

OTHER DIFFERENCES THAT AFFECT THE REGISTRATION PROCESSES

*DCVMN Common Technical Document
(CTD) Workshop*

Brazil, 18 to 20 June 2018

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This work has been produced by the Developing Countries Vaccine Manufacturers Network (DCVMN) in collaboration with the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) based on data available in the participating companies.

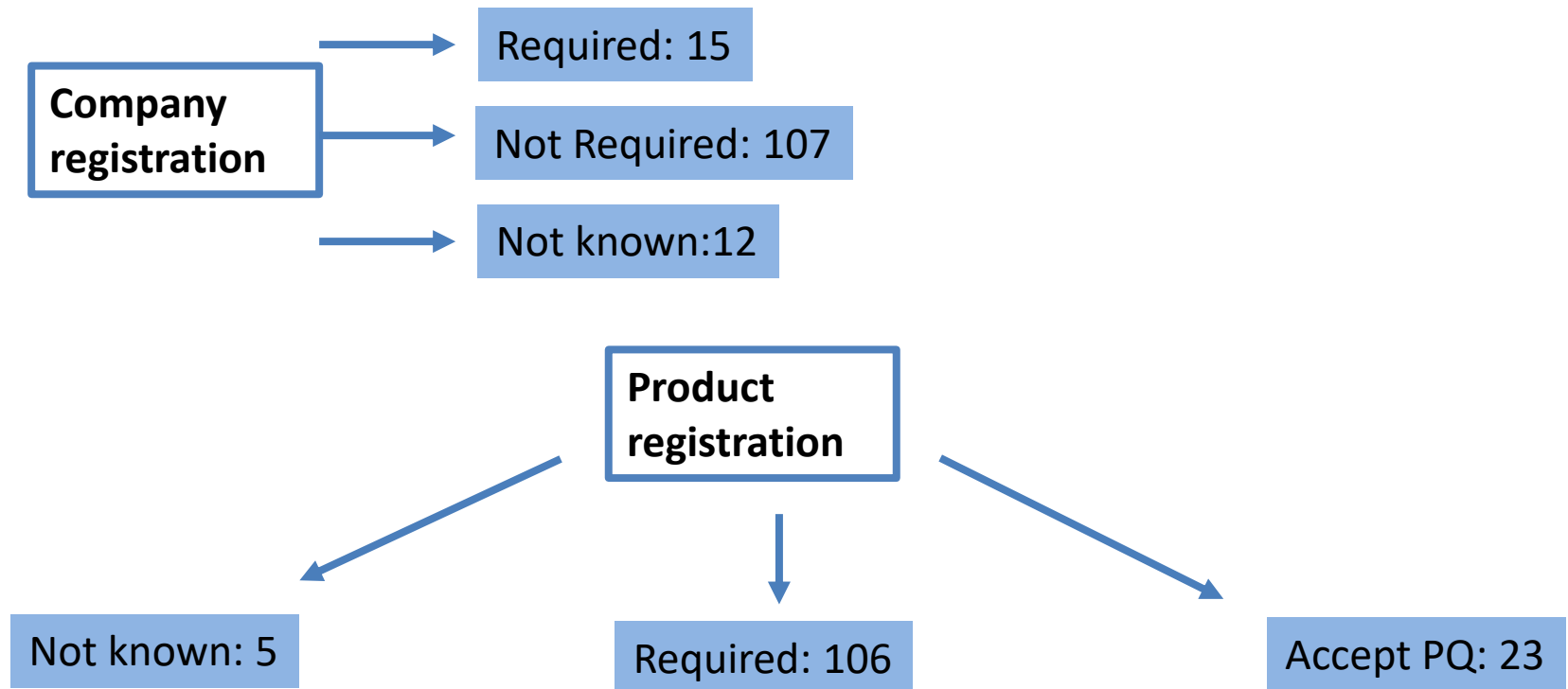
With funding from the Bill and Melinda Gates Foundation (BMGF)

HARMONIZATION vs DISHARMONIZATION OF REQUIREMENTS (ICH countries)

The process followed by countries for MA evaluation also differs. US and EU base the assessment on the review of the CTD and inspection if needed, Japan requires a previous license of the facilities, Canada requires licensing of the establishment, an on-site evaluation (for Biologics only) and testing of batches

