Norwegian Medicines Agency

Improving availability of needed medicinal products with low sales volumes and low profitability in Norway:

Survey of pharmaceutical industry

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1 Introduction

1.1 Background

In Norway and many other European markets, there is an unmet need for certain important/critical medicinal products. In this report, a needed product is in short defined as a product that is considered critical, but where we do not have a Marketing Authorisation (MA) for a marketed product. In some cases, the product might have a MA, but is not marketed. For certain critical products, more than one MA from different suppliers might be desired in order to decrease the probability of shortages in case there is supply disruption for one of the suppliers.

Call for needed products

The Norwegian Medicines Agency (NoMA) publishes a list called Announcement of needed products in Norway that contains products where the supply is currently unmet. This list should in no way be seen as exhaustive, and other products currently not marketed could most certainly qualify for this list.

Typical needed product

A typical needed product is an old, generic product with expected low sales volume. Such product is typically also associated with relatively low prices and consequently low or no profitability. Older antibiotics are one type of product that often falls in the category of low price and volume. Generics for smaller population groups such as children and products used for treatment of relatively rare conditions also often fall within this category. Since sales volume is one of the most important factors, availability issues are typically greater for smaller European markets such as the Norwegian market.

Benefits of MA-products

In some cases, such products can be made available through various national exemption schemes instead of being marketed with an MA. Solutions for exemptions often differs between member states and these can be acceptable solutions for some products. However, as a rule of the thumb, the best way to ensure a safe supply for a product in a given market is to have an MA. Product with an MA is then supplied by the Marketing Authorisation Holder (MAH). The MAH has a wide range of responsibilities, one of them being monitoring the supply and demand situation at any given time to avoid potential shortages.

Incentives and the survey

There are several measures available to National Competent Authorities (NCAs) that can act as incentives for the industry to market important medicinal products. The Norwegian Medicines Agency (NoMA) performed a survey among Marketing Authorisation Holders (MAHs) in the summer of 2022. The primary aim of this survey was to gain some better insight into what measures the industry find most relevant and attractive. This report aims to disclose a large portion of the results from the survey. It provides some conclusions on obvious observations and trends, but does not aim to perform any in-depth analysis of the results.

1.2 Incentives used by NoMA

Available measures to facilitate MA-procedures for needed products, such as expedited and prioritised procedures, can be used on a case-by-case basis by NoMA. Such measures are typically only used for

products that are currently published on the list of needed products mentioned above. Certain measures can in some cases also be used in order to get MA-product marketed or prevent a MAH from withdrawing the MA. One such measure is waiving the application fee. Others can be to accept deviations from certain requirements in guidelines related to quality, safety, efficacy, product information, etc. One general example for this could be if the product has been marketed and used for a very long time in one or several other European markets. Procedures can also be prioritised and shortened when circumstances allow it. A higher maximum price can also act as an incentive, and it is possible to accept such higher price pre-authorisation for products that are announced as needed products. Some incentives that are available in Norway and many other European countries are shortly described in a general manner below:

Prioritised procedure

Procedures for new marketing authorisations are typically assigned a slot time in accordance with available resources at the NCAs. As a result, the start time of a procedure (also called 'slot time') can in many cases be set several months after the first contact with the agency. There is no guarantee in receiving a slot time within a certain period. One incentive is to provide a prioritised slot time for the procedure. For Decentralised Procedures, *i.e.* European procedures involving several member states, the applicant also needs to find a Reference Member State that accepts the main responsibility for the procedure. For such procedures, it is therefore also important that at one member state accepts such a role.

Expedited procedural timelines

The timelines for different types of procedures (*e.g.* National Procedures, Decentralised Procedures, Mutual Recognition Procedures etc) differ. A typical procedure normally takes at least one year including clock-stops. The assessment phases of an expedited procedural timelines can to some extent be prioritised and shortened. How much shortened can differ significantly from case to case.

Fee reductions/exemptions

There are typically fees for various kinds of applications, for example for new marketing authorisations and variations. There are possibilities to reduce or waive these fees for needed products, *e.g.* where expected sales volumes are very low. The applicant should apply for a reduced or waived fee containing a short justification. The justification should explain the need of the medicinal product and contain financial estimates, for example manufacturing costs, expected sales prices and volumes for at least the next two years.

Accepting deficient documentation and deviations from guidelines

MAHs are required to keep the dossier up to date. It is expected to be continuously updated in accordance with current requirements and practice. Maintaining the dossier and keeping this up to date is a resource demanding activity. However, this requirement is not always fulfilled. This is especially true for products with low profitability that in turn might have a low focus from the MAH's side. As a result, many older products don't have dossiers that fulfil current requirements for a marketing authorisation application. Updating such a dossier to current requirements and standards is both resource demanding and costly. Exemptions from certain documentation requirements can in some cases be considered based on an overall patient safety evaluation.

Foreign language packages

Native language requirements for physical packages and leaflets are associated with various costs for the MAHs. Time limited exemptions from this requirement can be made in certain cases for products for hospital use.

1.3 The questionnaire

The survey that this report is based upon was performed as part of a Nordic project (Legemidler til barn i Norden). This project aims at increasing collaboration between Nordic countries for medicinal products for children. A questionnaire was designed in order to collect relevant responses. Useful feedback on this was received from both industry interest organisations in Norway, LMI and Farma Norge before it was submitted to the pharmaceutical companies.

A link to the questionnaire was sent to all MAHs with at least one MA in Norway and any representatives of these as registered in the Article 57 database. This database is maintained by the European Medicines Agency and contains pharmacovigilance contact information for all products that have been granted an MA in a EU/EEA member state. The total number of recipients were approximately 400-500 companies, including both MAHs and other representatives registered in this database. All MAHs were encouraged to respond no matter on the number- and kind of MAs registered in Norway. Both the industry interest organisations mentioned above, assisted in reminding their members of this survey.

The main challenge of a questionnaire is to ask the right questions and at the same time keep it simple. All questions identified as relevant should be asked. At the same time, asking too many questions and making the response options too complicated might decrease the response rate. Based on the general comments provided by many MAHs, it is indicated that the questionnaire managed to cover both relevant questions and response options to each question.

From earlier experience, the number of questions and detail/complexity of the questions should be balanced. Few questions may result in too little information gained whereas too many questions or too detailed/complex questions may result in incomplete or absent response. The response received here could therefore be further followed up with the industry.

2 Results

2.1 Responding MAHs

A total of 71 MAHs responded to the questionnaire, which is in line with expectations based on experience from earlier surveys performed by NoMA among MAHs.

Number of MAs per responding company

One question was to indicate how many MAs they have registered in Norway and if they have an office located in one of the Nordic countries. Due to the connection between the survey and the Nordic project on medicines for children, they were also asked if they have an MA for any paediatric medicines registered in Europe.

The size of the responding MAHs was evenly spread from those having just a few MAs to those having more than 30 MAs. Figure 1 shows the fraction of responders based on the number of MAs they hold.

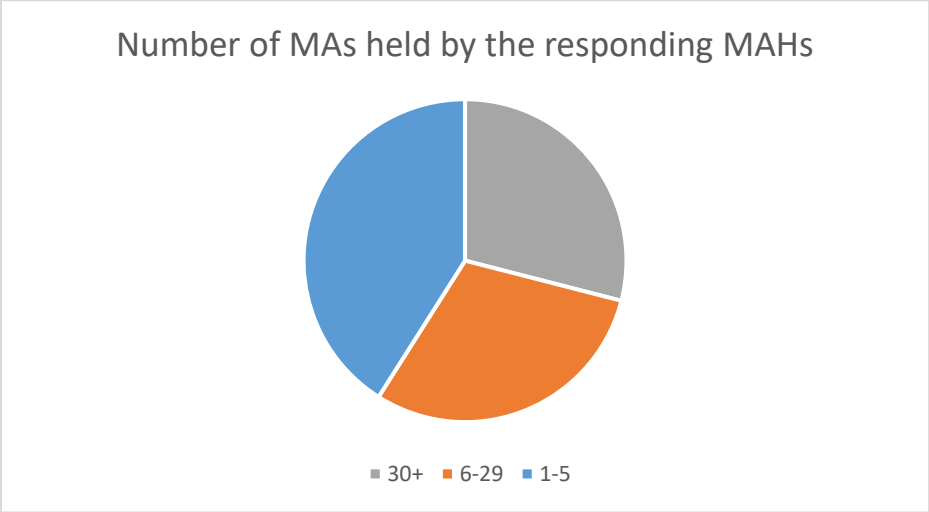

Figure 1. Depiction of the number of MAs held by the MAHs responding to the questionnarie

Although 71 responders constitute a minority of the total number of receivers of the survey, it should be mentioned that these at the same time represent a very large portion of the total market share in Norway, both in terms of numbers of marketed MA-products and total sales volumes.

Companies with products for children

75% of the responding MAHs have an office in a Nordic country and 62% have at least one paediatric MA-product.

Patent protected products vs generics

A couple of questions were related to measures in order to put products with an MA on the market. Since relevant measures for generic products differ significantly from measures for originators (patent protected products), two separate questions were designed to address each product category. The response to these questions also indicates if the company has generic products and/or originators. For example, if a company responded “not applicable” to questions related to generics indicates that the company only deals with originators.

Out of the 71 responses, 42 companies responded that generic products were applicable to them whereas 32 companies responded that originators are applicable to them. Thus, 3 companies considered both the generic and originator market to be relevant.

