr Chin began with a disclaimer that he has given a one-off consultation with GW Pharma to give some advice as to the design of their clinical trials, and that he was an investigator in the GW Pharma sponsored multi-centre international clinical trials.

- Often when people talk about cannabis they think of it as one thing, however there are many different types of cannabis, with different characteristics, and with more than 70 different psychoactive substances. Some of these characteristics can be dangerous, some can be beneficial, and getting that combination right consistently and being able to titrate them are critical issues. It is also a particularly emotive subject. Under the Hippocratic oath the first rule is “Do no harm”; whatever clinicians do should be safe and legal, and in order to determine if something is safe and legal we base it on the data that is available to us at the time. That is not to say that legal issues or safety issues should not be challenged - they should be – but it should be based on the data that is available at the present time. Dr Chin mentioned thalidomide and sodium valproate as examples of safety problems emerging after initial approvals.

- The Home Office current stance is that “it is unlawful to possess, supply, produce, import or export cannabis and any one of these cannabis plants except under Home Office License”. Cannabidiol (CBD) – a component of cannabis – in its pure form would not be controlled under the usual scheduling.

- Many CBD products do not fully disclose their contents or provide a full spectrum of analysis at an appropriate level of sensitivity to accurately and consistently determine their true content or controlled status. Against that background, the presumption has to be caution, and that a CBD-containing product on the internet, street corner or pharmacy could be controlled under the current HMO Home Office regulations as a result of possible other cannabinoid content.

- Epidiolex is a pure form of CBD. It contains a small component of THC, but it is less than 0.2%. The trials have been completed in two specific, severe types of epilepsy as well as an extended access programme. Overall the efficacy is about 40%. It is not 100% and does not work in everyone. It does have noticeable side effects, which are potentially quite serious. Most of the data that we have is based on pre-clinical or early clinical trial data and so we don’t know what effects CBD has on the developing brain. It is currently

unlicensed, however a decision of whether it will gain Food and Drug Administration (FDA) approval in the States will be announced in June. There has been an application submitted for licensing to the European Medicines Agency (EMA), which would oversee UK regulations, and the result should be known by the end of 2019. In the meantime, the company will consider individual applications on a named patient basis.

- Cannabinoids can cause brain injury and so controlled monitoring is required. For example, we use the opiate diamorphine, which is tightly regulated with very good quality control and used routinely in pain and palliative care - but we don't go out and buy heroin for patients. Instead we give a highly regulated, quality-controlled product. Pre-natal exposure to THC causes long lasting functional alterations that occur in the brain and affects learning and behaviour. Different cannabinoids can have positive and negative effects, so a drug's content and quality control are very important. We do not yet know exactly how epidiolex works and what the long-term side effects may be.

  Epidiolex has been well tolerated in animal models – it does seem to have a synergistic action and drug interactions with some other anti-epileptic drugs, in particular sodium valproate and clobazam, however with no major organ-related toxicity or observed serious adverse effects.

- Dr Chin gave an overview of the trials that occurred, detailing two studies; one in Dravet Syndrome and one in Lennox-Gastaut Syndrome which have been completed and published. There are on-going studies regarding Tuberous Sclerosis and infantile spasms.

- Dr Chin described an open label study of 214 patients, of whom 20% had Dravet and 19% had Lennox-Gastaut. Adverse effects occurred in 79% of patients overall, 20% had serious adverse events which suggests it is not a benign drug. Concerning efficacy, there was a median reduction in motor seizures of 36.5% which is equivalent or very similar to any of the other anti-epileptic drugs that come on the market. There are controlled trials which have now been published which look individually at Dravet and Lennox Gastaut patients. These were international multi-centre studies of epidiolex as an add on drug; participants received standard treatment plus epidiolex or placebo. Those people who were on the drug were more likely to have lower seizure frequency compared to those who were not on the drug. Also, parental views as to how much the children improved showed a significant improvement in patients who were on epidiolex. There was similar efficacy for both low dose (10mg/kg) or high dose (20mg/kg).

- Although the FDA report says there is sufficient exposure to assess adverse effect, this is only short-term data and so we don't know what long-term effects there are and what problems may be encountered in the future. The most common short-term effects are liver problems; some patients had raised transaminases and had to be monitored very carefully. Some patients dropped out of the studies because their liver levels were rising alarmingly. We don't know what would happen if they continued on that medication and if they would go into permanent liver failure. One of the most common reasons of dropping out was a much higher rate for infections, particularly lower respiratory tract infections and pneumonia. Both high and low doses were similar regarding efficacy, but side effects were dose dependant, so the risk of adverse effects was higher for those on the higher dose. There was a drug interaction between epidiolex and Clobazam. The liver function problems tended to be more pronounced in those on valproate and epidiolex at the same time.

