

## PROGRESS REPORT

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PROJECT:

TECHNICAL ASSISTANCE IN DEVELOPING A NEW LAW ON PHARMACEUTICALS IN R.MACEDONIA, HARMONIZED WITH EU LEGISLATION

PROGRESS REPORT CONTAINS

1. INPUT TO THE DRAFT (2) LAW

2. LIST OF NECESSARY BY-LAWS WITH THE DRAFT CONTENT

1. INPUT TO THE DRAFT (2) LAW

Comments/input on the Draft 2 (February 07) of the Law on Medicinal Products and Medical Devices provided as the outcome of the contribution of the Working Group on the Draft 1.

Comments on the Draft 2 will be put Chapter by Chapter and article by article wherever the relevant changes were identified.

### I GENERAL PROVISIONS

Art 1

The subtitle of this article should be "The scope of the Law". Provision on establishing of the Competent Authority on medicinal products and medical devices were removed and placed under the Chapter II. My personal opinion is that the establishing of the CA should also be mentioned under the scope of the Law. **This is pure national decision that depends only on national legal system.**

The same comment goes for the provision on defining the competent minister.

Art 2

New definition (46) of materiovigilance/vigilance of medical devices is announced but the term was not defined. I propose using the similar wording as for pharmacovigilance (39)

### II COMPETENT AUTHORITY

Several articles were deleted, probably in line with placing of such provisions within the legal system. **This is pure national decision**

### Art 3

I see that the decision was made to establish the Agency within the Ministry of Health as a Competent Authority for medicinal products and medical devices, and not as a public agency. **This is pure national decision that depends only on national policy.**

### Art.4

I see that the public invitation will not be obligatory for Minister before proposing Director of the Agency to the Government. **This is pure national decision that depends only on national policy.**

### Art.5

(2) I see that authorization of manufacturers and

(3) wholesalers of medical devices were introduced instead of notification. **It is not in line with dir 93/42/EEC**, but it could be justified by national needs concerning the existing situation on the market, but I also see that the wording in art 123 & 128 are not in line with this article. It should be clear whether authorization or notification is requested.

(9) English wording should be modified: "authorizations and/or **notifications...**" because the used term "reports" has different meaning.

(15) Listing of databases that are to be maintained was deleted and the sentence is now unclear. It is, on my opinion, **important to define databases that are to be established and maintained by the Competent Authority** because of clarity of legal text and because of accessibility of information (Free information act?) that is according to EU rules to be linked to the officially maintained databases.

(20) Obligation of Competent Authority to be aware of data on consumption of medicinal products and medical devices **must be supported by obligation of economic operators to provide the data** to the Competent Authority in later articles/provisions (to be added)

### Art 7

Following the hierarchy, Minister of Health should not ask for consent of Director (vice versa is more than acceptable) for appointing members of committees, but could ask for his proposal

Requirements for at least 10y of experience for experts/members of the committees is unnecessary obstacle for young people.

Both comments concern **pure national decision that depends only on national policy.**

Term (in English) "classified information" should be replaced by "confidentiality" (or similar) in order to be understandable. I believe that classified information are to be treated as confidential but it should be clearly stated in the text.

Art 8

The wording was slightly changed, (not relevant for functioning of the system) and concern **pure national decision**.

Art 9

See art 7: Following the hierarchy, Minister of Health should not ask for consent of Director (vice versa is more than acceptable) for appointing experts, but could ask for his proposal.

### CHAPTER III

Art 17

Provision concerning exception of parallel import was deleted because further articles on parallel import are deleted, so the Law will not regulate the parallel import. **It is not in accordance with EU legislative system (ECJ Cases)** but can be justified by by national needs concerning the existing situation on the market.

ex Art 55

Since the article in which all payments were regulated **was deleted**, it is **very important** to review all articles that foresee by-laws and payments of relevant procedures in order to assure the proper income for the CA.

