Conference room paper submitted by the Arab Republic of Egypt on strengthening international cooperation in addressing the non-medical use and abuse, the illicit manufacture and the illicit domestic and international distribution of tramadol

I. Tramadol, chemical structure, mechanism of action, uses and side effects

- Tramadol is a synthetic opioid medication used to treat moderate to severe pain. It has no effects on respiratory system and heart muscle but overdoses cause arrhythmia, cramps and coma. And it is not under international control.

II. Development of the abuse of tramadol

- The issue of tramadol has been highlighted in the INCB reports in the last few years, focusing on the emerging problem of tramadol in many countries, this paper starts by tracking the developments of the reporting on tramadol, to provide an insight on the developments in the subject as follows:

A. The Report of the International Narcotics Control Board in 2012

- The report starts shedding the light on the issue of tramadol in the paragraphs from 323 to 327, stating the following:

"Another development of concern is the increasing abuse of tramadol, a synthetic opioid not under international control, which has become a serious problem in a number of countries in Africa, notably Egypt. Abuse of tramadol has also been reported by Jordan, Lebanon, Libya, Mauritius, Saudi Arabia and Togo."
In response to that emerging threat and concerned by the increasing abuse of tramadol preparations in the country, the Government of Egypt placed that substance, as well as its salts and derivatives and preparations containing tramadol, under national control in 2012. Tramadol is also under national control in other countries, such as Jordan and Saudi Arabia.

According to information available to the Board, tramadol seems to be diverted mainly from international trade. For instance, Egyptian authorities seized in the country’s main seaports about 120 million tablets containing tramadol in 2011 and about 320 million tablets in the first quarter of 2012. The preparations were reportedly smuggled into Egypt mainly from China and India. Increasing amounts of seizures of preparations containing tramadol are also reported by Saudi Arabia.

In West Africa, a series of large seizures of tramadol preparations, totalling more than 132 tons of such preparations, were effected between February and October 2012. The preparations had been concealed in sea containers coming from India and were intercepted by the law enforcement authorities of Benin, Ghana, Senegal and Togo.

The Board is concerned about the growing abuse of tramadol in some African and West Asian countries and the increasing amount of trafficking in tramadol preparations to Africa, as evidenced by recent large seizures of such preparations in North and West Africa. The Board calls on countries in Africa and West Asia to take the measures necessary to address that problem and to furnish pertinent information on the extent and nature of the abuse of and trafficking in tramadol to the Board and WHO.’’

- The report continues to describe in more details the extent of the problem in different Member States in paragraphs 390, 391 and 586 as follows:

“Abuse of tramadol is a serious problem in a number of African countries, including Egypt, Libya and Mauritius. In 2011 and 2012, Egypt witnessed an upsurge in trafficking in tramadol. While in 2011, total seizures of tramadol preparations amounted to 120 million tablets, about 320 million tramadol tablets were seized in the seaports of Alexandria, Damietta and Port Said in the first quarter of 2012. The preparations are smuggled to Egypt mainly from China and India. The Libyan anti-narcotics agency reported that Libya is facing large-scale trafficking and abuse of tramadol; however, exact statistics are not available due to the current restructuring of the country’s law enforcement institutions. Abuse of tramadol preparations is also reported by Mauritius and Togo.

Under the UNODC/World Customs Organization Container Control Programme, a total of 24 containers with a total of more than 132 tons of tramadol preparations were seized between February and October 2012. All containers originated in India and were seized in West Africa. Of those, 16 containers were intercepted in Lomé, 7 containers in Cotonou, Benin, and 1 container in Dakar. A further container is being held in Tema, Ghana. Nineteen of those intercepted containers were ultimately destined for the Niger. Because part of the seized preparations might be counterfeit, forensic examinations will be conducted to determine whether the seized preparations actually contain tramadol.

