EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA Industry Survey summary results

Agenda point 3
Industry Stakeholder meeting on Brexit and operation of centralised procedure for Human and Veterinary Medicinal Products

Presented on 24 September 2018 by:
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Topics covered

- Industry survey format, timelines and response rate
- Industry survey results:
  - PSMF and QPPV
  - MAH transfers
  - Manufacturing changes
  - Quality control testing
  - Batch release site
  - OMCLs
- Risk assessment and next steps

Industry survey – Timelines and Response rate

- **22 January 2018** – The Industry survey was launched and sent to contact points for 690 CAPs corresponding to 176 MAHs. Industry survey was circulated to additional contact points for 4 CAPs (medicinal products that were authorised after cut-off date of October 2017) with a deadline for responses by 19 March 2018.
- The Industry survey received a **91% response rate** with a grand total of 662 CAPs responses (both H and V).

Total sent		
UK involvement	**CAPs**	**MAHs**
Human	**661**	**167**
Veterinary	**33**	**13**
Total	**694**	**180**

PSMF and QPPV (Human and Veterinary CAPs)

Results of Industry survey

Industry survey results - PSMF and QPPV response analysis (Human and Veterinary CAPs)

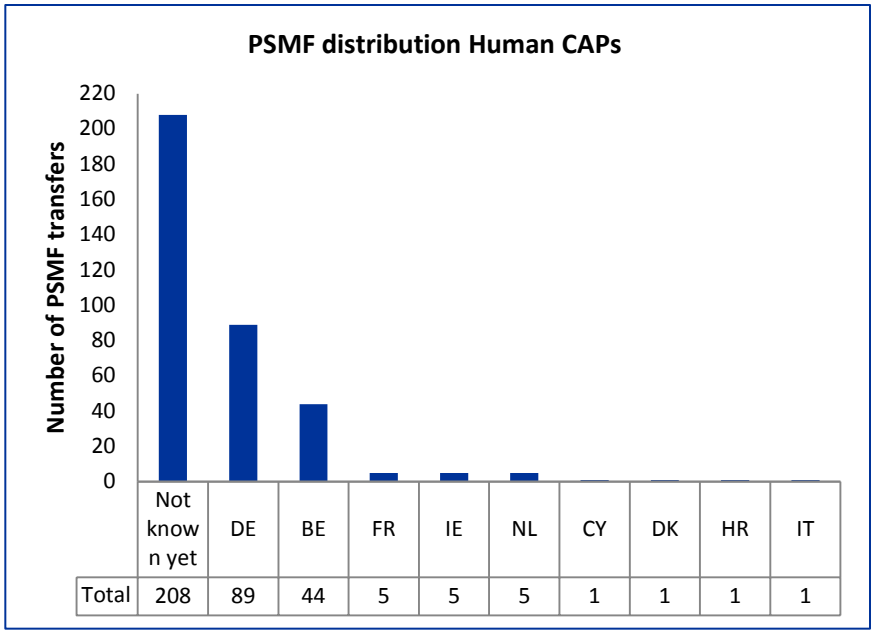
PSMF Human CAPs

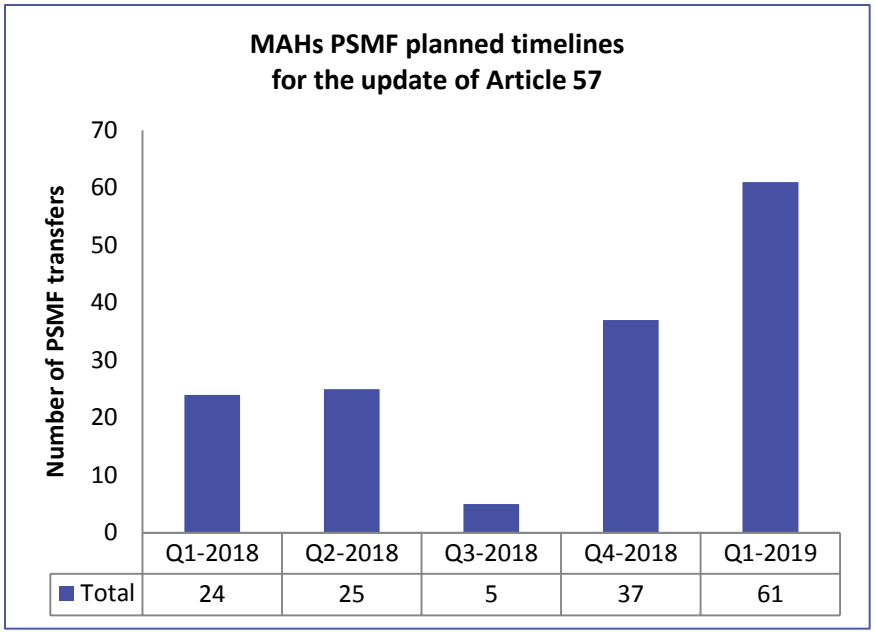
- 360 CAPs have Pharmacovigilance System Master File (PSMF) located in the UK and will change.
- Only 1 CAP has a PSMF located in the UK and did not response to the question.
- For 208 out of 360 CAPs, the new location is “Not known yet”.