Art 79

If provisions on parallel import were deleted form the text, words "**parallel import**" **should also be deleted** from the para 1 of the article

Art 96

I miss the previous wording : "**more great details**" in the by-law because basic requirements are given by the Law.

Art. 106

I see that Chapter on Medicinal Products waste was inserted again although it was agreed to delete the proposed chapter, because the issue "had been

regulated by another law". If the Chapter remains in the Law I would like to propose adding of some provision on collecting of **"old/waste medicinal products"** by pharmacies from individual users, since some provisions on pharmacies were added to the Law in the meantime.

Art 107

If provisions on parallel import were deleted from the text, words **"parallel import"** should also be deleted from the para 3 of the article

#### IV MEDICAL DEVICES

Art 119

There's an **error** in para 3 "medicinal devices" should be replaced by "medical devices"

Art 123

It s not clear if notification of manufacturers has been replaced by authorization. The article is not in line with art 5. **It should be clear whether the notification or authorization of manufacturers is required by the Law.**

Art 128

It s not clear if notification of wholesalers has been replaced by authorization. The article is not in line with art 5. **It should be clear whether the notification or authorization of wholesalers is required by the Law.**

Art 130

There's an error in numeration in para 5.

#### V INSPECTION

Art 143

**Not only inspections without prior announcement** are to be performed. It is possible and normally expected to announce regular inspections.

Art 146

Since all obligations and rights of inspectors are stated in art 143-145, **the introductory sentence in the art 146** is modified (wording "set out in horizontal legislation" is deleted), and **became unclear** because the competences

are to be considered as obligations and rights and vice versa. I propose "... in line with rights and obligations listed in art 143-145, have the following competences:"

**Parallel import should be deleted** from provisions on inspection

Art 148

**I do not understand** the purpose of the 1st para. Art 71 and 78 are the basis for revoking the manufacturing or wholesale license (in line with EU rules). It is not clear why to wait "the second mistake" after mistakes listed in art 146. Some of them are not so severe and can occur several times also to good economic operators. Some of them are very severe and can be treated in line with art 71 and 78 immediately.

Art 149

The term "drugs" should not be used

Art 152

Classified information should be understood as confidential information ???

## CHAPTER VI PENALTIES

I would recommend not to repeat the wording of all articles in this chapter (mistakes are possible if the text is repeated). I recommend references to the articles concerned.

**I highly recommend to review all the articles of the Chapter once again and add the missing violations that request penalties.**

**This chapter is pure national decision.** Nevertheless, I'll put some comments on the provided text:

(1) I do not see para 3???

(3) The provision is a part of marketing authorization requirements

(4)(5) If PhV requirements are not fulfilled by Marketing Authorisation Holder, the marketing authorization can/should be withdrawn, in line with art 33 (marketing authorization is granted only to person that fulfills the requirements)

(X) Violation of Art 37.2 All Changes/relevant information that may influence variation of marketing authorization or documentation submitted are to be authorized/notified. If not, it is a **SERIOUS** violation of the law (It is ca 70%

of the work of the Agency). Of course, also MA can be withdrawn in certain cases. Small changes are included in low penalties (art 155)?

(X) Violation of Art 50, if analytical, pharmacological-toxicological or clinical trials are performed by non-authorized institutions (included in low penalties (art 155)?

(X) Violation of Art 51 & 52 analytical, pharmacological-toxicological tests are performed not in line with relevant good practices (included in low penalties (art 155)?

(X) Art 55 should be introduced or included into (6)

#### Art 154

(10) Too low penalty?

(11) too low penalty?

(13) too low penalties if intentionally.

(X) Is violation of art 66 implied in marketing of medicinal product not in line with marketing authorization, or is missing?

(X) Violation of art 67 should be added (production of more than 100/day if declared as galenic products). - High penalty

(X) Violation of art 70 - reporting changes (if not, than high penalty) (included in low penalties (art 155)?