Based on this information, it is possible to divide responses to other questions both by company size (*i.e.* number of MAs) and between generic/originator companies. This is done where there are obvious differences in the responses to some questions.

2.2 Questions overview

The questions asked were divided into three parts in an attempt to cover the life cycle of medicinal products:

- The first part included questions related to the pre-approval phase, *i.e.* before a MA-application (MAA) has been submitted.
- The second part included questions related to the post-approval phase, *i.e.* once an MA has been granted. One of the issues here is that not all MA-products are actually marketed. Our

own statistics from October 2022 show that about 36% of all MAs granted via non-central procedures are not marketed. Non-central procedures comprise Decentralised Procedure (DCP), Mutually Recognition Procedure (MRP) or National procedure (NP). These procedures are most relevant for generic products. When excluding products approved via parallel import from this group, this figure decreases to about 31%. A few questions were therefore asked on measures available to get a greater proportion of the approved products available in the market.

- The last part of the survey had questions on how MAHs decide on- and handle withdrawals, and what the drivers for withdrawals might be. The response here could give a better overall insight and be helpful in any future initiatives to prevent MAHs from withdrawing needed products.

2.3 Questions on the pre-authorisation phase

Obstacles

The first question explored the biggest obstacles for applying for new MAs for needed medicinal products in Norway. Each responding company could select up to three options. The available options were likely not exhaustive but were based on factors that companies have perceived as hindrances in earlier dialogs with NoMA. The responses showed that all options available were relevant to some degree but unpredictability in maximum prices and sales volumes stand out as options selected by a large portion of the responders. The results are depicted in the figure below. The response has been divided between companies having 1-5, 2-29 and 30+ MAs. It is clear that the two options "Preparation, translation and/or maintenance of PI" and "Costs associated with serialisation" are factors seen as obstacles to a larger degree by companies having a smaller number of MAs.

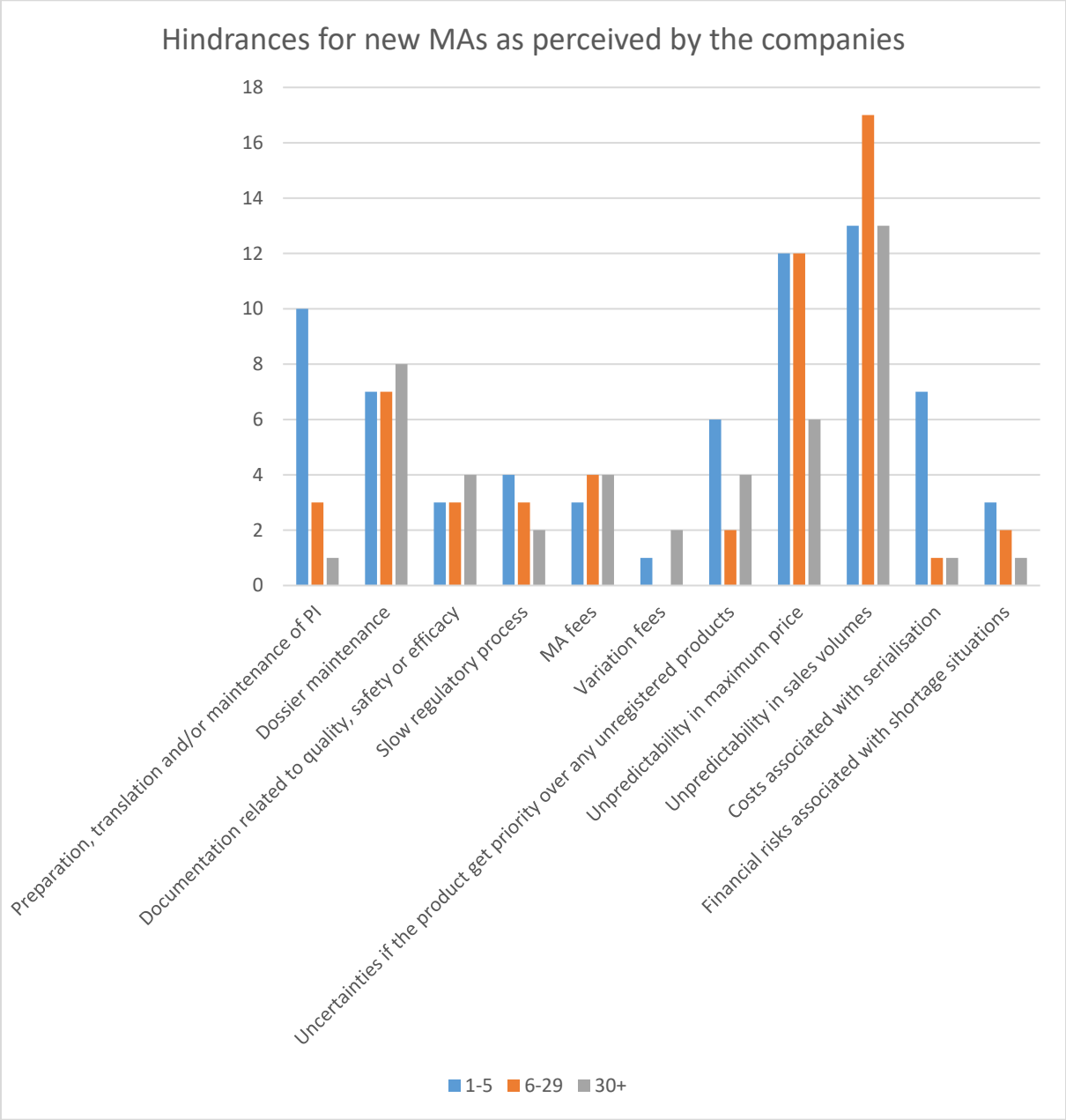

Figure 2. Hindrances for new MAs as perceived by the companies

Preferred incentives

The second question was very much related to the first one asking what incentives would mostly affect the company's willingness to apply for new MAs in Norway for needed medicinal products. Also here, up to three options could be selected.

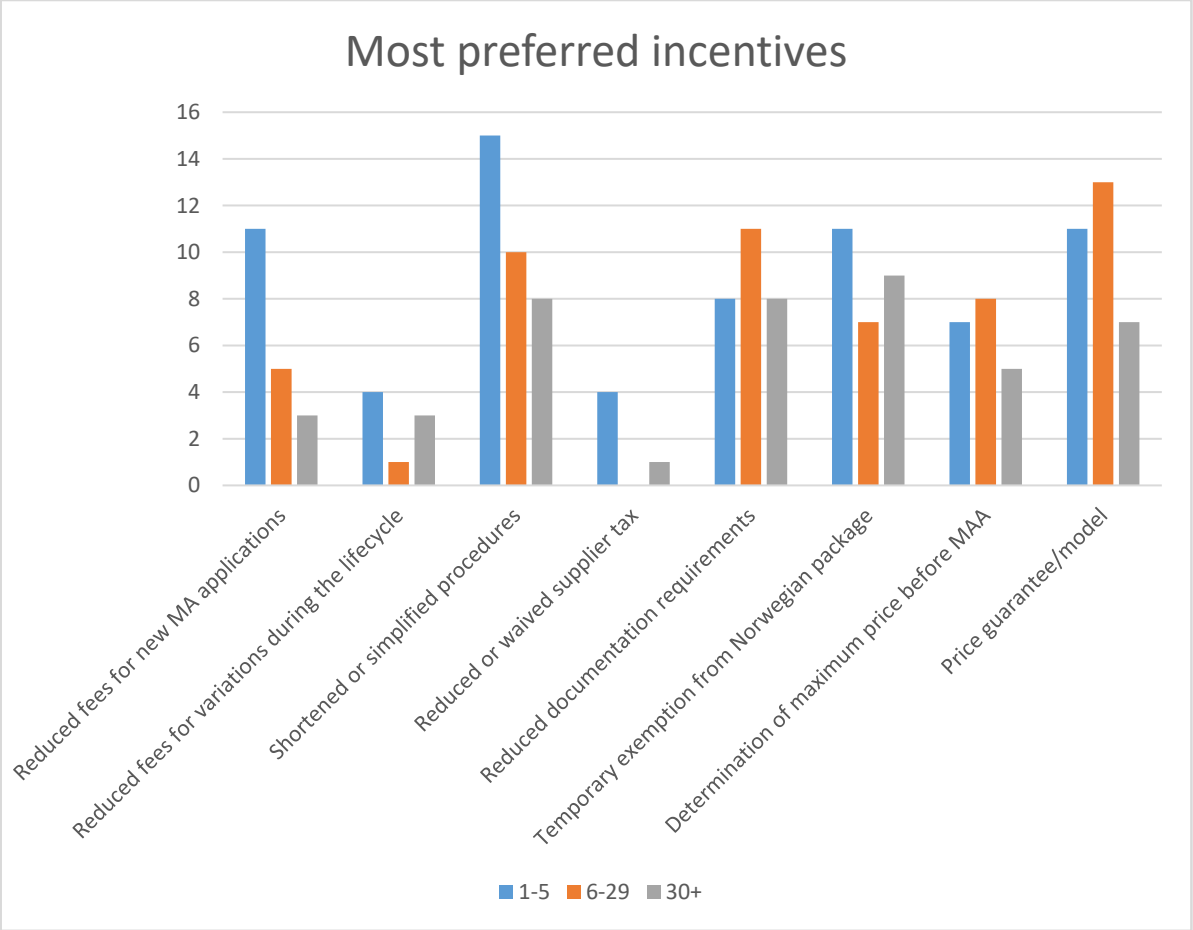

Figure 3. Summary of the most preferred incentives selected by MAHs

Incentives used in European procedures

A third question was on the importance of use of incentives or facilitations in European procedures, for example Mutual Recognition Procedures (MRP) or Decentralised Procedures (DCP). This could for example be a procedure receiving fast track or a procedure receiving faster assessment and where all National Competent Authorities (NCAs) involved agree to such timetable. The overall response shows that such measure could most likely have an impact on MAHs willingness to apply for MA for needed products. The only difference noted in response from companies of different number of MAs were that companies with 1-29 MAs had “very important” as the most selected choice whereas companies with 30+ MAs had “important” as the most selected choice.

