Open Letter IX, to Dr Ian Hudson, Chief Executive of MHRA

10 September 2017

ADHD drugs, MHRA and the Concerta scandal – suicides, suicide attempts and self-harm

With data from the new MHRA/EMA report about methylphenidate 9 June 2017

Dear Dr Hudson,

First I want to thank you for the inclusion in the latest MHRA/EMA report of my data from little Sweden about suicidality and self-harm in connection with methylphenidate.

In this excerpt from the final report (PRAC PSUR Assessment Report, 9 June 2017) my data from Sweden can be seen on pages 61-63. We find on page 62:

> **463 children and adolescents (10-19) made suicide attempts with methylphenidate or took overdoses of the drug in some other self-destructive purpose in the years 2011-2015,** (data from the he Swedish Poisons Information Centre, GIC).
> http://jannel.se/Methylphenidate%20PSUSA.June2017.PRAC.AR.excerpt.pdf

So we have *463* documented cases of suicide attempts/self-injurious behaviour for children 10-19 in the years 2011-2015 with methylphenidate from little Sweden, reported by me, a private citizen, from data obtained via FOIA requests to Swedish authorities.

To be compared with what *all* the manufacturers of methylphenidate products (Novartis, Janssen, Shire, Medice) report about the *total* number of suicides/suicide attempts/self-injurious behaviour with methylphenidate, for *all* countries world-wide, for (what it seems) *the last years* on pages 57-60.

I concluded in my earlier letter below (31 March 2017) that the MHRA/EMA assessment in this area will be based on false and completely unreliable data. And I was right as all interested readers can verify by comparing my figures with those from the pharmaceutical companies.

Case in point: Janssen (Concerta) reports (page 58) *77 cases of suicidal behaviour/self-injury and 8 completed suicides,* for the time period 31 October 2014-31 October 2016. In a table (page 60) we can find *195 cases of reported suicidality* (including 11 cases of suicide) with Concerta for a time period of *five* years (October 2011-October 2016). Janssen reports (in the underlying PSUR, forming the basis for the MHRA/EMA summary) a *cumulative figure of 43 suicides* with Concerta, from the International Birthdate of Concerta, 1 August 2000,
http://jannel.se/Methylphenidate%20PSUSA.June2017.PRAC.AR.excerpt.pdf

Case in point: Novartis (Ritalin) reports (in the underlying PSUR) 6 *cases of self-harm,* for the time period 1 November 2015-31 October 2016. The *54 cases* mentioned in the MHRA/EMA summary is found to be from a cumulative review – *almost from the beginning of time (!)* – from the International Birthdate of Ritalin, 6 October 1954. We can find the following data (in the underlying PSUR) – also from "the beginning of time": *233 cases of self-injury/suicide attempt/intentional overdose*, in addition to *40 reported suicides*.

Allow me to be rude and say: Shit in – Shit out! These figures are of course a joke, and all the resulting assessments based on them (supposed to be a reflection of reality) will be the same. Not only do they represent a *miniscule* proportion of the actual scene, the companies make a fantastic job of *minimizing even that miniscule proportion.* When the companies have "analyzed" these cases we have – as seen in the MHRA/EMA report – basically *nothing* left!

We can see (page 57) how Novartis explains away the 54 cases of self-harm (in some way separated from suicidality) by saying: "poorly documented", "additional risk factors", "underlying medical conditions", "concomitant medication", and they end up with *2 cases* (since 1954!) where "the causal role of Ritalin could not be ruled out".

And in the middle of this my data from little Sweden arrives. The data says that *463 children and adolescents in Sweden (10-19) made suicide attempts with methylphenidate or took overdoses of the drug in some other self-destructive purpose in the years 2011-2015, adding also 2016 we got the figure 553 children.* Included in my earlier letter below (but not in the assessment report) was the fact that only 3 (!) of these 553 cases had been reported to the Swedish Medical Products Agency (MPA), 0.5% of the cases!

Included in my earlier letter (but not in the assessment report) was also the fact that *33 persons* in Sweden committed suicide with methylphenidate in their body 2015. Adding the just released figures for 2016 (FOI request, National Board of Forensic Medicine) we get a total of **65 suicides on methylphenidate in the last two years in Sweden.** *None* of the cases was reported to the MPA!

