Conclusions RSNN Expert Meeting - Pharmaceutical Compounding, 21 May 2019

On May 21st, 2019, the RSNN organized an 'Expert Meeting' on the topic of pharmaceutical compounding which recently received significant attention in the media and in policy discussions. Traditionally, pharmaceutical compounding has been crucial in order to create a drug product with characteristics that are specifically tailored to an individual patient. Here the role of pharmaceutical compounding is complementary to industrially prepared medicine with a market authorization. However, in recent years certain movements have taken place through which topics such as the role of compounding pharmacies, the value of pharmaceutical compounding in *drug rediscovery*, pharmaceutical compounding during drug shortage and the meaning of pharmaceutical compounding as alternative for expensive registered drugs has gained increasing attention.

The RSNN invited fifteen experts and stakeholders in their personal capacity to discuss this topic in an informal setting. In daily life they work or have been working at governmental bodies, in business, clinical practice, universities or in branche organisations. In these roles they gained knowledge and experience around the topic of pharmaceutical compounding. The meeting was held under the Chatham House Rule.

The goal of the meeting was to identify relevant research questions from a regulatory science perspective. A regulatory science research question has the following characteristics: the question deals with the system of drug regulation or related matters; multiple stakeholders are 'owner' of the question; and lastly, answering the question helps to achieve the objectives of the system of drug regulation. In the coming period, the RSNN will take the initiative to gauge the support among various stakeholders for conducting relevant research that helps to answer the identified questions and thereby improving the opinion-to-data ratio and providing direction for discussions between stakeholders.

The regulatory science questions identified by the organizers of this expert meeting are shown by means of three themes.

1. TAXONOMY & BOTTLENECKS OF PHARMACEUTICAL COMPOUNDING

During the discussion it became clear that the field of pharmaceutical compounding covers a large diversity of products, for which the differences are not always taken into account. Depending on the type of product, the reason for compounding can differ and products can be compounded at different locations, such as the public pharmacy, the hospital pharmacy or in specialized compounding pharmacies. Besides this, pharmaceutical compounding can be an alternative to registered products, for example in the case of shortage or for economic reasons.

Moreover, there is diversity in the scale of compounding: for some drugs this will be done at a small scale while for other drugs a significant production volume will be reached. In order to get a better understanding of the current landscape of pharmaceutical compounding in the Netherlands, we need to categorize the drugs to which pharmaceutical compounding applies. Segmentation of pharmaceutical compounding can subsequently lead to more specific discussions for each segment.

Regulatory science questions covering Theme 1:

- Which categories exist in pharmaceutical compounding and how many products are covered within? Potential categories are therapeutic class, type of raw material, registered alternative/shortage, type of patients and mechanism/level of action.
- How many compounding pharmacies exist in the Netherlands (for each of the different categories described above) and which products can or can not be compounded by individual (hospital) pharmacies?
- Which type of pharmaceutical compounding creates bottlenecks? For example, as a result of compounding problems or the shortage of (delivery of) raw material.
- How will the compounding landscape develop in the future, taking into account the increasing amount of *personalized* therapies?

2. STUDY OF THE EUROPEAN/INTERNATIONAL CONTEXT OF PHARMACEUTICAL COMPOUNDING

Although the Dutch situation seems exceptional with regards to the knowledge, experience and infrastructure present in pharmacies, questions concerning the optimal use of pharmaceutical compounding arise in multiple countries in Europe. The latter includes the question if, and to what extent, pharmaceutical compounding can be used in situations when a registered alternative is available. The experiences around this topic need to be mapped in different countries, taking into account the individuality of the different healthcare systems. In addition, it can be useful to collect the knowledge in different

countries with regards to the research questions described in this report, such as the influence of pharmaceutical compounding on the innovation climate.

Regulatory science questions covering Theme 2:

- Which regulation exists in European countries with regards to the use of pharmaceutical compounding in general and compounding for specific populations, such as children? How does this regulation differ from the Dutch regulation? Is this regulation necessary or obstructing, considering the best benefit for patients?
- Can we identify international examples of how countries deal with pharmaceutical compounding as an alternative for registered products?
- How do other countries deal with drug shortage? Can we work towards a European approach, for example with regards to solutions for the availability of raw material?
- How does the Dutch expertise in the field of pharmaceutical compounding relate to this in other countries and what possibilities does this offer?
- Are there systems of pharmaceutical compounding outside Europe that could serve as an example for formulating European (national) policy?

3. ADVANTAGES AND DISADVANTAGES OF THE USE OF PHARMACEUTICAL COMPOUNDING

As mentioned above, pharmaceutical compounding plays an important role to create a drug product with characteristics that are specifically tailored to an individual patient, when an industrially prepared medicine with a market authorization is not (sufficiently) available. For the future we see a shift in the role of pharmaceutical compounding: while some stakeholders suggest pharmaceutical compounding as an alternative for (too) expensive registered products, others consider a significant role for the preparation of personalized treatments, or suggest a simplified route for registration to stimulate drug rediscovery. This raises new questions about making a trade-off between the advantages and potential disadvantages of pharmaceutical compounding. Another issue is how we can guarantee the quality of pharmaceutical compounding as effectively as possible.

Regulatory science questions covering Theme 3:

- How can we guarantee the safety, quality and efficacy of pharmaceutical compounding, and how does this relate to registered products? What can we learn from this with regards to risk perception and acceptance in a society? What role does the patient have in this discussion and how can it be filled in?
- Can the quality of compounding be increased by having local compounders specialize in a specific product?

- What incentives and barriers can we identify for registering products produced by compounding pharmacies, for example with a view on stimulating ‘drug discovery’?
- What information can we gather about the influence of the ‘pharmaceutical compounding climate’ in the Netherlands on the choices of companies whether or not to introduce a product on the market, also in comparison with other countries?

The results of this meeting will be processed by the RSNN in future research agendas that should contribute to informing policy discussions.