Any differences between generic and originator companies were also looked into. There was no difference of significance between these two categories of companies and the response has therefore been merged into the same figures above.

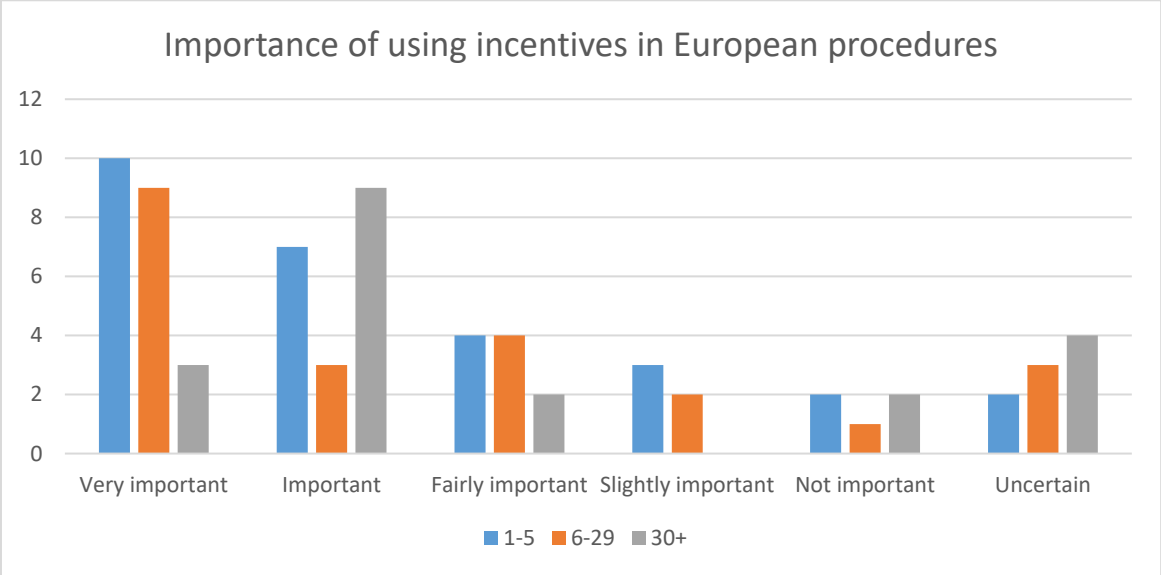

Figure 4. MAHs view of importance of using incentives in European procedures

Languages of packages

A couple of questions were also asked on possibilities for having other languages or a combination of languages on packages. Harmonised procedures open up for the possibility to get approval for other languages on packs than singular (*e.g.* only Norwegian). The responders were asked to rate the following three alternatives; English only packs, multilingual packs (*e.g.* some or all Nordic languages) and singular pack (*e.g.* only Norwegian). Each of the options could be assigned "most advantageous", "less advantageous" and "least advantageous". The results are depicted in the figure below. It is clear that English only or multilingual packs were preferred over singular Norwegian packs. There were no significant differences between companies with a small number of MAs as compared to a large number of MAs. Neither were there any significant differences between generic and originator companies.

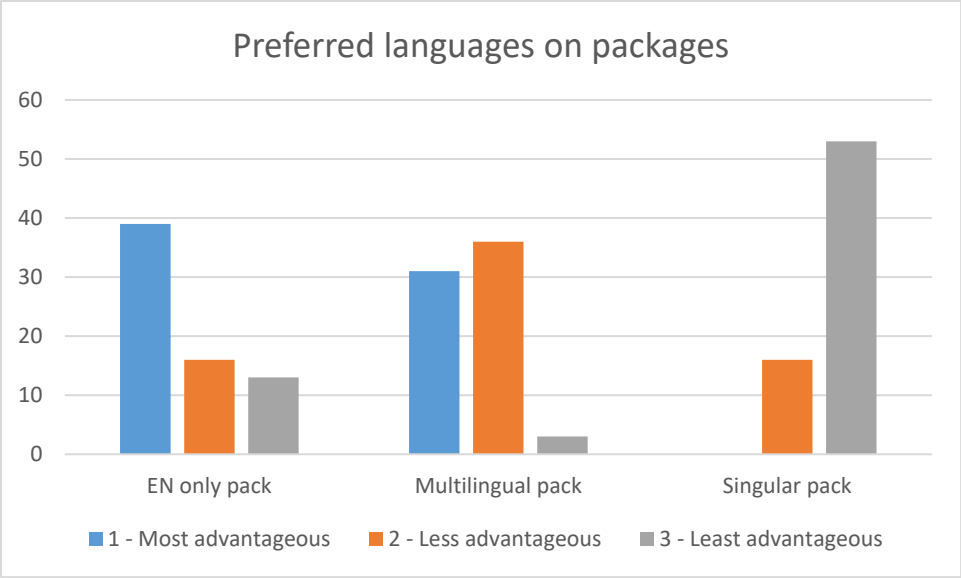

Figure 5. MAHs preferred languages on packages

Harmonised procedures also open up for the possibility to get approval for different combinations of languages on the inner and outer package. The responders were asked to rate different combinations of packages in the same way as above. The results are shown in the figure below. Also here, there were no significant differences in the response looking at either the number of MAs held by the companies or between generic/originator companies.

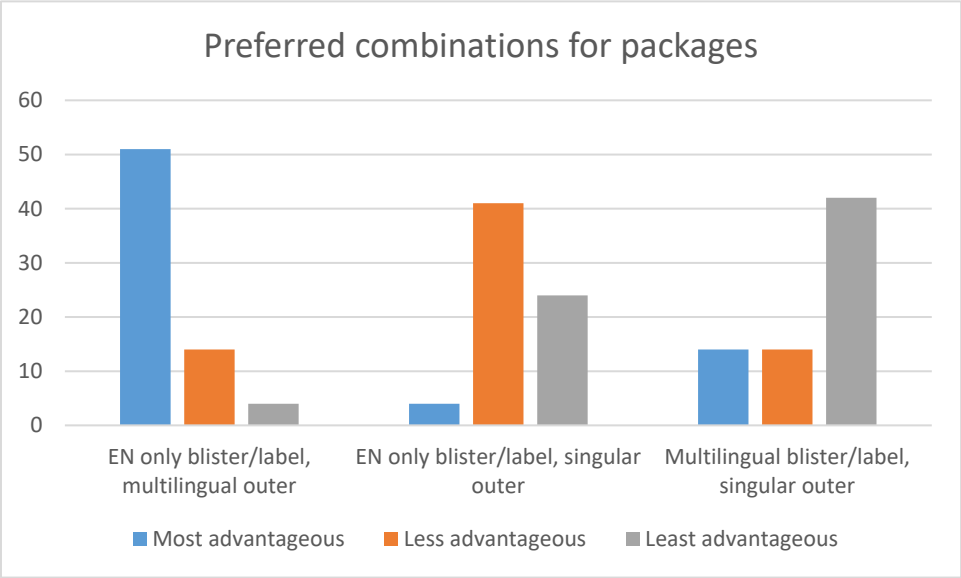

Figure 6. MAHs preferred combinations for packages

The last question in this section was related to electronic PIL (ePIL). Marketing products with only ePIL instead of a printed PIL could be a possible future. The companies were asked to compare ePIL to other incentives mentioned and what impact any possibility to have an ePIL have on their willingness to apply for MA and subsequent marketing of needed products in Norway. The following five options were given:

- Crucial - ePIL would alone act as a crucial incentive
- Major - ePIL would have a greater impact than most other incentives
- Medium - ePIL is comparable to many other available incentives
- Minor - many other incentives have a much greater impact than ePIL
- None - this would have no impact

The results show that most companies think that the possibility for ePIL instead of printed PIL would have some degree of impact. The response from companies with 30+ MAs lean towards a major impact whereas the response from others leans towards a minor impact.