Compare these 65 suicides from Sweden in 2 years with the 43+40=83 reported suicides from Janssen and Novartis for their drugs since the International Birthdate of Concerta and Ritalin.

We can in the MHRA/EMA report see that the assessors have a hard time handling the figures from Sweden. How can it be that *463 children* have been reported in this category for methylphenidate for little Sweden in five years, while Novartis reports *233 cases* for all ages, world-wide, since October 1954? How can it be that Janssen reports *77 cases* for all ages, world-wide for the last two years, while the corresponding figure for methylphenidate for the ages 10-19 for Sweden is *183* (for 2014-2015, see excerpt)?

The assessors don't know how to handle this, and so ask the Swedish MPA what to do with these figures. Remember, when reading below what happened, that the handling by the pharmaceutical companies (represented above by Novartis) is to claim say that the *quality* of the data reported to them is *so bad* that basically *nothing* is left after their analyses are done – 2 cases for Ritalin and self-harm since 1954! And even that was not "good enough"! Novartis tells us, via MHRA/EMA (page 57): "however these two cases did not fulfil the noteworthy case definition criteria". So we end up with 0 cases. And this is accepted by the MHRA/EMA!

The idea of the assessors to handle the disturbing figures from Sweden is obviously to invite the MPA (page 76) to do a similar job, as the one done by the pharmaceutical companies, of "making nothing" of the reported cases. We should, at this point, add that the Swedish MPA have contributed with, *absolutely no valuable data*, to the MHRA/EMA report. Shouldn't we expect the MPA, *with all its resources*, to give a lot more good data about the situations I have reported about the 463 children? Shouldn't we expect the MPA to use all the fantastic registers they have access to and make sure that Sweden *adds quality* to the European investigation with all its bad data? Instead the MPA explains to the worried assessors that they basically can ignore these 463 children!

In its "contribution" to the report the Swedish MPA says that the data (about the 463 children) "should be taken into consideration with caution … are based on the descriptions during the calls [to the Poisons Information Centre, GIC] and are not verified with healthcare records."

We get to know that GIC says that the specifics for a case "can vary from being very exact and precise … to pure guesses from people around the patient". As for the question about consequences of the intentional overdoses we are informed that one cannot always know if the consequence was hospitalization – even if the child was taken to the hospital in ambulance. Neither could one really know if the child had taken his/her personal medication or someone else's. And finally we are informed that the lack of such information [about other drugs or alcohol] in a case does not necessarily mean that e.g. alcohol or other drugs were not present." http://jannel.se/Methylphenidate%2520PSUSA.June2017.PRAC.AR.excerpt2.pdf

Why didn't the MPA try to get as much information as possible over to the MHRA/EMA about all these children, instead of using the Novartis approach above, of *making nothing* of all these serious cases?

- Why didn't the MPA require *all* data about these cases from the Poisons Information Centre (GIC)?
- Why didn't the MPA, as good as possible, cross check this information with other useful registers, like the Prescribed Drug Register and the National Patient Register?
- Why didn't the MPA in some effective way enforce the binding rules about reporting adverse events, including overdoses? After all 90% (73 of the 82 cases for 2016) came from Health Care Personnel (HCPs), and concerned children and adolescents requiring handling in emergency rooms; these cases should in other words be seen as *serious* adverse events.

If that had been done the MHRA/EMA would have known more *after* this assessment procedure than *before*!

My concluding questions:

1. Don't you think it is time for the MPA and MHRA/EMA to do *something*, knowing the true facts that 553 children and adolescents in Sweden made suicide attempts with methylphenidate or took overdoses of the drug in some other self-destructive purpose in the years 2011-2016? Instead of *doing nothing* and saying, as the MPA does (see letter below from 28 April): "The MPA is following the development and other available information and will signal/act when it is deemed correct to do so."

2. Will you now *request* that the Swedish MPA (with all its resources), for the next assessment procedure, is investigating and reporting the *full* data with *all relevant details* about suicidal behaviour and self-injury reported to the Swedish Poisons Information Centre (GIC) for *all age group*s and *all years*, crosschecking *all available registers* to get *the best quality data*?