QPPV Veterinary CAPs

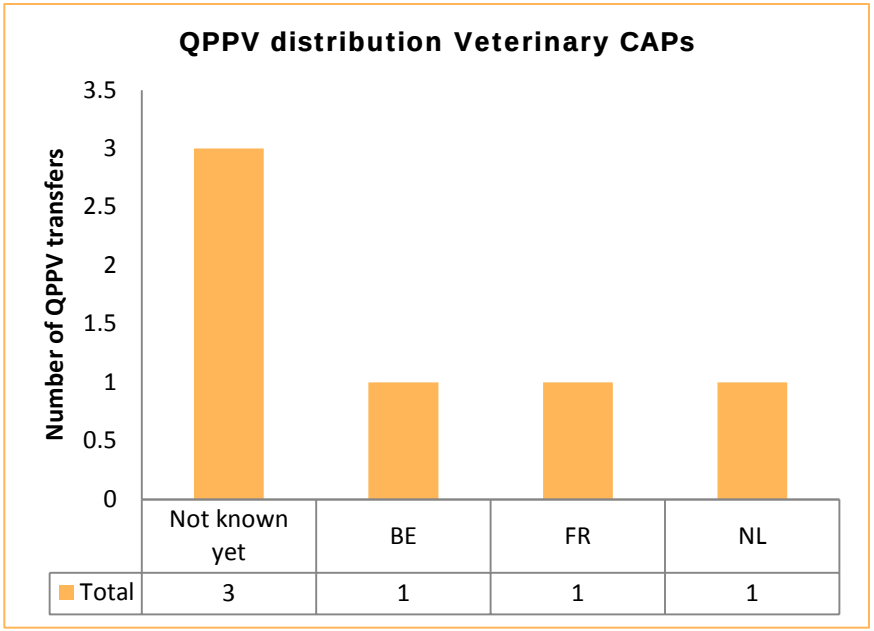
- 6 CAPs have QPPV located in the UK and will change.
- For 3 out of 6 CAPs, the new location is “Not known yet”.

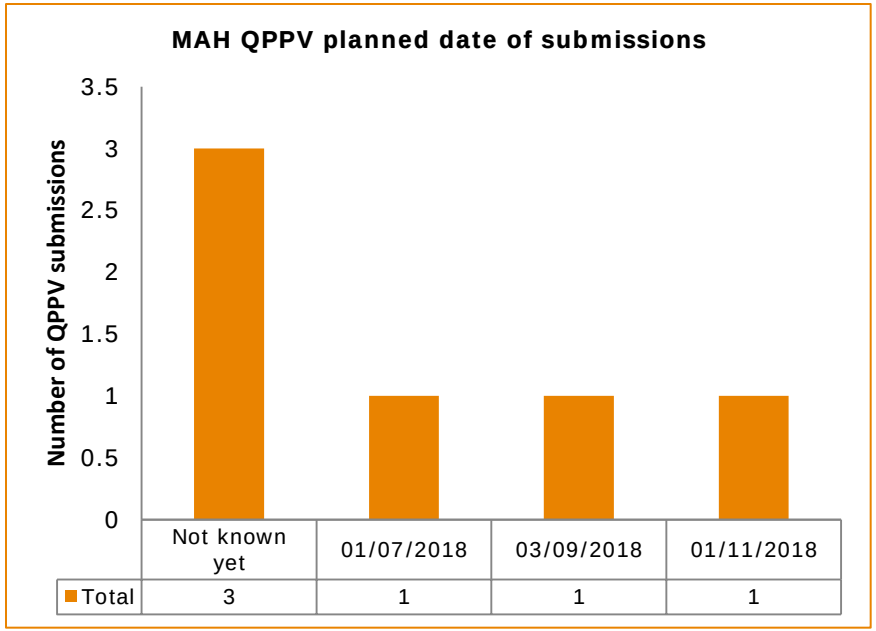
Industry survey results - PSMF (Human CAPs)





Industry survey results - QPPV (Veterinary CAPs)



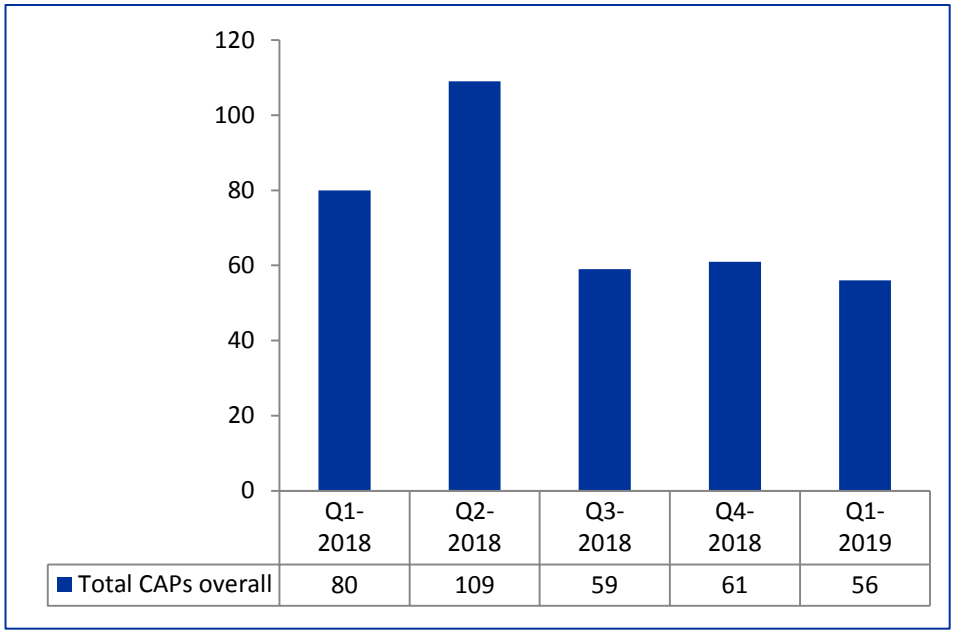


MAH transfers (Human and Veterinary CAPs)