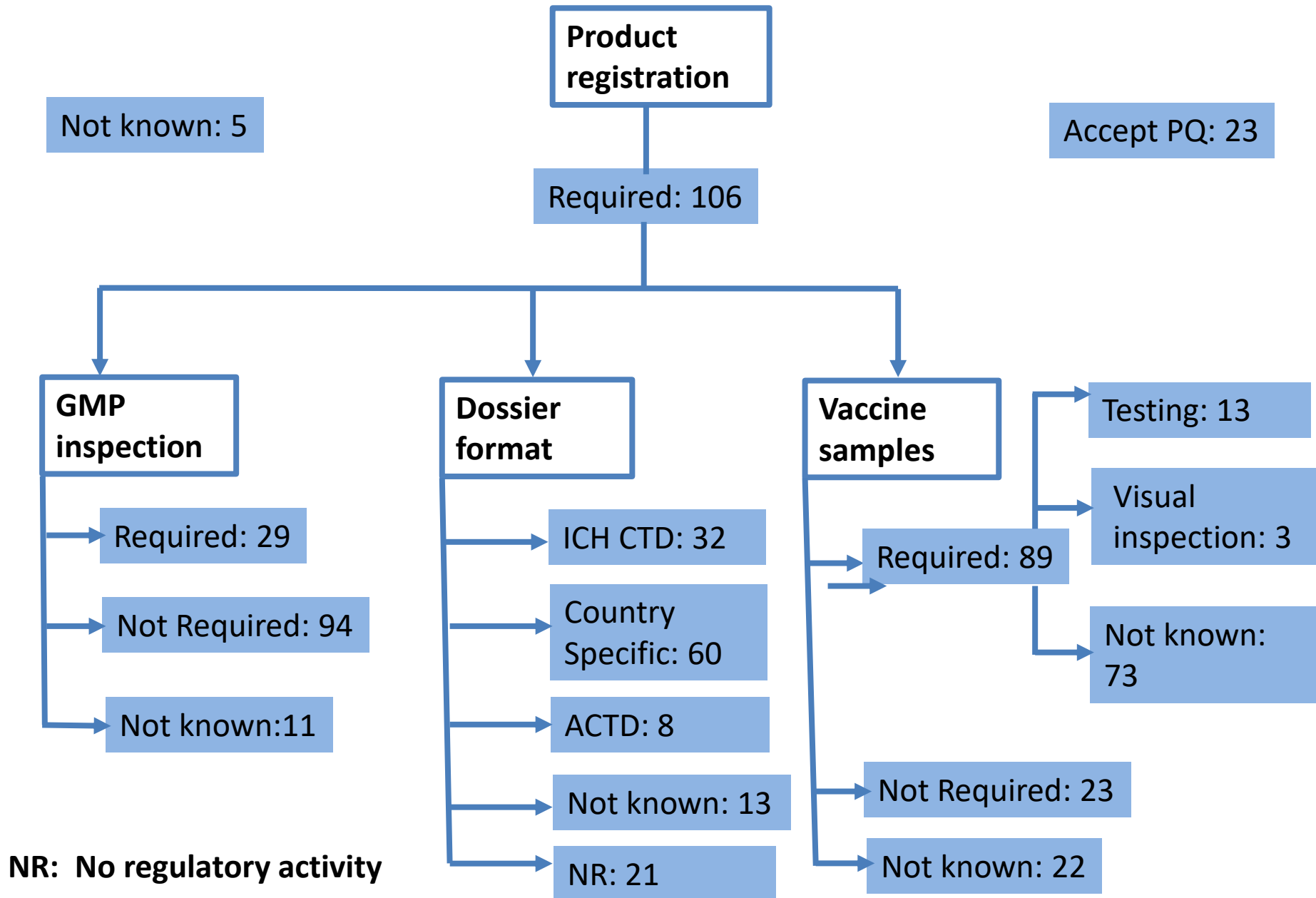
| Facility licensing | CTD review | Site inspection | Consistency testing |
|--------------------|------------|-----------------|---------------------|
| | USA | | |
| | EU | | |
| Japan | | | |
| | Canada | | |

Vaccine registration procedures in 134 countries



Countries assessed (supplied through UN agencies) N= 134

Vaccine registration (cont)



Analysis of the variability in registration procedures

- Requirement of company registration ahead of any product submission could be avoided, since it delays the product evaluation process unnecessarily. Countries with such requirement are encouraged to reconsider whether this company approval cannot be done in parallel to the product evaluation

Analysis of the variability in registration procedures

- The need for increased alignment in dossier format has been explained and demonstrated in the prior session. However, currently 32 + 8 countries have adopted the CTD with their “specific adaptations” and another 60 maintain their national formats and requirements
- There are at least 29 countries imposing “redundant” GMP inspections to companies and on products that have been already inspected by many other regulatory agencies (National, international, WHO, PICs, etc)

Analysis of the variability in registration procedures

- 89 countries require vaccine samples at the time of registration. However, testing is confirmed to be performed only in 13 of these countries and visual inspection conducted in an additional 3 countries; it is unclear the purpose for requiring samples during registration in the remaining 73 countries.
- Testing may be avoided during the registration step. Decision making can be based on reports from tests performed in the producing or other countries as available.
- Testing can be performed at the time of release of lots