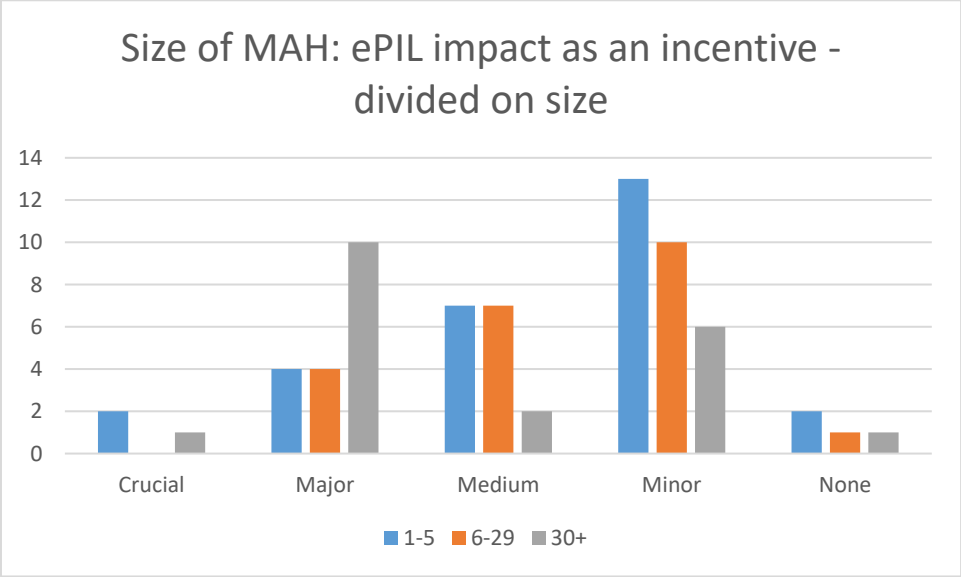

Figure 7. Level of impact that ePIL might have as an incentive, divided on size of MAH

When dividing the response between generic and originator companies, the generic companies tend to think that ePIL might have a slightly larger impact as compared to other incentives. When breaking down the numbers further and only looking at generic companies with 30+ MAs, the response leans even more towards a major impact. Out of all 14 generic companies with 30+ MAs, 9 responded that ePIL could have a major impact (not shown in any of the figures).

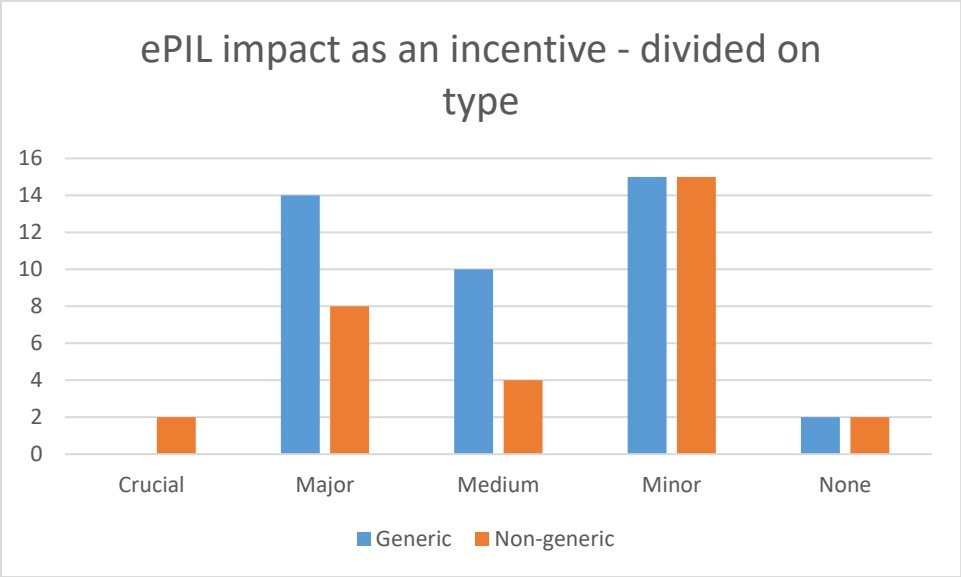

Figure 8. Level of impact that ePIL might have as an incentive, divided on type of MAH

2.4 Questions on the post-authorisation phase

A number of questions were also asked on the post-authorisation phase, *i.e.* once a MA has been granted. As mentioned in the introduction, one of the major issues here is that a large portion of products with a valid MA are never marketed.

Why MA-products are not marketed

The first questions were on what the main reasons are for not marketing certain products, although an MA has been applied for and granted. This was divided into two similar questions, one for generic products and one for originators. Up to two options could be picked. There was also the possibility to indicate if the question was not applicable. As already mentioned above, 42 companies responded that generic products were applicable to them, whereas 32 companies responded that originators are applicable to them.

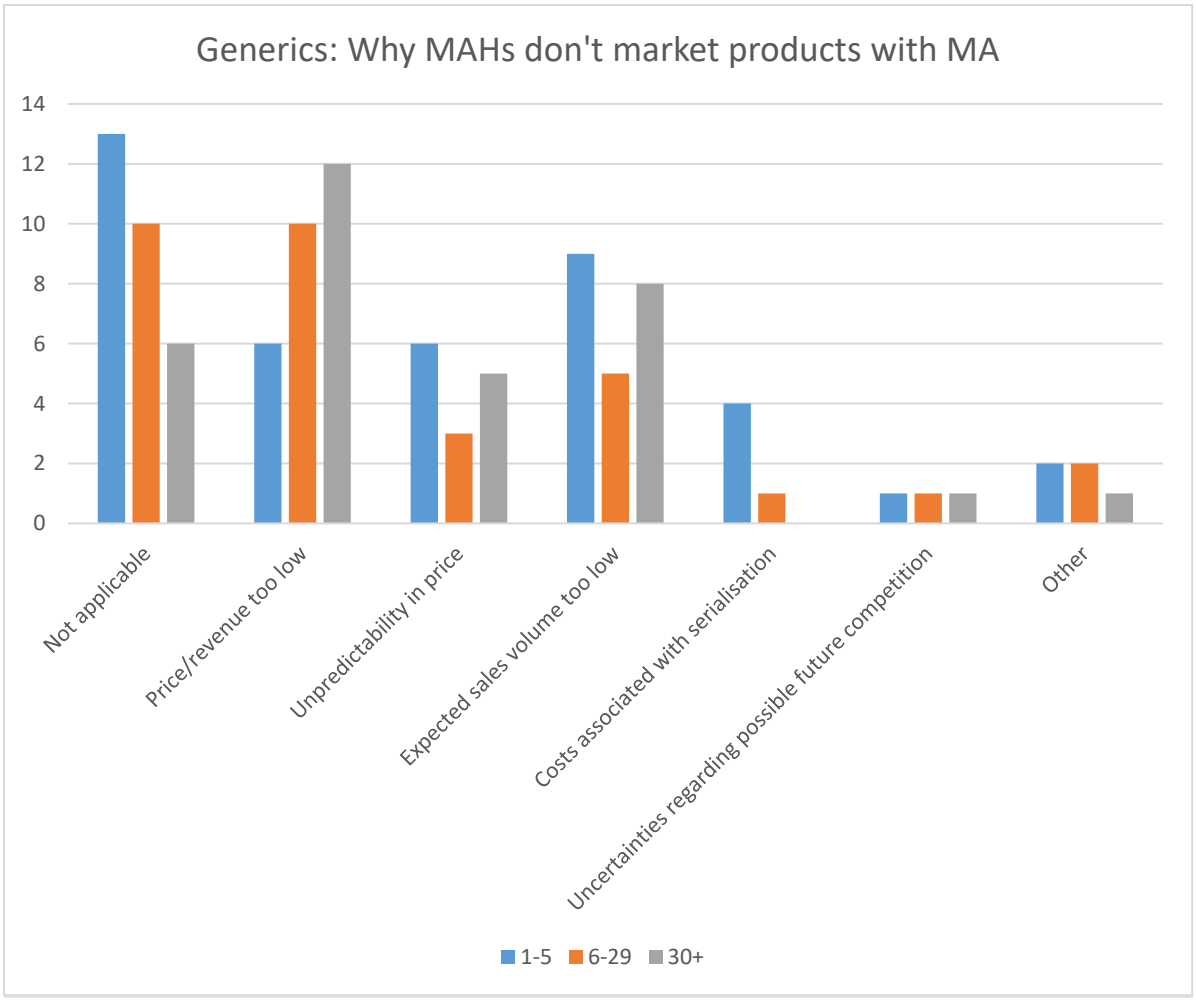

Figure 9. Why MAHs don't market generic products that already has been granted an MA