Results of Industry survey

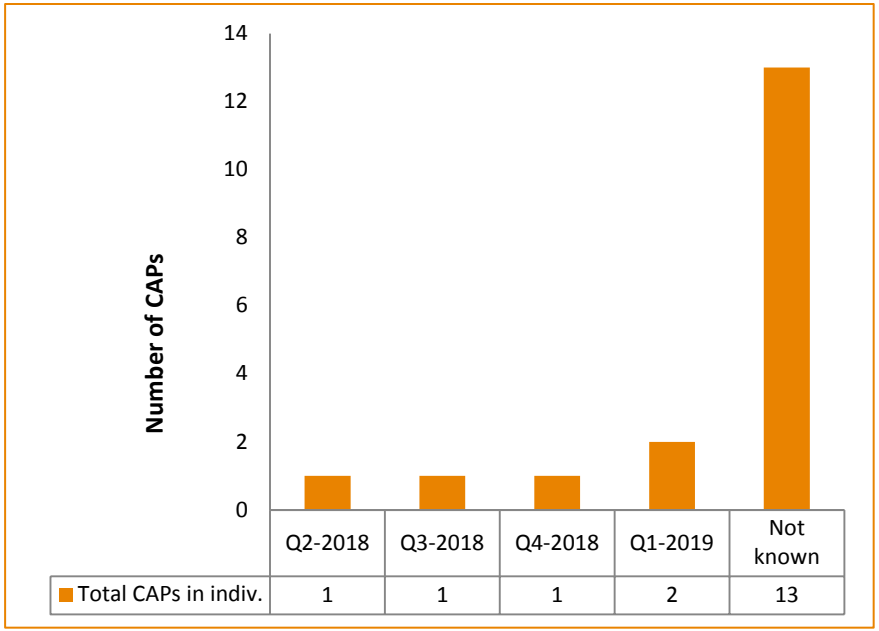
Industry survey results – MAH transfer response analysis (Human CAPs)

- Based on the survey, 63 MAHs of 365 human CAPs are located in the UK and will change to another EU/EEA Member State. 20 MAHs have SME status.
- The number of Brexit MAH transfer submissions represent 10-fold increase vs. normal yearly submissions.
- Workload of MAH transfers are overall spread within Q1-2018 to Q1-2019 ranging between 15-30% of submissions per quarter.
- 74% of MAH transfers have already been received (ahead of the timelines indicated by MAHs during the survey)



Industry survey results – MAH transfer response analysis (Veterinary CAPs)

- Based on the survey, 5 MAHs of 18 Vet CAPs are located in the UK and will change to another EU/EEA Member State. Two MAH transfers are related to MAHs with SME status.
- This represent 5-fold increase in the number of yearly MAH transfers (~3/yr)
- Workload of MAH transfers are overall spread within Q2-2018 to Q1-2019 with a high number of submissions with unknown date.
- 44% of MAH transfers have already been received (ahead of the timelines indicated by MAHs during the survey)



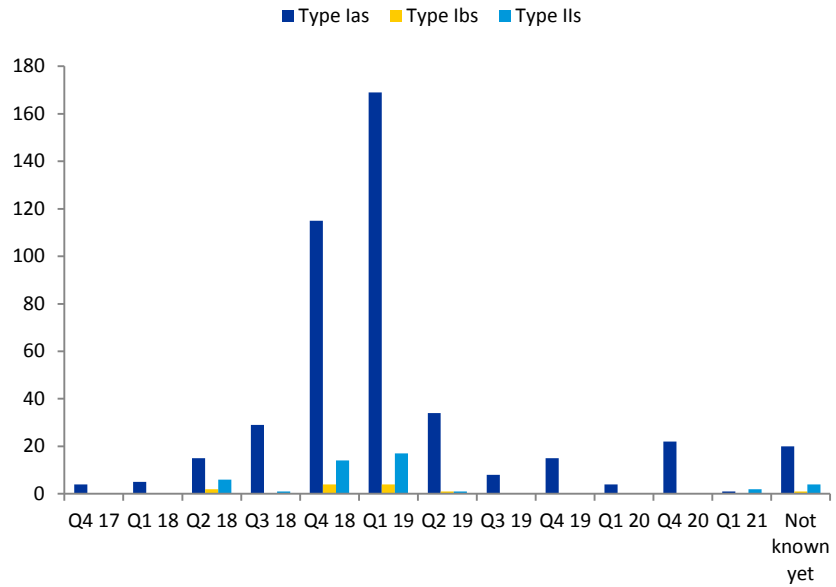
Manufacturing changes (Human and Veterinary CAPs)

Results of Industry survey and workload implications

Industry survey results - Manufacturing changes (Human CAPs)