- There is a question over whether, if you take a pure form of CBD, does it actually change and convert to a negative psychoactive substance once it is in the body? Now that trials with pure CBD are completed, further studies in humans are needed in order to see whether there are any signs of THC being produced. If you look at simulated gastric fluids

in an acidic environment, it would appear there is some CBD converted to THC, however other studies show no conversion. There has been conflicting evidence from rodent models, some of which show THC in the brain and/or blood, in particular at higher concentrations like 50mg and 60mg.

- In summary, there appears to be evidence that CBD does work but that it does not work in everyone and that there are concerns about the safety effect profile. There are questions about long term safety, efficacy, dosage and monitoring. Dr Chin felt that if it is being prescribed it should be regulated and monitored very carefully – we need to know what we are looking out for and how to do that.

4. The Convener thanked Dr Chin for his presentation and invited questions.

**Karen Gray** - mother of a child with drug-resistant Doose Syndrome, said she was taking a petition to Downing Street this week seeking to make medical cannabis available on the NHS. She said she is often asked why she has not bought him CBD available from health shops and that the reason is because of the risk of it interacting with the other epilepsy medications he is on. She would like to see medical cannabis available on the NHS for patients of epilepsy and other conditions. She felt it was important it was regulated and overseen by doctors, because of the risk of damage to the liver.

**Alex Cole-Hamilton** – As Karen's MSP, he was profoundly moved by her family's story. He was keen to hear views about the legislative landscape, the role of clinicians in this and what we can do within this country if at all to remediate that situation.

**Dr Chin –** said that clinicians are in the business to help families and it is really frustrating for them where three out of ten children don't respond to epilepsy medications and so they are fully supportive of wanting new drugs and modalities to emerge. So, clinicians welcome the possibility of drugs like epidiolex but again quality control must be paramount and being able to regulate and monitor very closely is essential.

**Aileen Bryson** – said that the Royal Pharmaceutical Society (RPS) would support a change in the legislation, which is reserved to Westminster, from schedule 1 to schedule 2 of the Act to allow more clinical research in this country, which she understands is being hampered in general not just for epilepsy but for any medicinal cannabis clinical trials for patient-facing concept. The RPS feels that research has been hampered, and their science team is very keen that legislation is changed to open up the possibility of more clinical research which is a significantly limited at the moment.

**Dr Chin** – said that the pre-clinical data was possible but that clinical trials were somewhat hampered by the way in which drugs needed to be escorted from one place to another with security guards because of the issue regarding schedule 1. Although epidiolex is considered a non-controlled drug because of the low THC component in it, in France for example the threshold is different, and it is considered illegal.

**Aileen Bryson** – the potential for any of the compounds to be investigated further is being hampered by the legislation which is very restrictive, making it difficult to allow human trials, which must be done; we may never know the vast extent of the risks or benefits until the global trials are undertaken on any drug and a huge number of people are taking it. There is a long way to go with this but the RPS would be supportive of the first step, which would be to change the legislation.

**Kenneth Gibson MSP** – thought that the length of time to get a drug to market was deeply frustrating for clinicians, however this is because you must firstly ensure that you do no harm before you can consider what benefits can actually be gained.

**Andrena Hughes** – asked whether, since the effect it has on the developing brain is unknown, would that be something that would be progressed further before experimenting in using it?

**Dr Chin –** replied that the pharmaceutical threshold for approval is a bit different from the clinical scenario and sometimes information that we would like as clinicians isn't exactly the same. For example, in terms of seizure control, from the pharmaceutical stand point we are interested in how effective this is after 12 weeks. As clinicians what we would also like to know is effectiveness after two years, 5 years - is it just a honeymoon period? From a pharmaceutical standpoint, all that needs to be shown is that it is safe in terms of what the short-term outcome is. What he would also like to know as a clinician are both the short-term and long-term side effects.

**Brian Rocks** – asked about the other 69 potential components within cannabis.

**Dr Chin** – Potentially you could have combinations of that 70 so you could have A+B, A+B+C – there are many, many different combinations that we could have - so we may look to see what are the ones that seem to be having the best effects.

**Anissa Tonberg** – asked a) whether FDA approval of epidiolex in the USA might expedite its approval in Europe, and b) if it does get licensed at the end of 2019 is it likely that neurologists might start to prescribe it on an off-label basis in adults?