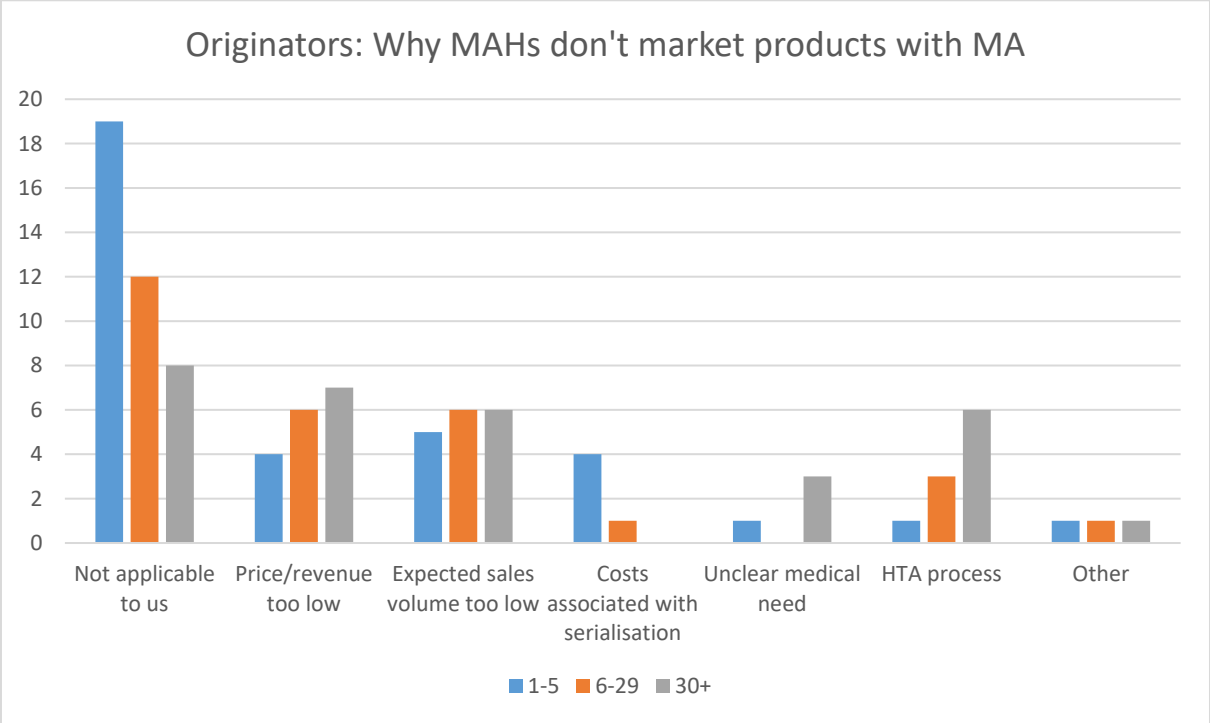

Figure 10. Why MAHs don't market originator products that already has been granted an MA

Price and volume

Too low price and sales volumes seems to be the two dominating factors why MAHs don't market products that already have a MA. Unpredictability in price also seems to be an important factor for generics. Also here, costs associated with serialisation is stated by some companies as a reason and it is clear that the importance of this factor increases with decreased size of the company. The HTA process for originators seems to increase in importance for larger companies.

Other factors

Some MAHs have also answered that other factors play an important role and the responders were given the opportunity to clarify this in a free text field. The response from both generics and originators showed that factors involving wholesalers are important. Examples are: no interest from wholesalers and the structure of wholesalers. Unpredictable and long tender periods are also mentioned as a reason for not marketing.

Closer dialog with NoMA

The last question in this part of the questionnaire was if a closer dialog with the Norwegian Medicines Agency and possible evaluation of incentives could have an impact on the willingness to market products where an MA has already been granted. The results are shown in the figures below, one divided on size based on numbers of MAs and one divided based on generics/originators.

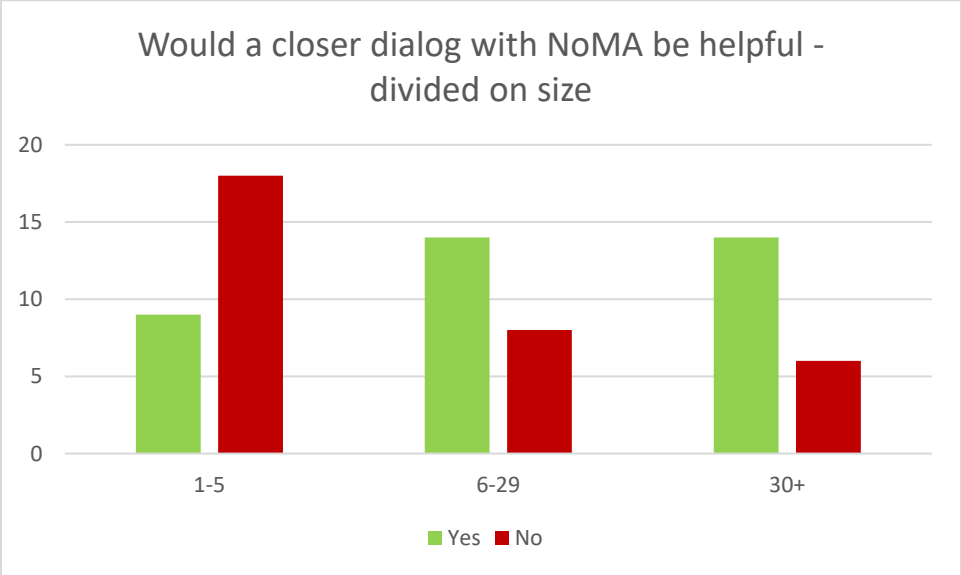

Figure 11. MAHs view on if a closer dialog with NoMA be helpful in connection with marketing needed products, divided on size of MAHs

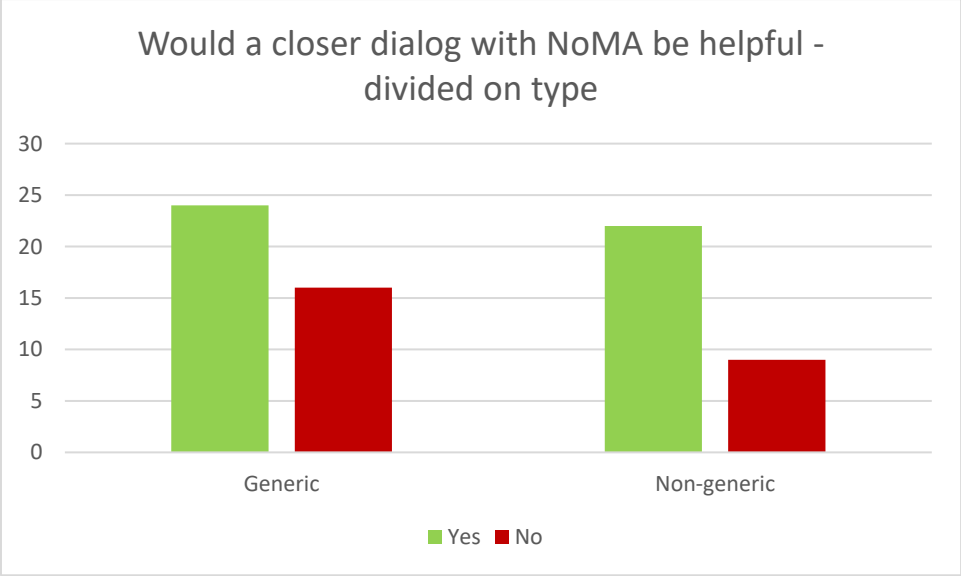

Figure 12. MAHs view on if a closer dialog with NoMA be helpful in connection with marketing needed products, divided on type of MAHs

The results clearly show that the optimism in having a dialog with the NoMA increases with the size of the MAH. Although a little bit more than half in total think that this could be useful, this figure is still surprisingly low. This is especially true for generics where measures in general are often easier to implement than for originators. The reasons for why almost half of the companies might not find this useful becomes purely speculative.

2.5 Withdrawals of Marketing Authorisations

The last part of the questionnaire contained questions related to withdrawals of MAs from the market. The response to these questions could to some extent also concern cases where the MA is kept but the product withdrawn from the market, *e.g.* for products approved in Centralised Procedure (CP).

Reasons behind withdrawals

The first question was on the reasons behind such withdrawals. Each MAH could select up to two options and the results are shown in the figures below.