Variations

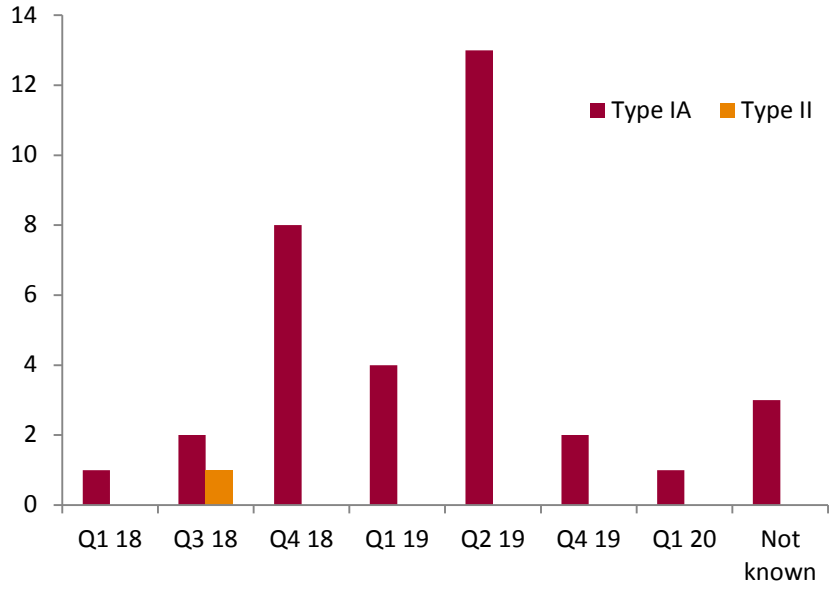
- Brexit related variations are estimated to be 441 Type IAs, 12 IBs and 45 IIs
- Type IAs and Type IIs: main workload will be in Q4-18 and Q1-19 with an expected 40-50% increase of IA submissions and 20-30% increase of quality Type IIs during this period
- 20 Type IA, 4 IBs and 3 IIs have already been submitted



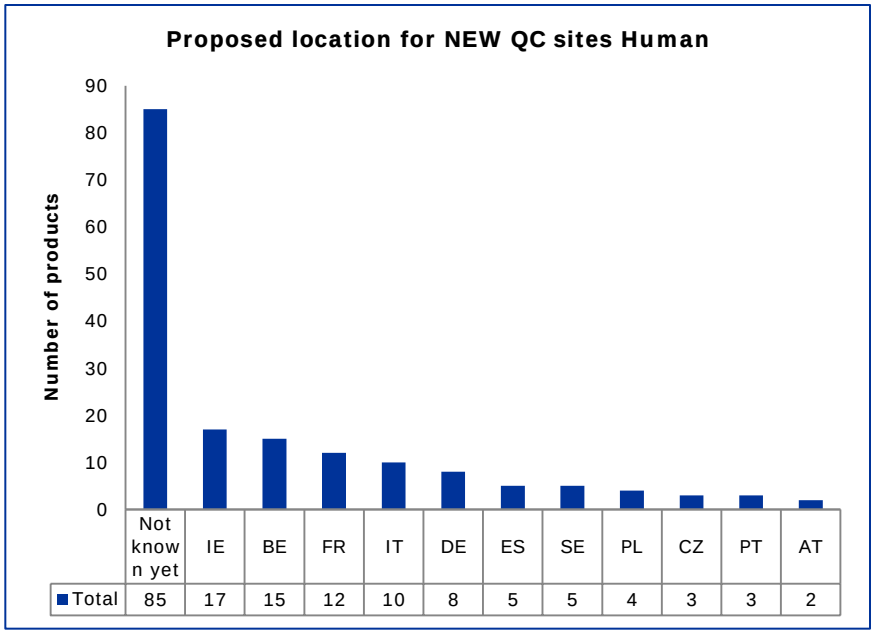
Industry survey results - Manufacturing changes (Veterinary CAPs)

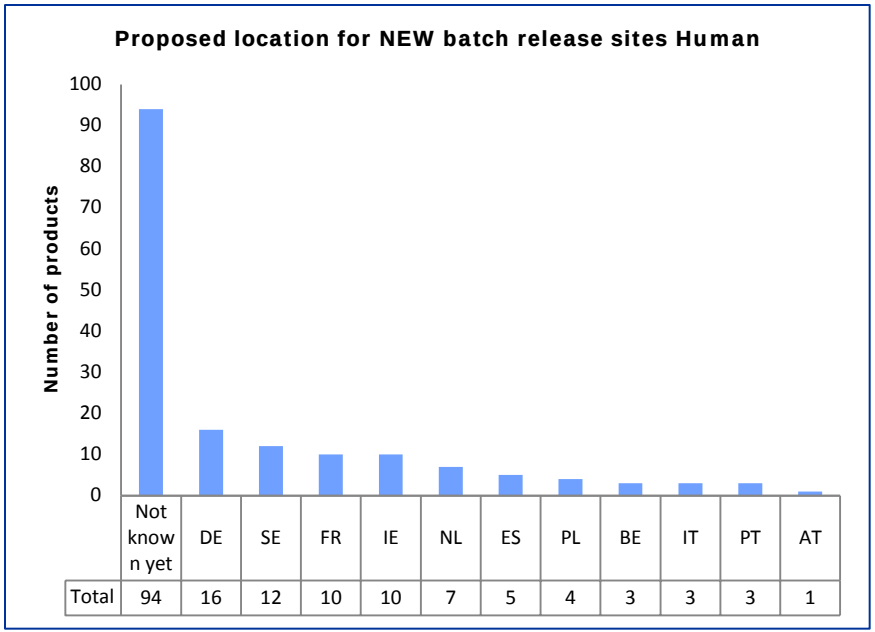
Variations

- Brexit variations are estimated to be 34 Type IA and 1 Type II variations. This represents approximately 14% of Type IA. The main workload is expected between Q4-18 and Q2-19
- 1 Type IA has already been submitted

