RSNN EXPERTMEETING "DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION"

On April 4th 2023, the Regulatory Science Network Netherlands (RSNN) expert meeting took place with the topic 'Direct Healthcare Professional Communication: Recommendations to improve impact'. The Direct Healthcare Professional Communication (DHPC) communicates new important drug safety issues to individual healthcare professionals (HCPs).

When new drug safety information becomes available through post-approval pharmacovigilance activities, regulatory authorities may decide that individual HCPs need to be informed in a timely manner. The decision to communicate can be at the suggestion of the marketing authorisation holder (MAH) or be required by national competent authorities or the European Medicines Agency. Generally, the content of the communication is agreed at the European Medicines Agency (EMA) by the Pharmacovigilance Risk Assessment Committee (PRAC) in collaboration with the MAH. Regardless of whether the new drug safety information is already known in the public domain (e.g., through publication of scientific or lay papers) and might be known by HCPs, a DHPC is sent shortly after regulators have decided that communication of the new safety information is of importance for maintaining the benefit-risk balance of the product. Together with the proposed target groups and within a European agreed timeline, national translations of the DHPC content are submitted by the MAH to the national competent authorities. DHPCs are issued for the following reasons: to notify suspension or withdrawal of the marketing authorization of a medicinal product for safety reasons; to communicate about new and important information about the usage of a medicinal product; to inform about new important risks of medicinal products; shortages or quality problems of a medicinal product [1].

In the Netherlands, the Medicines Evaluation Board (MEB) assesses the Dutch translation of the DHPC submitted by the MAH, for content and clarity, and whether the proposed target receiver groups are aligned with the Dutch healthcare system. The Dutch version of the DHPC is distributed in the form of a paper-based letter in an envelope with a white or orange hand logo as proposed by the MAH. The MEB thereafter confirms whether the proposed colour is appropriate for the DHPC content. The hand logos are displayed on both the letter and the envelope accompanied by the following text: "Belangrijke, niet-commerciële risico-informatie over een farmaceutisch product"; "Important, non-commercial risk-information about a pharmaceutical product'' [2]. An orange hand logo is used if the DHPC should stand out more, such as in the case of a restriction of an indication, a new contraindication, changes in dosing or infusion rates, extra physician or pharmacist visits being necessary, or a recall on a pharmacy or patient level [2]. A substantial part of Dutch DHPC is, however, sent with a white hand envelope.

Health care professionals' awareness of drug safety issues for which DHPCs have been issued and the impact of the DHPC on their prescribing behaviour is shown to be suboptimal [3-7]. In addition to the preference of Dutch HCPs for digital communication [8, 9], which is currently being implemented by the MEB following other European countries, there are other aspects that can be improved. The current communication strategy, regarding both the channel and timing of the communication, does not align well with the preferences of hospital-based HCPs, who are a frequently targeted by DHPCs [8-10]. Aligning the communication strategies with the preferences of the receivers may improve the uptake of the drug safety information. A previous study has shown that preferences of hospital-based HCPs for the moment of communication differ based on the characteristics of the drug safety issue [8]. Drug safety issues occurring less often, are less serious, and that do not need immediate actions are preferred to be communicated through periodic communication, such as a newsletter, instead of acute communication through DHPCs [8]. Such periodic newsletters could combine different drug safety issues and would be sent with prespecified time intervals. Communicating periodically grants the MAH and MEB more time to provide clinical implications to accommodate the HCPs who receive the new drug safety information.

The RSNN organised an expert meeting with the title: 'Direct Healthcare Professional Communication: Recommendations to improve impact'. The aim of the meeting was to discuss solutions to streamline regulatory risk communication in the Netherlands, and to optimise the effectiveness of DHPCs. The invited experts shared their knowledge, experiences, and personal views in accordance with the Chatham House Rules. The group comprised 16 experts from various backgrounds including academia, industry, governmental bodies, HCPs (including hospital pharmacists and one medical specialist), and a patient representative. This report provides a summary of the discussion held and is arranged thematically per question.

Is periodic communication a good addition to issue safety communication? And who should determine which drug safety issues qualify for periodic communication (professional medical association/MAHs/CBG?)

