Proposals for improvement of registration procedures

1. Pre-submission meeting*High Importance*

With regulators such as EMA, TGA or FDA -applicants are encouraged to request pre-submission meetings prior to filing to ensure understanding of requirements. Such meetings could be replicated to submissions worldwide, whilst keeping the following in mind:

- Make companies aware that havinga pre-submission discussion can facilitate registration (data[1] available from study shows that such meeting is not necessarily increasing possibility of success but discussions have positive impact in success rate afterwards)
- Make it possible to make in-country + reasonable time – currently in some countries it is impossible to discuss with regulators;so we need to make sure it should possible and in addition that this happenswithin a reasonable and established timeframe (timeframe could be linked to nature or request or medical need)
- Alignment and manage expectations: alignment between applicants and regulators on expectations, while managing expectations from both sides
- Minutes of such meetings should be formalised. Depending on the country such minutes would be binding on both the regulators as well as applicants.

2. Samples*High Importance*

Industry needs clarification on both the why samples are needed during the registration process, and the added value they provide to the NRA. If the samples are meant for testing then the request for samples by a NRA should be supported by the capability and capacity to critically evaluate such samples. Reliance on release of samples by a WHO lab or NCL / OMCL should serve the purpose instead of sample request with registration.If samples serve as tool for import or customs to verify and check for counterfeiting maybe the route of serialisation where more and more countries are going towards could be a solution. This is somewhat linked to import testing a well

3. **PQ** (*Discussed in another session*)

Prequalification should entail the following:

- A quick national registration (e.g. translation)
- “Automatic PQ” if there is an SRA or Functional RA approval (thus from a WHO acknowledged RA) and there is a need or requirement for national registration this should more or less be automatic or with a very limited review (verifying programmatic suitability)
- Facilitate CRP for vaccines should be firmly established (very limited uptake so far – and not clear of WHO has the resources to implement it for vaccines

4. Inspections*High Importance*

Similar to sample submission, there is a need to understand the reason whyextra inspectionsare needed for filing, and itsadded value; again, reliance on an existing functional NRA could be a solution to too many inspections. Also, the type of inspection needed need to be clarified (e.g. is it a site or product inspection or both).Another issue is that inspections are notconsistentwith the nature of a request (e.g. renewal for a product with 10 years, and suddenly that leads to site inspection).

https://www.ifpma.org/resource-centre/import-testing-position-papers/

– [1]*Eur J Clin Pharmacol (2010) 66: 39-48*

5. **Clinical trials***Medium Importance*

Unless there are relevant differences in ethnicitiesor other equally valid differences, there should be no need to repeat clinical trials which have adequately demonstrated safety and efficacy of the vaccine. There are also ethical issues around repeated clinical trials if there is no scientific or medical need to do this

6. **Non-clinical***Low Importance*

Redundant testing should not be required. With regards to animal testing, the“Three Rs” (replacement, reduction, refinement) should be rigorously implemented. Attempts must be made to develop alternate in vitro / in silico methods to obviate non-clinical testing. Joint effort is needed between industry to use alternatives but also with regulatory requirements still mandating the use of animals for release testing for example. Thus, although as an industry we have and we use levers to drive this change, regulatory authorities equally hold keys to accelerate the elimination of these in their requirements.

7. **Renewals***Medium/Low Importance*

Renewals are necessary in the interest of public health to ensure continued compliance with GMP. However, the process of renewal may be abbreviated / rationalized (e.g. for products with a long and good track record there should be an automatic renewal granted based on the risk approach). Need to understand the reason why a renewal is needed, and when those will be expected.

8. **Pharmacovigilance***High Importance*

Reliance is key; if a good pharmacovigilance system is in place, it could be a solutionfor a country’s need for clinical trials.

9. **Training and Sensitization of NRAs**

especially there is a large educational effort needed on vaccines for many regulators – they are specialising on small molecules but not necessarily on vaccines and have therefore requirements and requests which are not feasible or very difficult to comply with

10. **Administrative burden**

Do not compromise public health

Additional: company registrations, site registration (solution is to involve with first product registration)