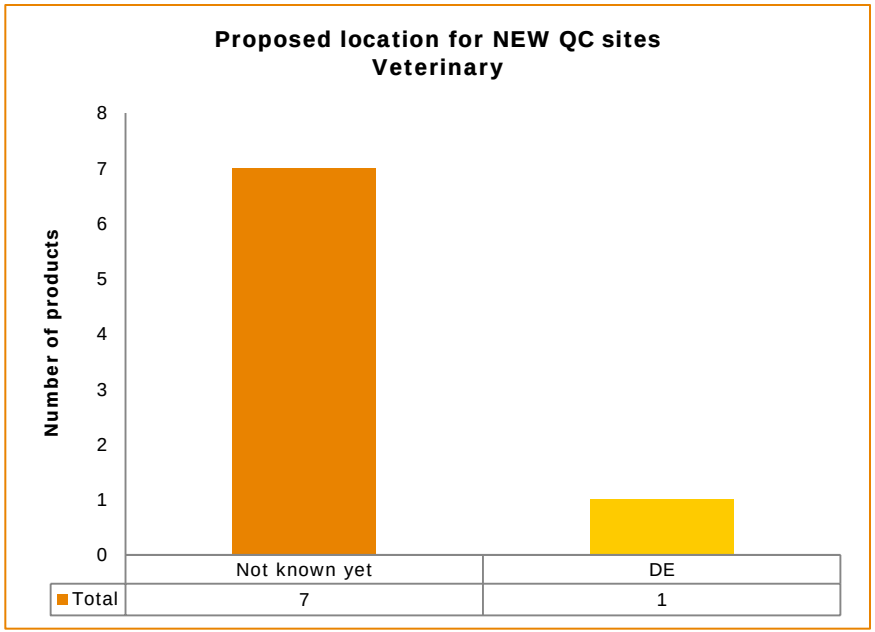


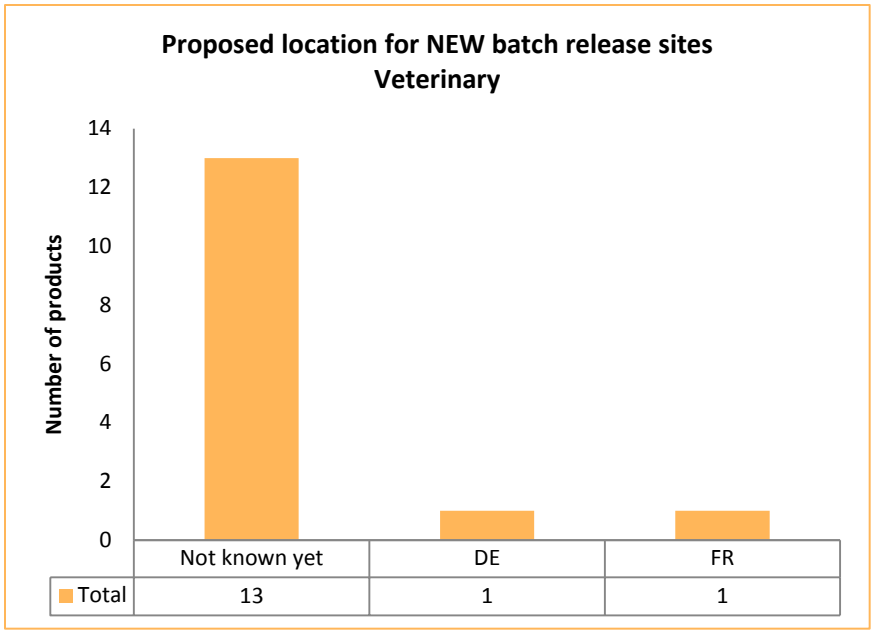
Industry survey results - QC Testing and Batch release sites (Human CAPs)