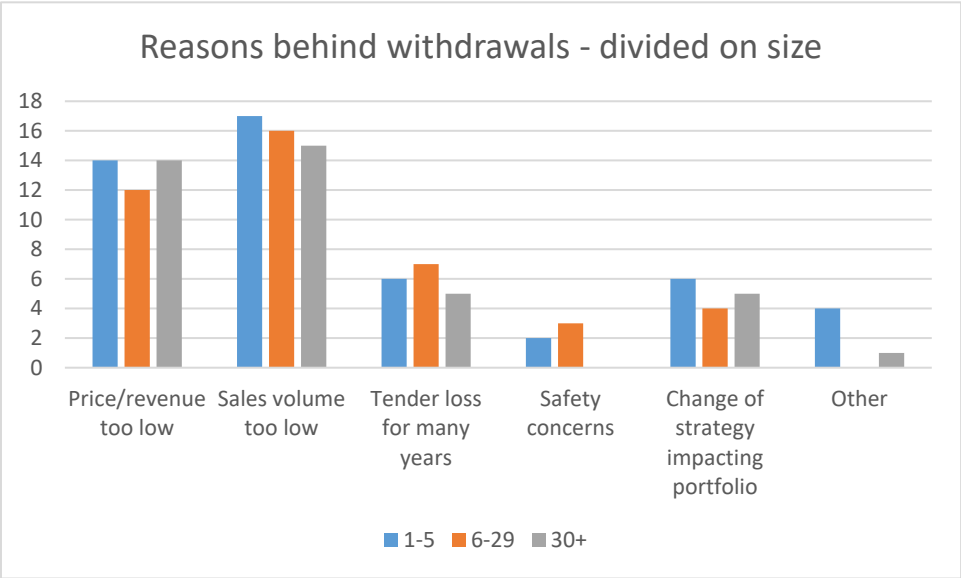

Figure 13. The general reasons behind withdrawals, divided on size of MAHs

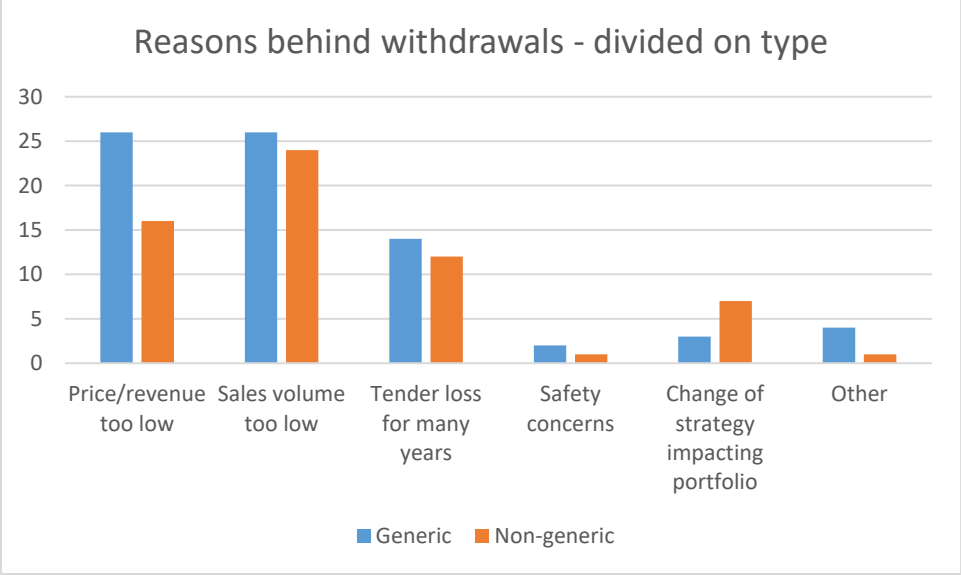

Figure 14. The general reasons behind withdrawals, divided on type of MAHs

The response show that there is not much difference between MAHs of different size or between generics and originators. The only clear difference is that price has a somewhat less impact for

products marketed by originator companies as compared to generic companies. Again, too low price and sales volumes are the two dominating factors. The MAHs could also select "Other" as a reason and specify this in more detail. Various costs are specified as reason in a couple of cases which can be more or less linked to price and sales volumes. Another example given is that the withdrawn MA is replaced by another MA.

Who decides to withdraw

The second question on withdrawals was where in the MAH's organisation the decision to withdraw a product is taken. It is clear from the response to the first question that the main reason for withdrawals is more of a business-case decision and typically not due to safety concerns. Many MAHs are part of an overarching company structure where the MAH is a company registered nationally and part of a bigger cluster of MAHs. In some cases, the MAH registered nationally has a relatively big local office and is free to make many decisions for each MA. In other cases, the local office is smaller or merely a post box and/or is not authorised to make decisions such as those related to withdrawal of an MA. For smaller MAHs, there might be only one organisation and office located somewhere in Europe. In such cases, the Norwegian MA and International/Regional office might be the same organisation.

Two options to this question were given; Norwegian MA holder or International/Regional office.

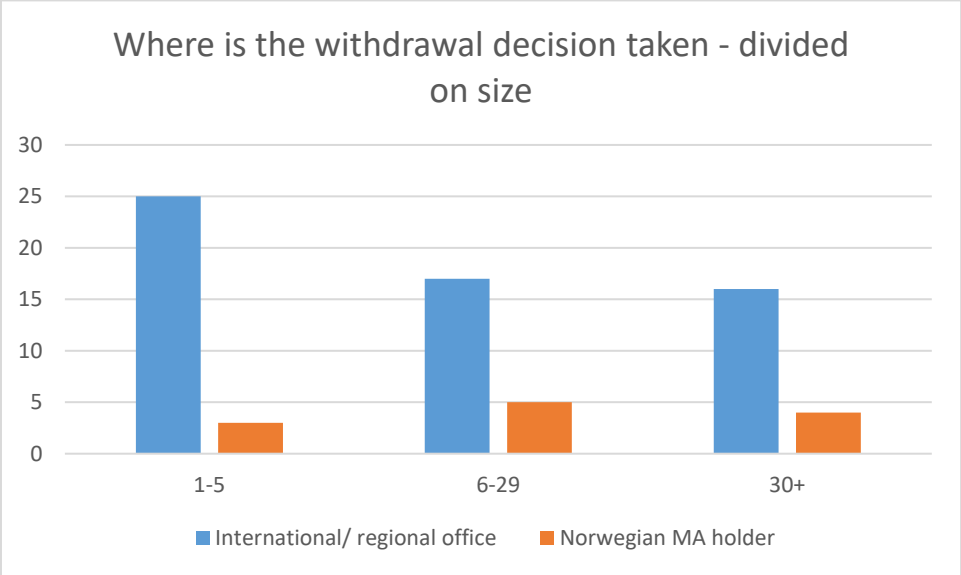

Figure 15. Where decisions for withdrawals are typically taken, divided on size of MAHs

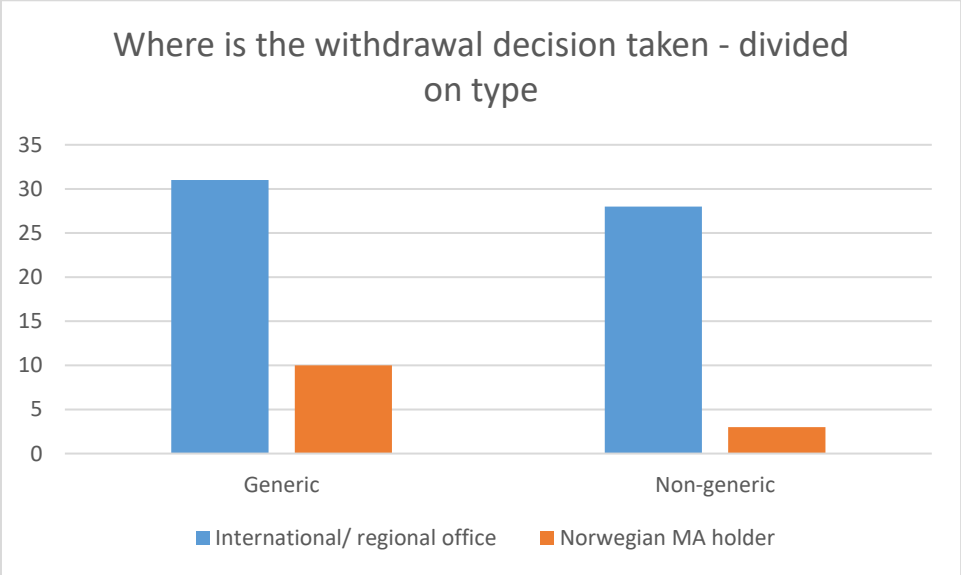

Figure 16. Where decisions for withdrawals are typically taken, divided on type of MAHs

The results show that for most MAHs, decisions on withdrawals are taken at an international or regional office and might be outside of the control of the MAH. For companies with generic products, a larger portion responded that decisions are made by the Norwegian MAH as compared to originator companies. When comparing different sizes of MAHs, a larger portion of the bigger companies (6+ MAs) indicated that such decisions are made locally by the Norwegian MAH as compared to the smaller companies (1-5 MAs).

Dialog with clinical community

The third question regarding withdrawals concerned to which degree the MAH has any dialog, collaboration or other interaction with the clinical community or experts on the clinical need before deciding to withdraw. The responders were given four choices between, from “not at all“ to “a great extent”.

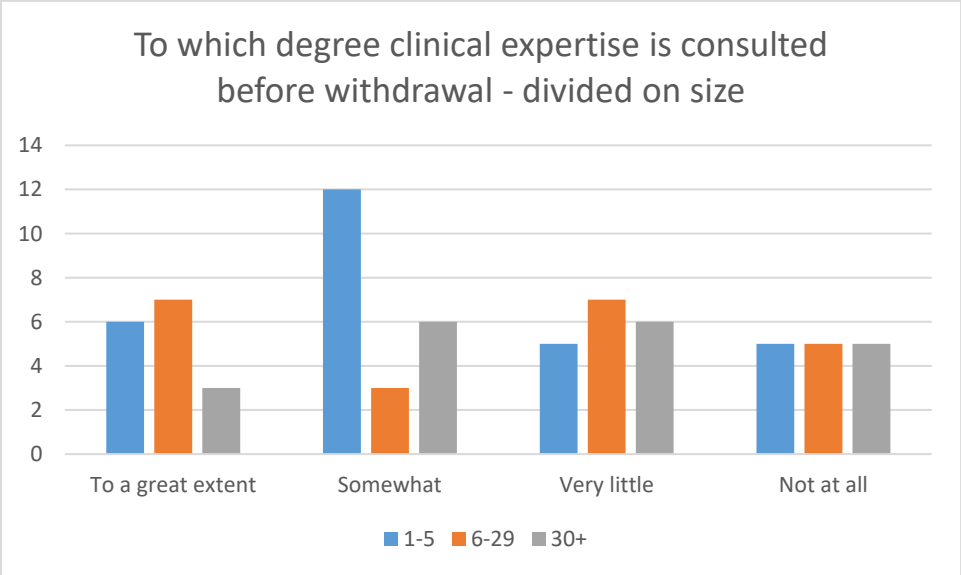

Figure 17. To which degree clinical expertise is consulted before withdrawal, divided on size of MAHs