The Government of Singapore has amended the Misuse of Drugs Act to expand the reporting obligations of medical practitioners. The amended Act requires medical practitioners to report the duration of treatment periods and the dosage and quantities of selected prescription drugs that are prescribed to suspected drug addicts, such as those containing benzodiazepines, zolpidem, codeine and substances not under international control such as dextromethorphan and tramadol. This additional information would assist relevant authorities in identifying possible trends in the abuse of prescription drugs. Furthermore, to facilitate the submission of such reports, a web-based electronic notification system has been introduced.”
The report gives attention to the measures taken by the Government of Egypt to address the problem, notably in paragraph 354:

“The Government of Egypt, concerned by the increasing abuse of tramadol, placed the substance, as well as its salts and derivatives and preparations containing tramadol, under national control in 2012. Furthermore, the Government’s Fund for Drug Control and Addiction Treatment has developed a national action plan against drug abuse for 2012-2016, for adoption by Parliament.”

The report then expresses clearly in paragraph 342 that tramadol has become a serious problem for a number of countries as follows:

“Abuse of tramadol, a synthetic opioid not under international control, has become a serious problem in a number of African countries, notably in North Africa. Trafficking of tramadol to Africa seems to be increasing as well, as corroborated by a series of large seizures of tramadol effected in West Africa in 2012, totalling more than 132 tons, of preparations containing tramadol coming from India that were intercepted in Benin, Ghana, Senegal and Togo during that year.”

Finally, the report, in its recommendations to the governments, recommends the following:

“The Board calls on countries in Africa to take the measures necessary to address this problem and to furnish pertinent information on the extent and nature of abuse of and trafficking in tramadol to WHO and the Board.”


The report of INCB in 2013 continues to explore the developments in the issue of tramadol, in paragraphs 325, 595, 596 as follows:

“Abuse of and trafficking in tramadol, a synthetic opioid not under international control, continues to be a serious concern in a number of countries of North and West Africa. The Egyptian authorities reported that they seized a total amount of 620 million tablets of tramadol in 2012, most of which were illicit shipments in containers coming from India through the ports of Dubai and Yemen. Benin, Ghana, the Niger, Senegal and Togo continue to serve as transit hubs for the smuggling of tramadol. From November 2012 until September 2013, about 84 tons of tramadol were seized from containers by joint port control units of Benin and Togo under the Container Control Programme of UNODC and the World Customs Organization. Of the 15 seizures made during that period by the joint port control units in Benin and Togo, in 14 cases, the containers from which the tramadol was seized had been sent from India and in one case, from China, and all but one of those containers were destined for the Niger. In most cases, the drug appeared to be a genuine pharmaceutical product, but the amount of tramadol contained in the medicine was greater than the regulated amounts. In certain other cases, seizures were carried out because the importer did not have the appropriate licence.”

“The misuse of tramadol, a synthetic opioid analgesic, in the Gulf countries is becoming a matter of genuine concern, with some countries even reporting tramadol-related fatalities. The trafficking and abuse of tramadol, which is not under international control, is being reported by many countries in the Middle East. Significant seizures of tramadol are regularly made by enforcement authorities in the region. In Jordan, tramadol is diverted from domestic distribution channels, at the retail level, and through sales without the requisite medical prescription.
According to information collected by the Board, tramadol has been placed under national control in almost all the countries in the region. The substance is already controlled under national legislation for psychotropic substances and/or narcotic drugs in Bahrain, Jordan, Qatar, and Saudi Arabia. In Lebanon, where more than 5 per cent of individuals in treatment for polydrug abuse are found to abuse tramadol, the authorities are considering placing the substance under national control.”

- The report then, in paragraph 597, calls on the countries of the MENA region to “remain vigilant vis-à-vis the apparently growing non-medical use and/or abuse of tramadol and urges countries where diversion and illicit trafficking already occur to consider the adoption of more stringent control measures over the trade in and distribution and dispensing of tramadol to ensure that preparations containing tramadol are dispensed for legitimate medical use and to limit their diversion into illicit distribution channels.”