That addition of periodic communication to the current form of communication through a DHPC could be of added value, was supported by the majority of the experts. It would especially be of use when the periodic communication would provide more context and clinical implications of the drug safety issue. For some academics and HCPs, periodic communication could even replace some of the DHPCs. The DHPCs sent in the white hand envelope would qualify to be solely communicated periodically, according to the HCPs. The distinction of which DHPC is sent in an orange hand envelope or a white hand envelope, is currently made by the MEB in collaboration with the MAHs. None of the experts were of the opinion that this process should be changed for periodic communication. However, due to

the legal obligations surrounding risk communication and the same level of transparency HCPs and patients deserve throughout Europe, periodic communication instead of some DHPCs could not be supported by regulators, industry representatives and the patient expert. If periodic communication of DHPCs were to be established, it should contain all DHPCs and be in addition to the DHPC.

Should periodic communication be digital and who should be the sender?

All experts agreed that periodic communication should be digital, for example sent by email. This way, different DHPCs could even be bundled per disease area. Multiple institutions were deemed appropriate as senders by the stakeholders, e.g. the MEB, the Netherlands Pharmacovigilance Centre Lareb, or professional medical associations. The MEB was considered most ideal, since they have the best overview of all communications/DHPCs within each period.

Who should the receiver of such (periodic) communication be? In other words, who should be responsible for the clinical implications of the issue/safety information in the hospital (individual HCPs/professional medical association/MAHs/CBG)?

Who the receiver of communication should be remained somewhat unclear. The handling of the DHPC within hospitals can differ amongst the hospitals. In case there is a clear procedure in place in which the DHPC is assessed for its clinical implications and this is communicated to other HCPs, it might not be necessary to inform all individual HCPs through a DHPC. The addition of periodic communication would most likely be relevant to the hospital pharmacists, since they currently receive every DHPC that is issued. If periodic communication were to be tailored on disease area, it would be interesting for patient groups to receive that as well.

Who should be involved in assessing and formulating the clinical implications, i.e., recommendations that go beyond newly identified safety information, but also how treatment could be affected considering also other available therapies (individual HCPs/professional medical association/MAHs/CBG)?

The DHPCs sent with a white hand envelope, were not always perceived as clear by HCPs. These DHPCs could benefit from additional information on the clinical implications and improved recommendations or should simply state that the DHPC only contains information the HCP should be aware of without immediate action expected.

Both industry representatives and the patient representative pointed out that the clinical implication of the DHPC is dependent on the patient and has to be defined between the HCP and the patient on a case-by-case situation. This is a process in which regulators and industry should not be involved. As pointed out by a regulator, providing additional information in the DHPC is only allowed when it is specific to the Dutch healthcare system. The patient

representative mentioned that patients throughout Europe deserve the same guidance, for which the same information should be communicated in each country. In case a DHPC is issued on a European level, when possible, recommendations are established in terms of restricting indication, new contraindication, dosing or monitoring advice. Ideally, these would include clinical implications, established on a European level.
In case of Dutch periodic communication, further clinical implications could be provided. The experts agreed that such clinical implications should be established without any involvement of regulators or MAHs. Ideally, it would be on the initiative of professional medical associations. It is unclear from this meeting if professional medical associations are willing to take on this role, since no professional medical associations took part in the meeting.

KEY MESSAGES:

- Periodic communication could add value to the current way of communication, because it generates the possibility (time) to provide more context on clinical implications. In general, WHE DHPCs would qualify for such periodic communication, preferably in digital format using email.
- Periodic communication was preferred by HCPs over the current immediate distribution of the WHE DHPC. However, other experts did not consider exclusively periodic communication feasible because the Dutch healthcare system would be informed about safety issues later as compared to other European countries. In addition, this strategy would not comply with the current EU legislation.
- The MEB would qualify to be the sender of periodic communication.
- Patients throughout Europe should receive similar drug safety communications/DHPCs sent to their HCPs, receiving equal care.
- Other than providing clear recommendations along with the safety communication, regulators and industry should not be involved in the interpretation of the drug safety information and decide on what the clinical implications should be because these are patient-dependent and have to be defined between HCP and patient.
- Professional medical associations and patient organisations could play a role in providing clinical interpretations, allowing all patients to benefit from it in the same manner.

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