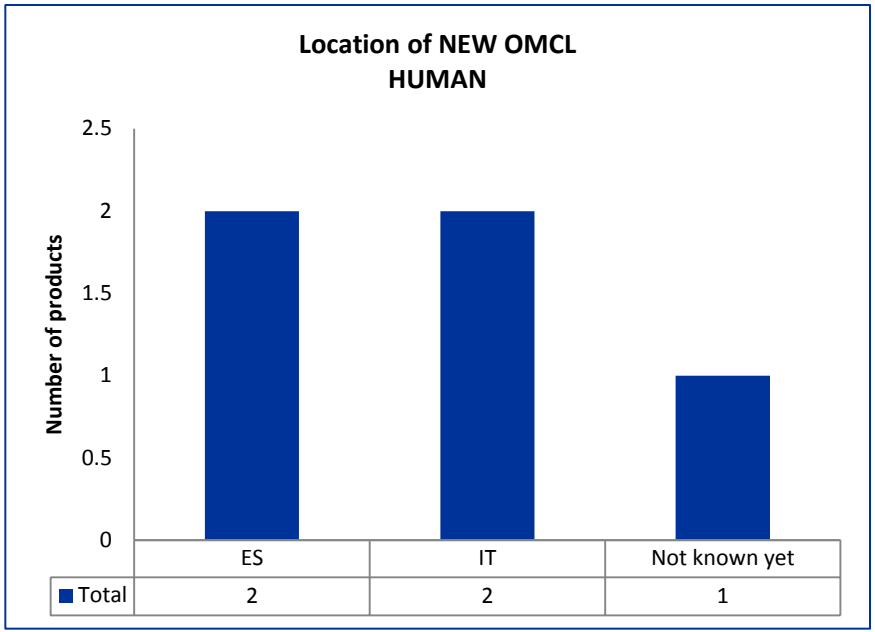


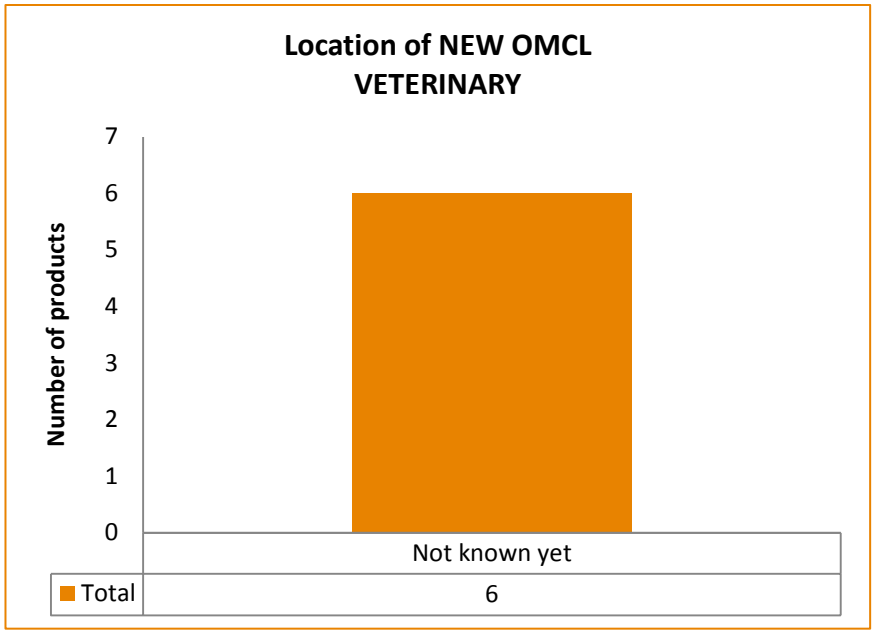
Industry survey results - QC Testing and Batch release sites (Veterinary CAPs)





Industry survey results - OMCL distribution (Human and Veterinary CAPs)





Risk assessment and next steps

Industry survey results - Risk assessment (1/3)

- The aim of the survey was to further identify the CAPs potentially “at risk” of supply shortages and obtaining information on the timelines for submission of the necessary regulatory changes.
- In line with the initial objectives set out for this survey, an analysis of the responses provided by the MAHs has enabled the Agency to define a list of potentially “at risk” CAPs.
- Of the 694 CAPs, 108 medicines (88 human and 20 veterinary) has one or more manufacturing sites located in the UK only without any other current alternatives, hence these medicines are considered to be “at risk” of supply disruption or shortages in the Union, if changes are not submitted and implemented in due time. EMA contacted MAHs of these concerned products to address any potential supply disruptions.
- EMA is monitoring the submissions of changes to marketing authorisation for all 694 CAPs, where necessary.

Industry survey results - Risk assessment (1/2)

- A risk matrix has been developed which includes different elements required to be changed before 30 March 2019.
- Risk matrix takes into account the outcome of the survey, including the timing for submission of the changes required.

Risk levels	MAH UK	SME	Secondary packaging	Quality Control	Batch Release	OMCL	UK: PSMF / QPPV / OD	Local rep.**
A	+	+	UK only	UK only	UK only	UK only	+ / -	+ / -
B1	+		At least one activity is UK only				+ / -	+ / -
B2			At least one activity is UK only				+ / -	+ / -
C	+			UK also	UK also	UK also	+ / -	+ / -
D				UK also	UK also	UK also	+ / -	+ / -
E	+ / -						+ / -	
F								+
G	On time							

** Not included in Industry survey

Industry survey results - Risk assessment (2/2)

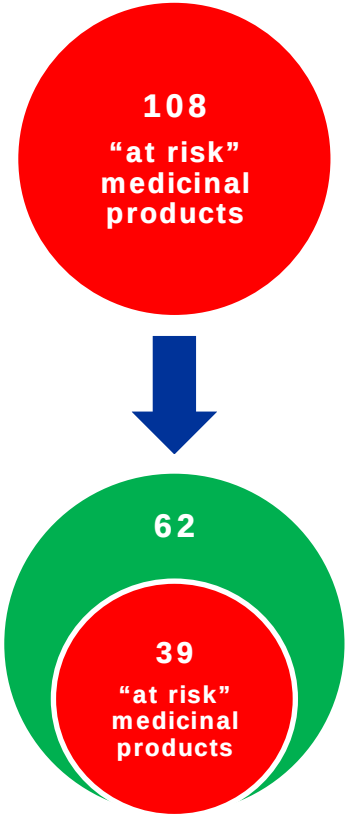
EMA contacted MAHs to address any potential medicinal products supply disruptions