3. Will you make sure that true and reliable data from trustworthy authorities in other concerned member states are also included in the assessment procedure, and that these reliable data are taking precedence over the false and unreliable data submitted by the pharmaceutical companies?

Yours sincerely,

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Open Letter VIII, to Dr Ian Hudson, Chief Executive of MHRA

28 April 2017

ADHD drugs, MHRA and the Concerta scandal – suicides, suicide attempts and self-harm

With data for the ongoing investigation about methylphenidate and self-harm

Dear Dr Hudson,

Thank you for your answer dated 4 April 2017. I really appreciate to hear that the information I have provided will be included in your assessment about of suicides, suicidality and self-harm in connection with methylphenidate. You have earlier (14 November 2016) also stated that the information I submitted in the area was "invaluable in the overall assessment" (even if providing "limited case by case detail").

I am now writing to inform you that the information submitted by me seems to be the only invaluable information from Sweden to be provided in relation to this issue.

My questions to the Swedish MPA and its PRAC Member (Liminga), about what important contributions we can expect from the MPA for this investigation, get a very disappointing answer. The Agency (Fornstedt Wallin) says in a letter dated 25 April: "The MPA is following the development and other available information and will signal/act when it is deemed correct to do so." The Agency also points out that the important information I have submitted has "limitations".

This answer tells me that you will get *no* contributions from the Swedish MPA in form of data relating to the issue of suicides, suicide attempts and self-harm (from the country with the best possibilities to do so). We can even ask if you will get any *comments* from Sweden; in the earlier assessment reports it seems as if Sweden has no interest, has nothing to say.

I have identified that "553 children and adolescents (10-19) made suicide attempts with methylphenidate or took overdoses of the drug in some other self-destructive purpose in the years 2011-2016." I have contributed with the information that 33 persons in Sweden committed suicide 2015 with methylphenidate in their blood at the time of death; 10 of these persons were in the age group 15-24.

The MPA and the concerned pharmaceutical companies (having the same information for Sweden) will contribute with *3 (!) adverse event reports* about suicide attempts/self-harm in connection with methylphenidate treatment (for the age group 10-19). The MPA will contribute with *0 cases of suicide* in connection with methylphenidate treatment.

I would say the contributions from the MPA have some serious "limitations", and I again hope you will request the data from the Agency that I asked for in my earlier letter (below).

Yours sincerely,

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Open Letter VII, to Dr Ian Hudson, Chief Executive of MHRA

31 March 2017

ADHD drugs, MHRA and the Concerta scandal – suicides, suicide attempts and self-harm

Dear Dr Hudson,

I should have come back much earlier, but the secrecy stamps from MHRA and the Swedish Medical Products Agency (MPA) have made it impossible to gain access to the important facts *about suicides, suicide attempts and self-harm in connection with methylphenidate treatment.*

It's first now, four month after your answer (below) that we can compare the data from the pharmaceutical companies with the reliable data from Sweden about suicides, suicide attempts and self-harm, revealed in my investigation.

As you know the manufacturers of methylphenidate (Concerta, Ritalin, Equasym, Medikinet) were ordered by the MHRA and the EMA Pharmacovigilance Risk Assessment Committee (PRAC) to *"undertake a cumulative review of all cases of self-injurious behaviour"* in connection with their products (1). These reviews were to be presented in the next Periodic Safety Update Reports (PSURs), to be submitted to the MHRA/EMA in the end of 2016.

We could thus, in these reports, expect to get *exact data* about *all* cases of self-injurious behaviour (including suicides and suicide attempts) in connection with methylphenidate prescription world-wide known to the companies, from the International Birth Date (IBD) of the products.

As you also know I have investigated the cases of "suicide attempts or overdoses in some other self-destructive purpose" in connection with ADHD drugs, presented to the Swedish Poisons Information Centre (GIC). This for the population of children and adolescents (10-19) for the years 2011-2015. The investigation revealed that we had *463 individual cases of "suicide attempts or overdoses in some other self-destructive purpose" for these young persons for methylphenidate in these five years!*

In your earlier letter you acknowledged the receipt of this information, and said it was "invaluable in the overall assessment of these events" though providing "limited case by case detail". You also said that these reports were "considered to be spontaneous occurring post-authorisation" and would be "taken into consideration in our ongoing monitoring of the issue of suicidal and self-injurious behaviour with methylphenidate".

