GLOBAL CHARACTERISTICS OF THE RABIES BIOLOGICAL MARKET IN 2017

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BACKGROUND

In December 2015, the global community set a goal to reach "zero human rabies deaths by 2030". In response, WHO, OIE[1], FAO[2] and GARC[3] established a global framework that advocates for countries to incorporate rabies elimination activities into their health systems and leverages existing tools and technologies to be used in their implementation. Consequently, the demand for rabies biologicals is likely to increase. However, the global needs for biologicals are unknown and the capacity of the pharmaceutical industry to fulfil these needs remains to be determined.

This survey was sent out to rabies biological manufacturers to gather important information related to current, and future, market capacity as well as product characteristics. This information will be used to evaluate the feasibility for establish human vaccine and RIG biological banks for Rabies, the possible expansion of the OIE dog vaccine bank and inform countries in the development of their national rabies elimination plans.

OVERVIEW OF FINDINGS

Market characteristics

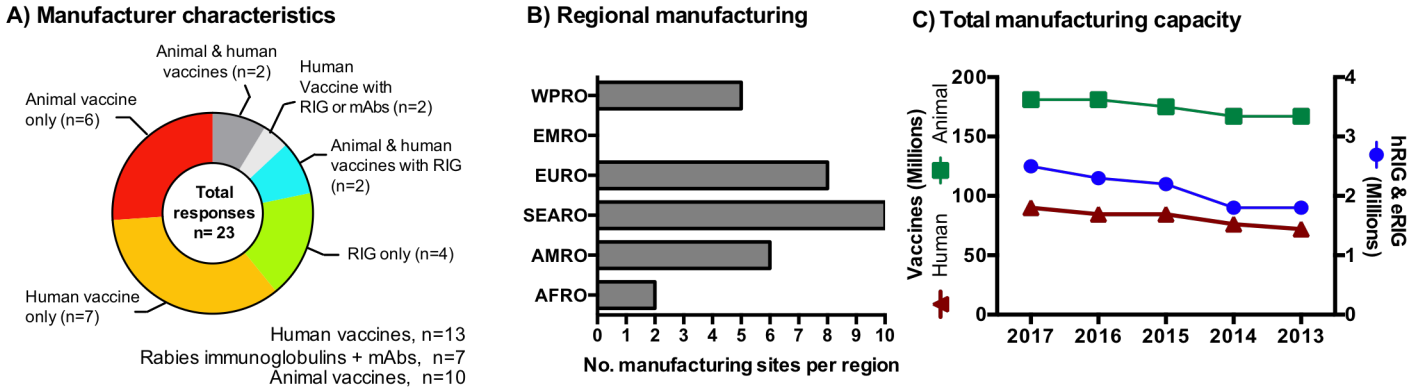

Figure 1: Summary statistics of respondents of the Rabies biological manufacturer's survey

- Out of the 23 respondents, most manufacturers produced only one type of rabies biological (Figure 1).
- South East Asia Region (SEARO) and Europe (EURO) have the highest number of manufacturing sites. With India and China most likely highly represented (Figure 1B and data not shown).
- The rabies biologics market capacity increased by 28, 19 and 8% since 2013, with a 2017 capacity of 90, 2.5 and 181 million vials for human vaccines, RIG and AV, respectively (Figure 1C and data not shown).
- The number of RIG doses produced was dramatically lower than vaccines, and reflects lower demand compared to vaccines. Only 2% of bite exposures receive passive immunization (Figure 1C)[4].
- ~80% of all manufacturers indicated they could increase production by > 50% on average.
- In 2017, one manufacturer indicated a mAb production capacity of 2 million vials - 4 fold higher than RIG average (Figure 1C and data not shown).
- Vaccine and RIG lead times ranges were 42-420 days, and 30-420 days, respectively. Many producers could store biologicals on behalf of clients (data not shown).

Altogether, these results suggest that a lack of demand from countries to provision health facilities is stopping market expansion. Producers can support increased demand for rabies biologicals from countries, providing they accurately forecast their supply chain needs and provide companies enough time to complete production cycles.

The possibility of increasing capacity and the ability to store biologicals on-site on behalf of clients will facilitate the development of global human rabies biological banks by WHO and its partners.

[1] OIE: World Organisation for Animal Health
[2] FAO: Food and Agriculture Organization of United Nations
[3] GARC: Global Alliance for Rabies Control
[4] Warrell, M. (2012) **Travel Medicine and Infectious Disease** 10: 1-15.

World Health Organization

Characteristics of Rabies Biologicals on the market

Table 1: Characteristics of Rabies biological products available world-wide

	Route of administration (No. responses)					Shelf life (months)				Temperature (% positive response)	
	IM	IM; ID	IM;SC	SC	oral	12	18	24	25-36	Storage 2-8^{0}C	Thermo-Tolerance
Human vaccines	4	9	N/A	N/A	N/A	0	1	3	8	9 (100%)	69%
RIGs & mAbs	4	3	N/A	N/A	N/A	0	0	2	4	7 (100%)	57%
Animal vaccines	1	N/A	4	3	1	1	2	2	4	7 (87.5%)[2]	29%

	Formulation (No. &percentage responses)		Biological source material (No. responses)			Vol. per vial (ml)
	Liquid	Lyophilized	cell line	Equine plasma	Human plasma	Mean ±SEM
Human vaccines	1 (8%)	12 (92%)	Cell-line derived n=13			0.69+/- 0.07
RIGs & mAbs	6 (86%)	1 (14%)	2	2	3	3.13+/- 1.13
Animal vaccines	9 (100%)	0	Cell line derived n=9			1.02 +/- 0.09

All responses were aggregated and presented as the total number of responses per category. Percentages were calculated relative to the number of responses available, empty values were excluded. IM is intramuscular; ID is intradermal; SC is subcutaneous. SEM is standard error of the mean, N/A not applicable; [2]one respondent provided -20^{0}C.

- Most human vaccines were lyophilized while dog vaccines were available as liquids. Only 29% of animal vaccines had thermotolerance compared to 69% for human vaccines (Table 1).
- Most human vaccines could have vial monitors (n=8), but only 1 and 2 manufacturers stated this was possible for RIG or animal vaccines, respectively.
- Out of the 13 human vaccine products only 3 were WHO pre-qualified to allow for purchase by procurement agencies (data not shown)
- Many were suitable for Intra-dermal (ID) administration, which are more cost-effective in high through put health facilities (Table 1).
- Despite the availability of human RIG (n=3) that causes less adverse events, equine RIG producers (n=2) remain on the market. This is likely to be due to the decreased purchase cost. Two mAbs are in production, although currently only one product has been approved by national regulatory authorities.

Given the similarity of many product characteristics and assuming equal cost per dose, vaccines suitable for intradermal (human) or sub-cutaneous (Dogs) injection with longer shelf lives, and a degree of thermotolerance will have the competitive advantage. More companies should seek to obtain pre-qualification status for their human vaccines to facilitate purchase by procurement agencies.

The future availability of mAbs on the market will improve global immunoglobulin supply long-term due to improved safety profiles and their scalable technology. Yet, post-market surveillance is still required to clearly demonstrate their effectiveness in preventing human rabies deaths. As such, polyclonal blood derived immunoglobulins will be the market mainstay for the foreseeable future. Engagement of national regulatory authorities and regional regulatory networks, under the guidance of the WHO, is needed to develop processes to facilitate the approval of rabies mAbs.

No information was gathered on purchase, but it is likely to play an important role in country's decision-making processes.

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