**(14) No service without compensation should be put on economic operators !!!! "For free" does not mean "without compensation" - as written in the text !!!!**

**(The article 73 regulates products that can be supplied/distributed by wholesalers. Among others, products that are not paid by end-users (e.g. medicinal products given for free to a hospital or to group of patients)**

**(15) Some penalties are extremely low !!!(e.g. to perform wholesale /manufacturing activity without license),**

(X) violation of art 78 (2)?

(X) violation of art 81 - if medicinal product is retailed elsewhere than in pharmacies !!!!!!! Important.

(X) violation of art 83,84,85 - is violation of this article considered to be marketing not in line with marketing authorization requirements?

(X) is it clear that import of batches for which Q control according to art 100 has not been performed is to be considered as violation and is to be sanctioned?

(X) If the chapter on Medicinal products waste is reintroduced, some penalties concerning the chapter should be introduced too.

#### Art 155

Low penalties were introduced for some violations that are not minor.

Art 156

Article **should be deleted** because no EU country is punishing doctors that have not reported adverse reactions. Education of HC professionals is the only measure that is to be taken, not punishment

**I would highly recommend the review of the Chapter together with provisions of the Law.**

## CHAPTER VII TRANSITIONAL MEASURES

The Chapter is not available. Transitional provisions are of vital interest of the system.

### 2. LIST OF NECESSARY BY-LAWS WITH THE DRAFT CONTENT

#### **1. By-law on classification of medicinal products**

The content: Classification of medicinal products according to the method and place of their dispensing

#### **2. By-law on marketing authorization procedure**

The content: The contents of the application, types of the application, the procedures and the requirements for obtaining a marketing authorisation for medicinal products as well as fees to be paid

#### **3. By law of renewal of marketing authorisation**

The content: The contents of the application, the procedure and the requirements for renewal of a marketing authorization as well as fees to be paid

#### **4. By law on variations of marketing authorisation**

The content: The types of variations/changes of marketing authorization or/and its documentation, content of application/notification and procedure for notification or approval of the changes of marketing authorisation for medicinal products or already provided documentation as well as fees to be paid

#### **5. By law on registration for traditional herbal medicinal products**

The content: The content of the application, the procedure and the requirements for obtaining a registration for traditional herbal medicinal products and the form, contents of the required documentation and conditions

for recognition of marketing authorisation issued in the EU as well as fees to be paid

**6. By law on registration for homeopathic medicinal products**

The content: The contents of the application, the procedure and the requirements for obtaining a registration for homeopathic medicinal products, the form and contents of the required documentation, conditions for advertising and labelling of the products, conditions for recognition of marketing authorisation issued in the EU as well as fees to be paid

**7. By law on generic substitution of medicinal products.**

The content: The manner and procedure for substitution of medicinal products in pharmacies.

**8. By law on the content of the information on medicinal products to be published in the Official Journal of the R of Macedonia.**

**9. By law on the transfer of marketing authorisation**

The content: The procedure for transfer of marketing authorisation, content of documentation to be submitted and procedure for verification of prescribed conditions and other requested data as well as fees to be paid.

10. **Guidances** for good manufacturing practice including a good control laboratory practice, good laboratory practice and good clinical practice in clinical trials and good pharmacy practice.

**11. By law on requirements to be fulfilled by investigational institutions for medicinal products**

The content: The requirements for authorisation of medicinal products investigational institutions concerning staff, equipment, facilities and the verification procedures as well as fees to be paid

**12. By law on analytical testing of medicinal products.**

The content: The principles and procedures for pharmaceutical chemical-biological and microbiological testing of medicinal products.

**13. By law on pharmacological-toxicological testing of medicinal products.**

The content: The principles and procedures for pharmacological-toxicological testing of medicinal products.

**14. By law on clinical trials of medicinal products**

The content: The manner, principles and procedure for clinical trials, content of documentation to be submitted and procedure to be followed, protection of investigational subject as well as fees to be paid.