It was of course very good to know that the information I had submitted was regarded as "invaluable" and was to be taken into consideration in the coming assessment by MHRA/EMA. But the assessment report from MHRA/EMA raised many serious questions requiring further investigation. We could for example in the assessment report read (page 25): *"Whilst overall the numbers of self-injurious reports may be low, self-injury can have serious consequences."*

Yes, self-injury can *indeed* have serious consequences, *but* what about *"overall the numbers of self-injurious reports may be low"*? I have revealed and presented alarming data about 463 individual cases (10-19) of self-injurious behaviour for methylphenidate in little Sweden (2011-2015) – not exactly a "low number"!

So what do the pharmaceutical companies actually report to the MHRA/EMA; what are the figures about suicides, suicidal behaviour and self-injury *forming the basis for the assessment* by the agencies? How could it be – considering my alarming data from little Sweden – that the instances of self-injury could be deemed to "be low" in the world-wide prescription of these drugs, from their birth?

The secrecy stamp on reported suicides and self-harm

The secrecy stamp first made it impossible to get an answer to any of these questions.

The Swedish Medical Products Agency (MPA) got the Periodic Safety Update Reports (PSURs) from pharmaceutical companies in the beginning of 2017, but refused to release the data about the *number* of suicides, suicidal behaviour and self-injury in these reports. The MPA explained that the MHRA had objected to release the data about the *number* of reported cases of suicidal behaviour and/or self-harm contained in these reports.

It's been said (Goldacre, Bad Pharma, 2012) that drug regulatory agencies have *a "dangerous obsession with secrecy"*, and what could be a better example of this than putting a secrecy stamp on the cumulative number of suicides, suicide attempts and self-injurious behaviour reported by the manufacturers of methylphenidate drugs. Drugs that we know have been involved in 463 cases of "suicide attempts or overdoses in some other self-destructive purpose" for children and adolescents in Sweden.

The MPA even explained that the release of these data – *just the number of cases* – would cause disturbance in Sweden's relations with another country (UK)!

I don't know who at the MHRA decided that this information was sensitive to such a degree that it would hurt the relations between Sweden and the United Kingdom would it be released. What I *do* know is that it would have been impossible to compare the data reported by the pharmaceutical companies with my data from Sweden – had the MHRA and MPA been *successful* in their "dangerous obsession with secrecy".

The newly updated investigation for Sweden

I have now updated my investigation for Sweden up to 2016 and can report:

- 553 children and adolescents (10-19) made suicide attempts with methylphenidate or took overdoses of the drug in some other self-destructive purpose in the years 2011-2016, (data from the he Swedish Poisons Information Centre, GIC).

- Only 3 (!) of these 553 cases were reported to the adverse events register at the MPA.

In your November letter you said the earlier data I gave, though "invaluable", provided "limited case by case detail". In order to give even more valuable data to the MHRA/EMA review I can provide the following data for the added 82 individual cases for 2016:

- 73 of the 82 cases (90%) came from Health Care Personnel (HCPs), and concerned children and adolescents requiring handling in emergency room; these cases should in other words be seen as *serious* adverse events.

- Only one (a 14-year old girl taking Ritalin) of these cases were reported, as required, to the adverse events register at the MPA.

- Concerta was the drug mentioned in 63 of the cases, Ritalin in 14, Medikinet in 8 and Equasym in 3.

- Some examples from the notes for individual cases:
  "hard to breath …heart beating",
  "14 of 18 mg Concerta",
  "feel strange and does not want to live anymore",
  "hope she will die",
  "pain in the heart and cannot breath properly",
  "18 of 54 mg Concerta",
  "hallucinating",
  "not possible get in contact with",
  "11 Concerta 54 mg with suicide purpose",
  "with suicide purpose".

It should be noted that the Swedish Poisons Information Centre (GIC) is an agency administratively *under* the Medical Products Agency (MPA). The MPA can without much effort make a full evaluation of all the 553 cases presented to the GIC for the years 2011-2016.