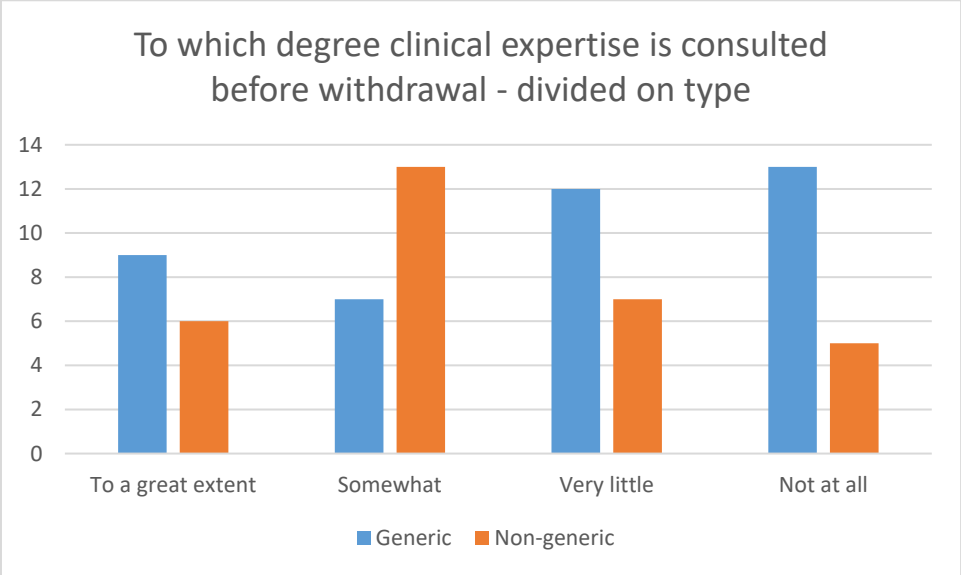

Figure 18. To which degree clinical expertise is consulted before withdrawal, divided on type of MAHs

The response is relatively evenly distributed over the four alternative answers. There is no obvious trend when looking at the size of the companies. However, there seems to be a larger portion of originator companies consulting expertise as compared to generic companies.

MA transfer before withdrawal

The fourth question was on to which extent the MAH tries to sell the legal rights and transfer the MA to another company before a product is withdrawn from the market. Doing so may enable the product to stay on the market without being withdrawn. The results are depicted in the figures below.

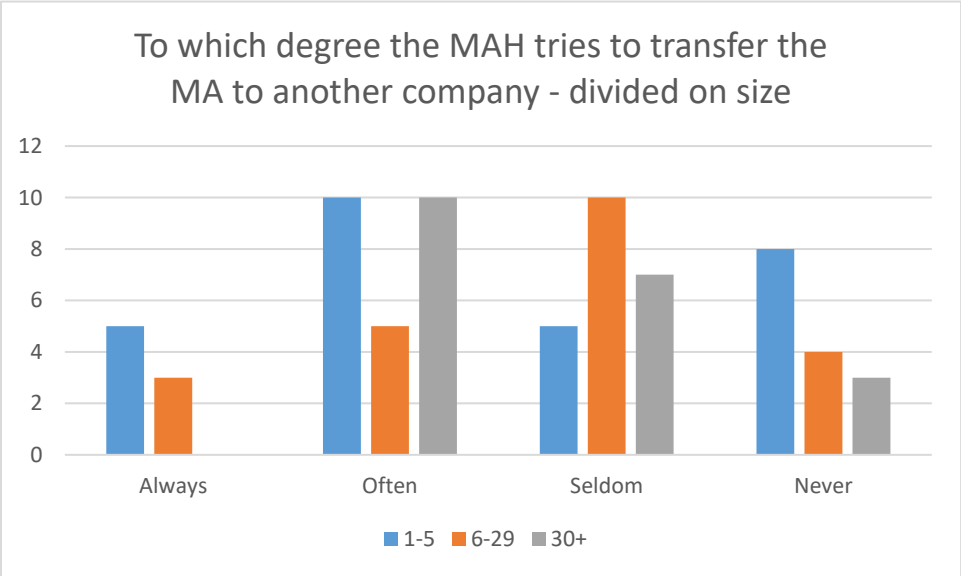

Figure 19. To which degree the MAH tries to transfer the MA to another company, divided on size of MAHs

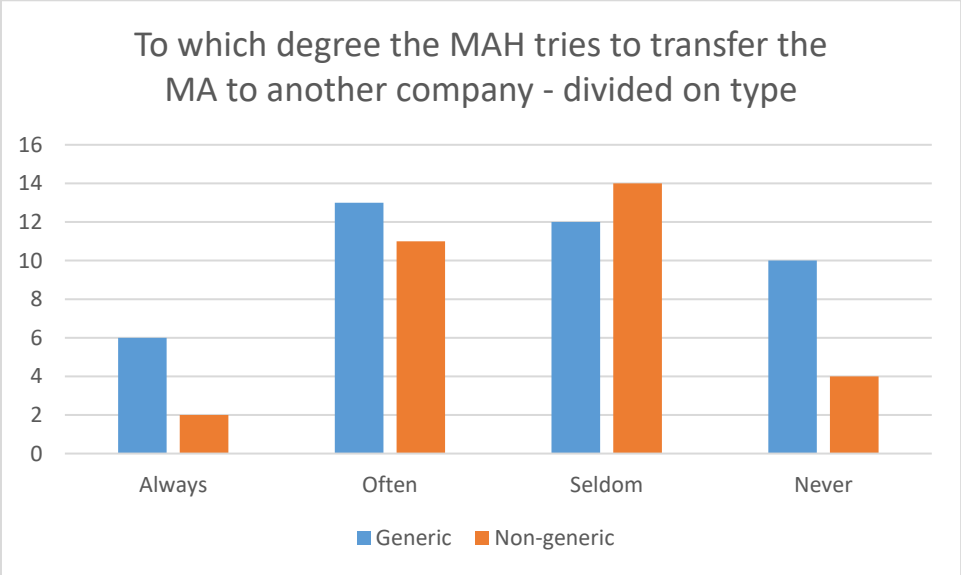

Figure 20. To which degree the MAH tries to transfer the MA to another company, divided on type of MAHs

The response is distributed from always to never, but shows that most companies to some extent try to sell and transfer MAs before finally withdrawing the MA or product. There are no obvious trends when looking at both size of the companies and comparing generic and originator companies.

Closer dialog with NoMA

The final question was whether a closer dialog with NoMA and evaluation of any incentives could have an impact on the company's decision to withdraw products from the market. Several incentives are the same as those incentives that can be used for applications for new MAs. The response is summarised in the two figures below.

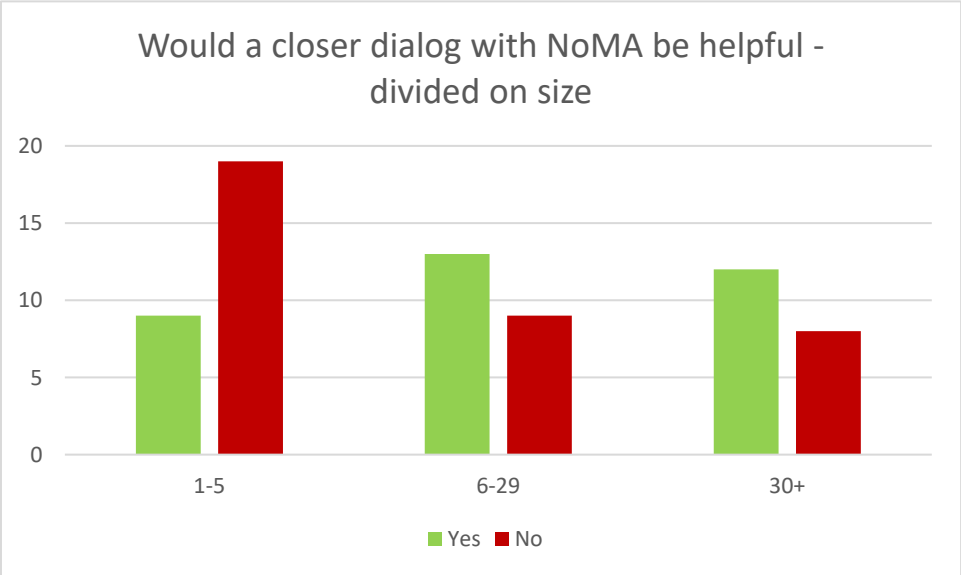

Figure 21. If MAHs think a closer dialog with NoMA be helpful, divided on size of MAHs

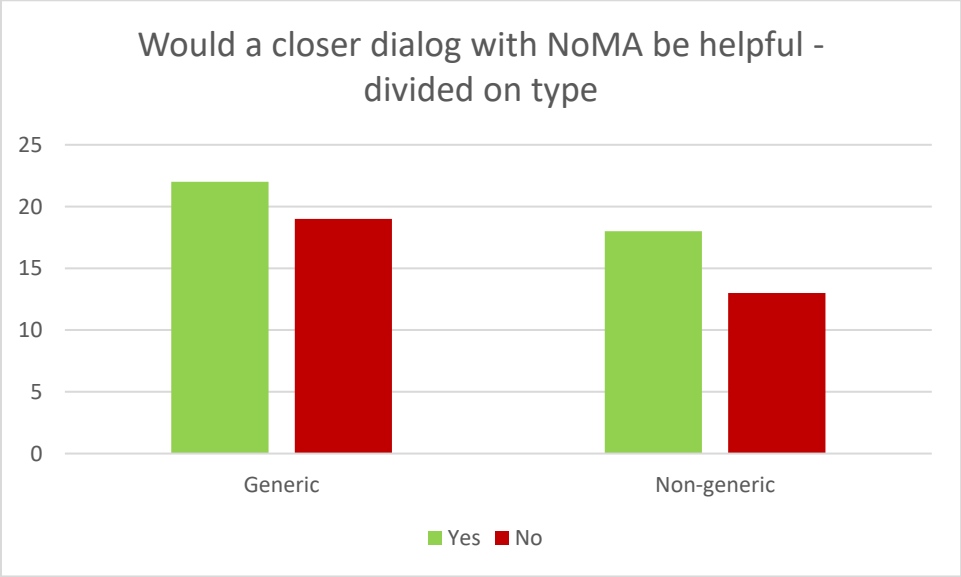

Figure 22. If MAHs think a closer dialog with NoMA be helpful, divided on type of MAHs

The response to this question and the trends is very similar to the earlier question on a dialog regarding incentives that could have an impact on willingness to market MA-products. A larger portion of bigger companies (6+ MAs) think that a dialog on incentives might have an impact as compared to smaller companies (1-5 MAs). Any difference between generic and originator companies is negligible.