**Dr Chin** – a) The EMA (European Medicines Agency) tends to be a bit more rigorous compared to the FDA and it is currently hard to say whether it would be fast-tracked or not. The company would need to apply for fast tracking and the usual thing is to show that something has potentially life-changing potential. b) The license application submitted to both the EMA and the FDA was for licensing above the age of two in Lennox Gastaut and in Dravet Syndrome. The trials cover both adults and children so it should be able to be supplied for adults for those two specific conditions, but there are a number of different drugs that have been approved for those conditions and are used off-license, so it seems likely that it will also be prescribed off-license.

**Alex Cole-Hamilton –** it's understandable why the Misuse of Drugs Act would restrict physical trials in the UK, but is there not basic data from other parts of the world where they have been exploring cannabis therapies for epilepsy and or is this just a new field that we are just exploring now?

**Dr Chin -** investigations into cannabis in epilepsy is a relatively recent field, e.g. in the past 10 to 15 years. Investigators need to be confident that what we are doing is being done robustly. When the open-label studies were done in which everyone knew what they were getting, there were subgroups within that in which parents were asked if their child improved or not. Parents reported an improvement when in fact when those same patients were put under video monitoring, there was no improvement. However the gold-standard of placebo randomised controlled trials requires a big enough cohort so that results are not by chance, and that is why those trials are so very difficult.

**Kenneth Gibson –** Pharmaceutical Industry has to be cautious because there have been disasters over the years, like Thalidomide, which has cost the industry billions of pounds and brought discredit upon it. So what is important is not just that the clinical trials are undertaken but that they are undertaken in jurisdictions that are recognised by other jurisdictions. There are certain countries in the world where you can do trials but they might not be recognised - for example in Europe.

**Kim Workman –** said that her son has severe, treatment-resistant epilepsy and wanted to highlight the impact on his education and social life. She welcomed whatever could be done to expedite approval of epidiolex so that people can try it.

**Anissa Tonberg –** asked if Dr Chin could explain why CBD potentially being converted to THC in the brain is not good.

**Dr Chin –** replied that THC is one of the 70 cannabinoids, it is psychoactive and is the component mostly responsible for the highs and also a lot of the negative aspects of cannabis, such as psychosis and other mental health disorders. THC has long term effects on brain receptors, so it exerts a physical structural change that occurs and has a long-term effect on cognition and learning. It is a big worry if we now have a drug which doesn't contain that when it is ingested, but which changes and converts once it reaches the acidic environment of the stomach. There are questions over whether this then enters the blood stream and crosses the blood-brain barrier. Studies on this have been conflicting or do not mimic the human situation, however it seems imperative now that children on epidiolex are monitored to see if there are any signatures for THC in their blood or urine.

**Sylvia Lawrie –** the mother of a woman with intractable epilepsy, asked whether the children that were on the trials who are still on the cannabidiol are being monitored?

**Dr Chin –** clarified that he was part of a multi-centre trial and currently the trials and their follow-ups have been completed. However, clinicians who have been involved in the trial and are following patients up in terms of what their seizure control has been following continued use of the medication and whether their development continues. If children who took part in the trial gained benefits from the drug - whether seizure or cognitive improvement – they were given the option to continue it outside of the trial.

**Karen Gray** – said she felt that currently available epilepsy medications have lots of bad side effects and thought that trying cannabidiol would be a good option. She wondered if any attendees disagreed that medical cannabis should be available on the NHS?

**Dr Susan Duncan –** thought that at the moment it should only be available in exceptions, she felt from listening to Dr Chin that the evidence so far is not overly convincing and that further evidence is required before spending public money. She felt that we do not really know what the full side-effects might be because the current data covers a very short time period.

**Kenneth Gibson** – thought people might take the view that it is not a first line of treatment, it is something that people would like to try when their children have been on all other forms of therapy and that has not worked. The research suggests that it can make a difference, however trials also suggests that in some people there are negative effects, so it would have to be looked at in an individual basis even if it was available on the NHS.

5. The Convenor reminded attendees that if members of the group want to have questions asked of MSPs in Parliament, or raise issues as parliamentary motions, they can send them to the Convener, or their own MSP, or Anissa the CPG Secretariat.
6. The Convenor reminded attendees that the next meeting will be held in September and will feature the Minister for Public Health and Sport, making it a good opportunity to put forward questions to the Minister and make a difference.
7. The Convenor asked attendees to raise any ideas of issues they want to have discussed at future meetings, for example epilepsy and social security is something we want to look at soon. He closed the meeting by thanking attendees for their questions today.