- The report keeps tracking the seizures of tramadol in 2013, mentioning in paragraph 297 that “The abuse of tramadol, a prescription opioid not under international control, continues to raise concern in a number of African countries, notably in North Africa. In 2013, tramadol was placed under national control in Egypt, where the abuse of the substance was widespread. According to data provided by the Egyptian authorities, seizures of tramadol decreased from 650 million tablets in 2012 to 27 million tablets in 2013. This downward trend is reportedly attributed to the new stringent measures in place regarding the substance. Reportedly, the abuse and trafficking of tramadol have also recently been increasing in Libya. In addition, Nigeria has reported abuse of tramadol and has now scheduled it as a controlled medicine.”

- The report continues in paragraph 581, noting that “tramadol, a synthetic opioid that is not under international control, has been placed under national control in most countries in the Middle East. Tramadol is a prescription-only medication and is already controlled under national legislation on psychotropic substances and/or narcotic drugs in Bahrain, Jordan, Qatar, and Saudi Arabia. Abuse of tramadol is reported by many countries in the West Asia subregion.”


- The report mentions in paragraph 341 that “The abuse of and trafficking in tramadol, a synthetic opioid not under international control, continues to represent challenges to a number of countries in Africa, notably in North Africa and West Africa. In 2014, more than 43,578 kg of tramadol were seized by the joint port control units of Cotonou, Benin, and Tema, Ghana. In February 2015, the joint port control unit of Cotonou seized 13,612 kg of tramadol, which had arrived from India and had been destined for the Niger. Seizures of tramadol in Egypt declined significantly, from 435 million tablets in 2012 to 157 million tablets in 2014. According to the Egyptian authorities, the decrease could be attributed to the fact that tramadol had been brought under national control in 2013.”
III. Situation in Egypt

A. Legislative framework to address the issue of tramadol

- Despite the fact that the substance is not under International Control, the Egyptian Anti Narcotic General Administration (ANGA) has monitored with interest the developments in the tramadol market, intercepting the illegal trafficking and seizing a large quantity of the substance over the last five years.

<table>
<thead>
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<th>Year</th>
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<td>2011</td>
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<td>2012</td>
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<td>2013</td>
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<td>2015</td>
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<tr>
<td>2016</td>
<td>521,057,333</td>
<td>23,972</td>
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</table>

The statistics of tramadol seized quantities from (2010 -2016) in the Arab Republic of Egypt.

- Based on data of abuse and illegal trafficking, tramadol was first placed in Schedule III as annexed to the Egyptian law on Drugs, paragraph (D). This made it necessary to get a permit from the central administration of pharmaceutical affairs in the cases of importing and exporting of tramadol. The permits were given according to the annual consumption plan of each company.

- The Egyptian competent health and law enforcement authorities exerted their efforts to ensure the availability and control over the required legal quantities of tramadol for patients to prevent the establishing of the illegal markets of that drug. However, depending on the data received about the increased abuse of the substance, tramadol was later placed in the schedule II, and then currently, tramadol is already placed as schedule I according to the ministerial decree no. 125/2012 of the Egyptian drug law.

- The Egyptian authorities believe that the negative consequences of tramadol abuse necessitate that its control be expanded beyond a national control mechanism to be included under international control. In 2013, the Egyptian government proposed to the CND during its 56th session, a draft decision to support the international cooperation to prevent non-medical use of tramadol.

B. Medical and psychological effects of tramadol abuse in Egypt

- According to national statistics, tramadol is one of the most abused effective pharmaceuticals among addicts in Egypt. Tramadol is among sedatives used as a painkiller in the cases of bone deficiencies and cancer.

- Based on these statistics, the Egyptian health and Academic institutions have held various studies on the matter, the results are as follows:
Research on the medical and psychological effects of tramadol:

Research and studies are being held periodically in the laboratories of the Egyptian Ministry of Health, according to the results on the abuse of tramadol are the following points:

- Tramadol affects the noradrenaline and serotonin receptors. The most important receptor is (O-desmethylmetabite of tramadol “ODT”) which is an opiate receptor with an effects on the Central Nervous System that might lead to dependence on the substance.

- Mansoura university did a survey study in (2008-2010) on the effect of drugs on the heart muscle through urine and blood analysis. The result ensured that tramadol was present in 42.2 per cent in the blood samples, the study concluded that the increase in tramadol abusing leads to increase in intoxication and heart failure death averages in Egypt.