It should most definitely be noted, as mentioned earlier, that only 3 (!) of the 553 cases (0.5%) were reported to the adverse events register – all of them should have been reported.
In addition to the data above, about suicide attempts and self-injurious behaviour, we should add some words about the *number of completed suicides* in Sweden in connection with methylphenidate treatment. The main purpose with this note is to be able to *compare* the figures with those reported by the pharmaceutical companies.
We find for the year 2015:

- 33 persons in Sweden committed suicide with methylphenidate in their blood at the time of death; 10 of these persons were in the age group 15-24 (data from toxicology analyses done by the National Board of Forensic Medicine).

- *None* of these cases were reported to the adverse events register as a suspected adverse event.

What did the pharmaceutical companies report to the MHRA/EMA?

And we come to *the data reported by the pharmaceutical companies to the MHRA/EMA.*

These are the figures about suicides, suicidal behaviour and self-injury forming the basis for the MHRA/EMA assessment.

The figures so sensitive that it would hurt the relations between Sweden and the United Kingdom would they be released.

The figures about *all* cases of self-injurious behaviour (including suicides and suicide attempts) in connection with methylphenidate prescription world-wide, known to the companies, from the International Birth Date (IBD) of the products.

Completed suicides:

Concerta (Janssen) 43
Ritalin (Novartis) 40
Equasym (Shire) 23

In total: 106

Suicide attempts, self-injurious behaviour*:

Concerta (Janssen) 154-347
Ritalin (Novartis) 93-241
Equasym (Shire) 37-82
Medikinet (Medice) 21-39

In total: 305-709

***** After long negotiations with the European Medicines Agency (EMA) I have finally got access to these figures. However EMA cannot give data about *the number of individual cases* for suicide attempts, suicidal behaviour, intentional self-injury, intentional overdose – only *the total of reported adverse events.* As *one* individual can fall in more than one of these categories I have had to report it as above. The number of reports of self-injurious behaviour (including all categories) is in other words *minimally* 305 and *maximally* 709.

These are the cases of suicides, suicidal behaviour and self-injury forming the basis for the MHRA/EMA assessment.

Let's make it even clearer by presenting these figures about methylphenidate and the ones from Sweden in a table:

Number of cumulative cases of self-harm world-wide reported by the pharmaceutical companies	**Number of cases of self-harm Sweden for children and adolescents (10-19) 2011-2106**
305-709	553
Number of cumulative cases of completed suicides world-wide reported by the pharmaceutical companies	**Number of cases of completed suicides found in toxicological analyses in Sweden for 2015**
106	33

The MHRA/EMA assessment is based on false and completely unreliable data

I have with *limited* resources (the Freedom of Information Act) proved that the MHRA/EMA assessment is based on false and completely unreliable data.

I have also proved that the "dangerous obsession with secrecy" includes the hiding of these data about suicides, suicidal behaviour and self-injury – easily exposed as false if made public.

The MHRA/EMA is looking *in the wrong direction*, and can let the pharmaceutical companies conclude that the number of self-injurious reports is *low*, and so can continue to say that there are no reasons to be concerned.

My concluding questions:

1. Will you make sure that the updated information I have given about Sweden is right away included in the investigation and is given full attention?

2. Will you make sure that the Swedish MPA (with all its resources), for the current assessment procedure, is investigating and reporting the *full* data with *all relevant details* about suicidal behaviour and self-injury reported to the Swedish Poisons Information Centre (GIC) for *all age group*s and *all years*?

3. Will you make sure that true and reliable data from trustworthy authorities (like the Swedish GIC) in the concerned member states are included in the assessment procedure, and that these reliable data are taking precedence over the false and unreliable data submitted by the pharmaceutical companies?

Yours sincerely,

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Those not familiar with the Concerta scandal should read the full story, starting with page 19, the letter from 14 February 2014
http://jannel.se/MHRA.Concerta.July2016.pdf

1. EMA/MHRA, "Lead Member State PSUR updated preliminary assessment report Methylphenidate", released in June 2016, http://jannel.se/methylphenidatePSUSA2015.pdf (see page 7).