**15. By law on manufacturing of medicinal products**

The content: The content of the application, the procedure and the requirements for obtaining a manufacturing licence for medicinal products, as well as fees to be paid

**16. By law on wholesaling of medicinal products**

The content: The contents of the application, the procedure and the requirements for obtaining a wholesale licence for medicinal products, conditions for recognition of other laboratories batch analysis, as well as fees to be paid

**17. By law on import of medicinal products**

The content: The content of the application, the procedure and the requirements for obtaining an authorisation for import of medicinal product, as well as fees to be paid

**18. By law on authorisation of pharmacies**

The content: The principles and procedures for authorising pharmacies including e-pharmacies, until The Law for Pharmacies is established as well as fees to be paid.

**19. By law on labelling of medicinal products and information to patient**

The content: The contents of the outer and inner package, the structure and the content of patient information leaflet and procedure and criteria for exceptions

**20. By law on pharmacovigilance**

The content: The manner and procedure of reporting adverse reactions or events, manner of reacting to them, duties of medical professionals, marketing authorisation holders and the legal person from the second paragraph of this Article, manner of reporting and contents of periodical safety updated reports and manner of organisation of the system of pharmacovigilance.

**21. By law on advertising of medicinal products**

The content: The requirements and manner of advertising of medicinal products to general and professional public as well as control of advertisements as well as fees to be paid.

**22. By law on national supplement of Ph.Eur that shall be published in the Official Gazette of the R of Macedonia**

**23. By law on quality control of medicinal products**

The content: The content and procedure of quality control of medicinal products, carried out by the authorized control laboratory for the quality control purposes, conditions for recognising analytical control performed by other laboratories, method of sampling and expences for quality control as well as the method of keeping evidence as well as fees to be

**24. By law on pharmaceutical waste (?)**

The content: The manner of disposing of pharmaceutical waste

**25. By law on pricing of medicinal products**

The content: The method of determining/forming prices of medicinal products, method of price control and method of reporting medicinal product

**26. By law on classification of medical devices**

The content: the conditions for and manner of classifying medical devices according to their potential risk for users, their nature, power source connection and other characteristics, terms of duration of their use on human beings, of manner and place of dispensing and classification of *In vitro* diagnostic medical,

**27. By law on the essential requirements for medical devices**

The content: the essential requirements, i.e. general and specific requirements that medical devices must meet

**28. By law on the conformity assessment procedure for medical devices**

The content: The content of the requests and procedure for assessment of conformity of certain types of medical devices with the general and specific requirements as defined the Laws and its by-laws, and contents of the conformity assessment certificate of medical devices

**29. By law on notification of manufacturers of medical devices**

The content: The form of documentation to be submitted for notification of manufacturers of medical devices including requirements concerning premises, equipment for manufacturers of medical devices, the as well fees to be paid.

**30. By law on notification of wholesalers of medical devices**

The content: The requirements concerning premises, equipment, staff and notification documentation for registration of wholesalers of medical devices as well as fees to be paid.

**31. By law on notification of specialized stores for medical devices**

The content: The requirements concerning premises, equipment, staff and notification documentation for registration of specialized stores for medical devices as well as fees to be paid

**32. By law on the register of medical devices and economic operators dealing with medical devices**

The content: The contents of the register of economic operators that deal with medical devices, the availability of the data from the register as well as expenses associated with recording

**33. By law on labeling of medical devices**

The content: The contents and the manner of labeling the outer and inner packing of medical devices, as well as contents of the instructions for use,

**34. By law on clinical trials of medical devices**

The content: The required documentation and the procedure of notification of clinical trials, changes of notified clinical trials, reporting adverse reactions and events or incidents, requirements that shall be met by legal persons entitled to carry out clinical trials of medical devices, procedure of their verification and oversight as well as expences/fees associates with the procedures

**35. By law on vigilance of medical devices**

The content: The manner and procedure of reporting undesirable effects during the use of medical devices, types of reactions to them, duties of medical staff and suppliers, as well as manner of organizing a system of monitoring undesirable effects of medical devices and reactions to them, i.e. the system of materiovigilance.

**36. By law on advertising of medical devices**

The content: The conditions for and manner of advertising medical devices to the general and professional public