- Mansoura university did a study in 2015 that confirmed that tramadol is one of the main reasons of epilepsy and convulsions for adults who visit the clinics in the academic hospital. Another study confirmed in 2016 that 78.75 per cent of the convulsions patients admitted to the hospital have a history of tramadol abuse.

- Egyptian clinical researches and studies also indicated that tramadol use disorder is associated with physical withdrawal symptoms and compulsive behaviour despite awareness of the abuser of dangers and harmful effect. Accordingly it is considered a dependence disease as it has the following elements (probability of abuse — withdrawal symptoms — set back — compulsive disorder — gradual increase in quantities used). Tramadol dependence could have comorbidities with other mental health problems including depression and schizophrenia.

- The results of Ain Shams university study about substance use among patients with dual diagnosis indicated that 80 per cent of cases abuse tramadol, 14 per cent abuse tramadol only. 40 per cent abuse tramadol and hashish, 26 per cent abuse tramadol and other substances. The study indicated that 86 per cent of the sample schizophrenia patients abuse tramadol, 89 per cent of the sentimental bipolar disorder patients abuse tramadol.

National demand on tramadol treatment:

- According to the report of the national observation of drugs in 2015, there is an increase in the average numbers of people seeking treatment for tramadol, currently ranking as the number one substance for demand for treatment.

- The statistics confirmed that in 2015, about 11,756 out of 17,166 addiction patients (around 68.5 per cent) sought treatment from tramadol addiction in governmental facilities.

Tramadol-related deaths:

- The formal reports of the clinical toxicology centre of Ain Shams university indicated increasing in tramadol-related deaths in 2011 and the later years. Reports confirmed that in 2011, tramadol was considered the first and the main reason of drug-related deaths.

- Reports on tramadol-related deaths in Egypt show a gradual increase, which can be viewed as follows:

  - In 2010, tramadol-related deaths were as follows: 5 cases out of 691 were affected by tramadol acute intoxication.

  - In 2011, 9 cases out of 1,595 were affected by tramadol acute intoxication.
During 2012, 14 cases out of 1,581 were affected by tramadol acute intoxication.

During 2013, 15 cases out of 1,412 were affected by tramadol acute intoxication.

During 2014, 30 cases out of 1,580 were affected by tramadol acute intoxication.

**IV. Recommended way-forward**

- **Noting the** increase in tramadol abuse and its possible harm and consequences as reflected by national studies and reports from other countries, as well as the lack of international control of control and lack of national legislations prohibiting it in several countries. Accordingly, illegal trafficking from the countries of production to the countries of consumption by the organized criminal groups is still prolific (including for money-laundering purposes).

- **And recalling the following international documents:**
  - CND resolution 56/14, on strengthening international cooperation in addressing the non-medical use and abuse, the illicit manufacture and the illicit domestic and international distribution of tramadol.

- **The recommended set of actions by this paper include:**
  - Member States are invited to pay special attention to the problem of the diversion of tramadol from licit medical use, where it persists, to monitor emerging trends in the abuse, diversion, illicit manufacture, illicit domestic and international non-medical distribution and to assess the extent of this problem within their own national borders;
  - Serious consideration should be taken by the Member States to controlling the use of tramadol by placing it on a list of substances controlled under their national legislation, while simultaneously ensuring access for medical and scientific purposes, consistent with the international drug control conventions;
  - Member States are also invited to adopt appropriate comprehensive measures aimed at detecting and countering the diversion and trafficking of tramadol, including trafficking through the Internet, in accordance with national legislation;
  - Member States are encouraged to consider adopting an import and export authorization system for licit international trade in tramadol while ensuring access for medical and scientific purposes;
  - Member States are encouraged, on the basis of the principle of common and shared responsibility, to share information and to cooperate at the bilateral, regional and international levels with a view to detecting and controlling the diversion of tramadol from the licit market, in particular by strengthening cooperation in law enforcement activities and by fostering cooperation among the relevant national health authorities;
  - INCB, WHO and UNODC are advised to gather further information and data on the abuse of tramadol, and report regularly on the matter to the coming regular session of the CND.