Risk levels	Human Products Submissions after 30 March 2019	Vet products Submissions after 30 March 2019
A-B2	88	20
C	35	3
D	68	0
E	73	8
F	3	28
Critical level	Submission before 30 March 2019	Submission before 30 March 2019
G	388	3

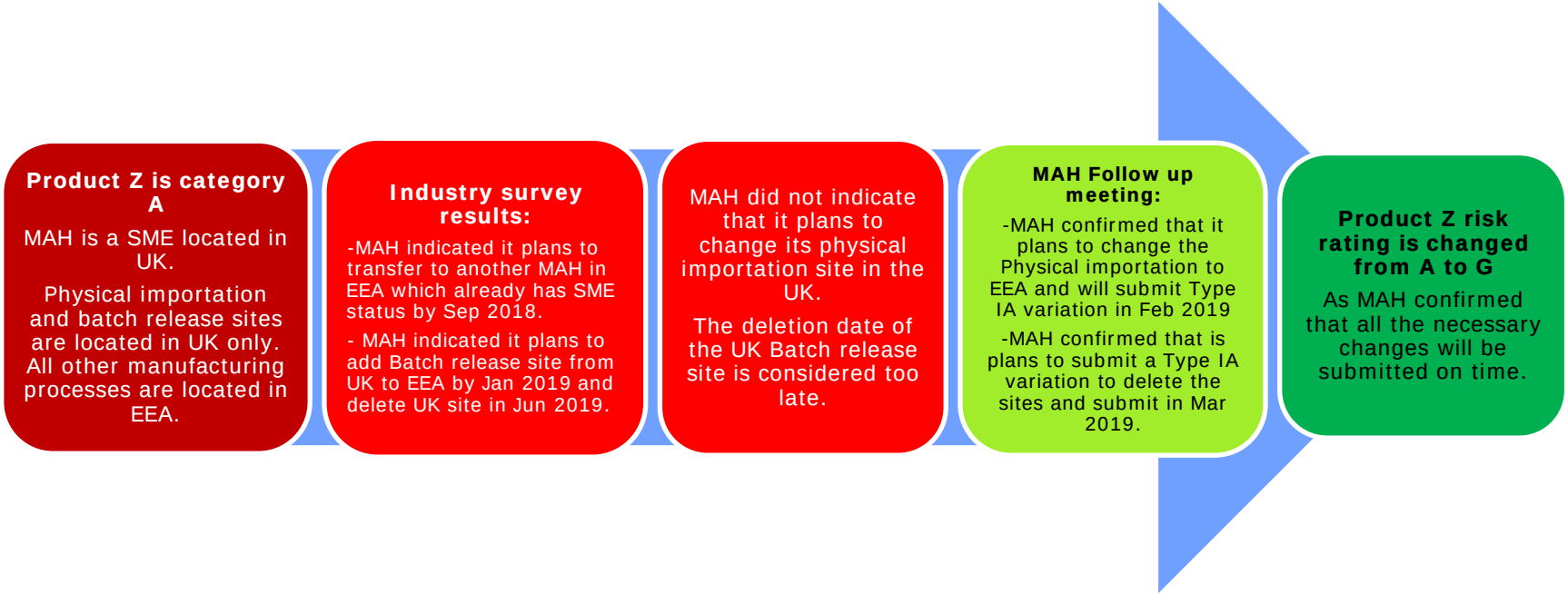
EMA is monitoring the submissions of changes to marketing authorisation, where necessary