Comments from MAHs

It should be mentioned that each of the above three sections had a final text box for general comments or other thoughts. Many MAHs have provided thoughtful and useful comments and feedback for consideration. The comments explain to some extent the responses provided. The feedback varies, and there are no obvious trending subjects or issues. For this reason, these comments will be further analysed and processed by NoMA, but are not further commented in this report.

3 Analysis

The response to the questions in this survey certainly provides clarification to why we don't get MA applications for certain needed products. It also gives a good overview of typical reasons for why certain MA products are not marketed or withdrawn from the market. At the same time, the response to many questions might raise new questions and concerns not covered by the survey. A follow-up of many questions together with the industry will give even better clarity and insight into the issues covered so far.

3.1 Observations from the response

The first part of the questionnaire contained questions on why companies are not applying for MAs for needed products and what measures are deemed most relevant. Prices and sales volumes are dominating factors. The issues are that they are either too low or not sufficiently predictable. However, the results show that all measures mentioned have been selected by some companies to a certain degree. In our experience, some companies are more interested in direct costs such as fees and other

costs payable to the government whereas others consider prioritised and fast procedures more relevant. Results from this survey seems to confirm the perception that all measures can be relevant to some extent. Different companies have different approaches when building business cases. It could perhaps also be assumed that some companies might have different approaches and value the measures differently, from case to case. It is therefore important to have all measures available, even though some measures in general could be considered more relevant than others.

Lower documentation requirements

The use of various measures, for example lowered requirements on documentation, are usually limited to National Procedures where the decision making is normally easier. The results show that a majority of companies think that measures used in European Procedures would increase the willingness to apply for MAs for needed products. The objective of the project on paediatric medicines (Legemidler til barn i Norden), mentioned earlier in this report, is to increase the collaboration on these measures between the Nordic countries. The results of this project should not be limited to paediatric medicines and could be further investigated for all needed medicinal products.

Prices and sales volumes

The second part of the questionnaire had questions on why MAHs do not market products for which an MA already has been granted. Also here, expected low price and sales volumes seem to be the dominating factors. Unpredictability of the price level also seem to be an important factor. Although not specifically included as an option in this part of the questionnaire, unpredictability in sales volumes was the most selected factor when the companies were asked why they don't submit MA applications for needed products (first part of the questionnaire). This is in agreement with our experience in NoMA.

The third part of the questionnaire contained questions on why products with MA are withdrawn from the market. Again, prices and sales volumes are the dominating factors. Since many companies have several offices around Europe or constitutes of clusters of companies all over Europe, we also asked where the decision to withdraw a product is typically made.

Influence on withdrawal decisions

The point of such decisions can be important due to various reasons. It indicates who to correspond with regarding any withdrawal decisions. From our experience, MAHs with local offices also tend to be more concerned with the local national market and whether their products are critical for patients in the specific market. In general, the further away a withdrawal decision is made, the less chance it is for a NCA (National Competent Authority) to have any influence on that decision. Our experience also indicates that there is often a delay from the time point a decision is taken until the actual MAH for the local market is informed of the decision. This means that the further away from the local market a decision on withdrawal is made, the more proactive any work to prevent such withdrawals need to be.

Dialog with NoMA

Somewhat more than half of the total number of responding companies think that a dialog with NoMA could be useful in connection with the different major decisions during the life cycle of the products. This figure is surprisingly low. The reasons can be many. For example, that the incentives available are not sufficient or that the company is not aware of such incentives. It can also be based on earlier experience from contact with authorities or from procedures. One reason could be that the decision to not market a product with an MA has already been taken and that this is out of hand for the MAH. For withdrawals, the reason could be that the process of withdrawal is too far gone, for example due to discontinuation of production. Another could be that the MAH doesn't think that the measures that we have at hand would help.

3.2 Possible measures

There is currently no available measure that can single-handedly solve the situation with unavailable needed products. As mentioned, the response indicates that different companies value different incentives differently. The “tool box” should therefore include all measures available to be applied on a case-by-case basis.

3.2.1 Regulatory

Simplified procedures

The responses show that simplified and shortened procedures is the most popular measure. A typical non-centralised MA-procedure takes around one year. In some cases, especially where issues are identified during the procedure, the time to complete a procedure can take even longer. Lengthy procedures have two main drawbacks. The first one is that the product will not be available to the market until the completion of the procedure where a MA has been granted. The other main drawback is that lengthy procedures often are very resource demanding for both the NCA and the applying company. Among the measures available to date, expedited procedural timelines could therefore be seen as the most effective incentive.

Expediated procedures

For the same reason as those mentioned above, it is also important to prioritise the start of procedures (the slot time) for needed products. The benefit of expedited procedural timelines can be severely diminished if the procedure cannot be started within a reasonable time.

Documentation requirements

Reduced documentation requirements was selected by 27 companies among the top-3 incentives. This is associated with documentation related to quality, safety and efficacy. Maintaining up-to-date documentation for a product requires expertise within a number of fields. Therefore, the documentation for old and non-profitable medicinal products is often not maintained or fully up-to-date. The regulation requires an updated documentation to current standards when applying for MA in a new country, an exercise which is quite costly. This is a major hindrance to availability of older products, meaning that acceptance of documentation that is not living up to the standards of current guidelines might be necessary. Collaboration and agreement among the Nordic countries on ‘risk-based’ acceptance of sub-optimal documentation on case-by-case basis, could also be a possibility to explore further.

Product information

MAHs should be encouraged to use multilingual packages to a greater extend as this enables the MAH to sell the same batches in several European member states. In certain cases, it might be necessary to approve the use of a foreign language on the physical package as part of the MA-approval. This is primarily feasible for products intended for hospital use and approvable for a limited time period.

The introduction of electronic product information (ePIL) fully replacing paper leaflets is currently discussed at European level and would simplify the manufacture of medicinal products. However, this measure will require legislative changes on a European level and will not be available for some years. It also requires that the same MA exists in the countries involved. There are currently several ongoing pilots in European member states that can hopefully provide more experience.

Many of these measures require deviations from normal practice and regulations, which is established in order to safeguard patient safety through provision of well-documented drug products. These deviations could be seen as an increased risk to patients. However, the risk of using any such measures

should always be assessed together with the current risk of unavailability. It should also be kept in mind that most products relevant for such measures are already approved, marketed and available for patients in other European member states.

3.2.2 Price and volume

Price

As expected, the price is an important factor throughout the life cycle of a medicinal product. This includes not only the actual price level, but also predictability of the price and hence the income. Unpredictability in maximum price is, as already mentioned, the second most selected hindrance for new MAs. Today, all registered, prescription-only medicines must have a maximum price before they can be marketed. The MAH must apply for a maximum price when the product has been granted MA. Determination of maximum price before the submission of an MA application could introduce more predictability for the MAHs and would not introduce any risk to the patients. Looking at the incentives for new MAs, a price guarantee model is considered a more popular incentive than determination of maximum price before application submission. Even if a higher maximum price is approved, there is no guarantee that the whole profit will go the MAHs, but the MAHs will have better bargaining power with the wholesalers. On the other hand, a price guarantee model has an impact on the price wholesalers need to pay MAHs for the product.

Volume

Sales volume is the other main factor that has an impact on availability. Too low sales volume or unpredictability in sales volume might inhibit application for a MA, marketing a product and maintaining the MA. Even a very high price might not be able to compensate for a low sales volume. Some products such as antibiotics can be extra vulnerable since these are products that we actively try to restrict the use of. When looking at long term solutions, it might therefore be necessary to look at models that also take volume into account.

NoMA has currently limited measures available related to price and volume, and potential measures would require changes to the national legislation.

3.2.3 European and Nordic collaboration

As already touched upon, one factor that has an impact on availability is the size of the market. Small markets tend to be much more vulnerable than larger markets. Collaboration between several member states on, for example, regulatory measures could act as an incentive itself for companies to apply for MAs. This is also strongly supported by the response to this survey, where a majority of companies think the use of incentives in decentralised European procedures could play an important or very important role. It is therefore important to explore the possibilities for better collaboration with other member states. An example is a collaboration between the Nordic countries that also have relatively small markets. This could be anything from a simple common list of needed products to collaboration in non-centralised procedures.

3.3 Acknowledgements

NoMA is deeply grateful to all MAHs that have taken the time and effort to provide very useful and helpful information and insight into the issues covered by this survey. The results will be further followed up with the industry where needed.