Follow up with MAHs on “at risk” products

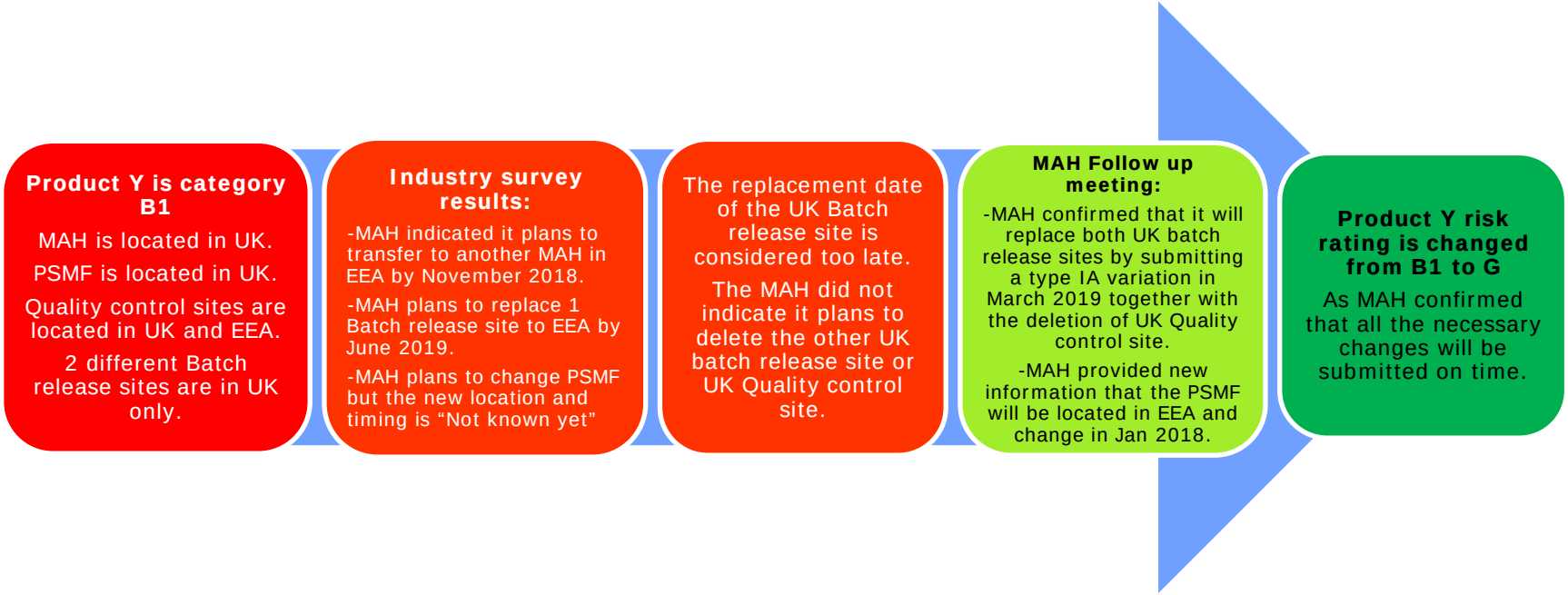
- Follow up meetings for **108** medicinal products were organised with 54 MAHs (45 Human and 9 Veterinary)
- A total of 51 teleconferences took place (43 Human and 8 Veterinary). A small number of MAHs provided information by email.
- As seen from the feedback provided by MAHs, plans are changing for a number of companies since the launch of the survey and many companies will make the necessary changes before 30 March 2019.
- **39** medicinal products (25 Human and 14 Veterinary) are currently considered “at risk” and may have potential supply issues.
- 6 Human products have been already withdrawn or will be withdrawn before 30 March 2019. 1 Veterinary product will not renew its Marketing Authorisation.



Follow up with MAHs on “at risk” products
Example of risk level change from A to G



Follow up with MAHs on “at risk” products
Risk level change from B1 to G



Feedback from follow up meetings with MAHs

Main points raised not covered in the Q&As session:

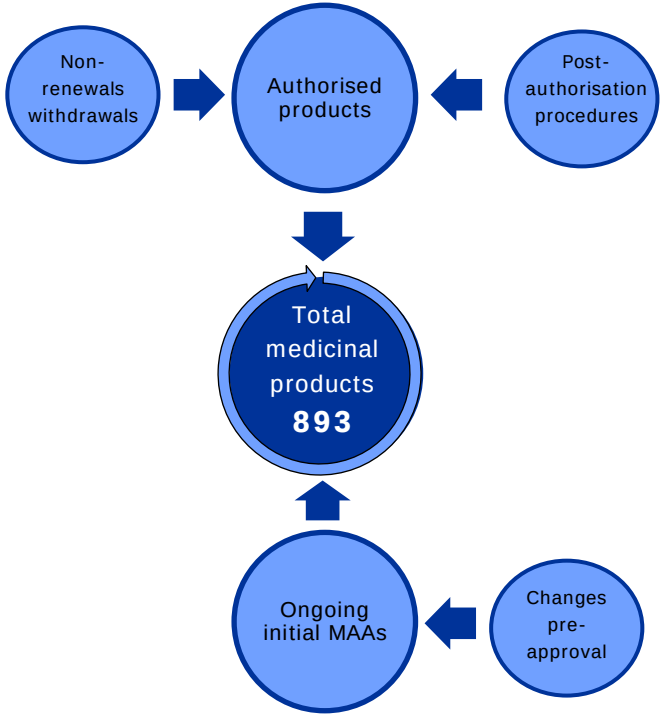
- Clarification that regulatory changes to MA are required regardless of the product's marketing status including products exempted from sunset clause.
- Deletion of UK sites responsible for quality control for finished product, physical importation and batch release from the MA is required after 29 March 2019 (submission of Type IA within 2 months).
- A few MAHs informed about their plans to divest on certain products. These MAHs will need to timely inform EMA as the new MAHs will need to comply with the regulatory requirements for the product on time.

Next steps and methodology for criticality assessment

- Further clarification from the MAHs is pending and may change the number of products “at risk”.
- In addition, information provided by MAH may move products from a “non-at risk” category to a “at risk” category as well as delays in the planned submissions.
- Following feedback from the MAHs, the products still considered as “at risk” (currently 39 products) will undergo a criticality assessment.
- Criticality assessment will be performed by looking at the therapeutic use and availability of therapeutic alternatives for each medicinal product.

Tracking and monitoring of Brexit related changes

- EMA has been and will continue to monitor and track the submissions of required changes for **all 893 Brexit affected CAPs.**
- Currently **65 products** have completed all the necessary changes in order to comply with the legal requirements.
- MAHs are reminded of their legal obligations to inform EMA on supply issues and product withdrawals.
- Furthermore, MAHs are requested to timely inform EMA on any changes to their current plans.



Any questions?

Further information

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