Comparison of application forms from 8 countries

Table 4- Contents of application forms in 8 countries

| A | INFORMATION ABOUT THE APPLICANT AND DISTRIBUTOR | A | INFORMATION ABOUT THE PRODUCT | A | STORAGE CONDITIONS SHELF LIFE | A | PACKAGING, LABELLING, INSERTS | A | REGULATORY STATUS |
|--|---|---|---|---|---|---|-------------------------------|---|---|
| 6 | Company name | 8 | Commercial Name | 7 | Proposed shelf life | 2 | Samples | 3 | List of countries where API is registered |
| 7 | Name of manufacturer of active substance | 8 | Pharmaceutical Form | 6 | Proposed shelf life after opening | 5 | Label and insert | 5 | Reference control of finished product |
| 8 | Name of manufacturer of finished product | 8 | Physical description of pharmaceutical form | 6 | Proposed shelf life after reconstitution | 3 | SPC | 4 | Name of control authority |
| 6 | Name of marketing authorization holder | 8 | Commercial presentation | 7 | Proposed storage conditions | 5 | Secondary packaging | 3 | Date and number of registration in origin country |
| 2 | Any manufacturer in world in production of accessories | 8 | Indication | 6 | Proposed storage conditions after opening | | | 5 | List of countries in which finished product is registered |
| 3 | Other manufacturer involved the production of the product | 3 | Pharmacotherapeutic group | | | | | 3 | International certificate |
| 3 | Name and address of the agent in the country | 8 | Route of administration does and dose regimen | | | | | 3 | Date of submission in the country |
| 3 | Contact person for defects and recalls | 6 | Container closure and administration device | | | | | 0 | Appointment date and time |
| 6 | Person/company authorized for communication between the MAH and NRA | 3 | Kind and sources of strains used | | | | | 2 | Information regarding experts |
| | | 3 | GMO declaration | | | | | 2 | Scientific service of the MAH |
| | | 8 | Qualitative quantitative composition | | | | | 3 | Certificate pharmaceutical product |
| | | 7 | Active substance | | | | | 5 | Reference pharmacopeia |
| | | 4 | Manufacturing details | | | | | 3 | Specific monograph of active substances |
| | | 4 | List of materials of animal origin and human origin | | | | | 3 | Did you apply for scientific advice before submission |
| | | 3 | Active substance master file | | | | | 6 | Type of application |
| | | 2 | Vaccine antigen master file | | | | | 4 | Annexed documents |
| | | 4 | Clinical trial summary | | | | | | |
| | | 4 | Detail of overages | | | | | | |
| A: No of countries that require the information listed out of the 8 countries compared | | | | | | | | | |

Comparison of application forms from 8 countries

There is information that is required by the majority of countries, while other is required only by one or two countries. The expert group considered that a model application form can be proposed as a contribution from manufacturers to the alignment of requirements.

OTHER COUNTRY SPECIFIC REQUIREMENTS

- ✓ Eight countries require local clinical studies as part of the registration process
- ✓ Some countries require prior approval in accepted reference markets (e.g. EU, US, Canada, Japan, Australia, Switzerland, etc)
- ✓ Some countries require translation of the full submission, others require local language for selected parts of the submission
- ✓ In general, country specific requirements for labelling
- ✓ Labelling normally required in local language
- ✓ Requirement of national commercial agent in most countries
- ✓ Huge variability in format and contents of application forms
- ✓ Diversity of requirements for documentation and its legalization
- ✓ Some countries require MA and commercialization in Country of Origin or in reference countries
- ✓ Timelines for approval vary from 6 to 36 months depending on the countries

POTENTIAL FOR IMPROVEMENT

The DCVMN-IFPMA working group met again on 11 and 12 January 2018 to work on proposals for alignment of requirements

1. Alignment of CTDs across countries and regions
 - The participants worked on the development of a proposal for alignment of the numbering system for module 1
 - The proposal for alignment of modules 2-5 is based on the suggestion to follow ICH (EU) guidelines for numbering and content and suggestions on where to fit country specific requirements that may not be included in the EU guidelines.
2. Model application form
 - A model (standard) application form is being developed
3. Suggestions for improvement of registration procedures are also being developed

POTENTIAL FOR IMPROVEMENT (2)

1. Challenges observed are described in a paper submitted for publication in Vaccine Journal
2. A Proposal with suggestions for improvement is being developed for publication and sharing with key stakeholders (WHO, ICH, ASEAN and other Regional economic blocks) as well as with supportive stakeholders (UNICEF, GAVI, donors, PATH, MSF, etc)
3. Potential support from WHO with presentation of issues and proposal for alignment at the coming International Conference of Drug Regulatory Authorities (ICDRA) to be held in Dublin in 2018

Acknowledgements

Working Group Members: Mary Allin (Pfizer), Abdulaziz M.M Almotiri (Arabio), Paula Barbosa (IFPMA), Nirav Amitkumar Chokshi (Zydus Cadila), Monique Collaço de Moraes Stávale (Bio-Manguinhos), Samir Desai (Zydus Cadila), Shubhangi Ghadge (Serum Institute of India), Tarek Ibrahim (Arabio), Seon Gyeong Jeong (LG Chem). Matthew Marsden (Pfizer), Mic McGoldrick (Merck), YIJIE Qu (CNBG), Christophe Saille (former GSK), Mira Uton (Biofarma), Qiaoruo Xiong (CNBG), Nora Dellepiane (Consultant), Paula Barbosa (Secretariat IFPMA), Sonia Pagliusi and Ching Chia Ting (Secretariat DCVMN)

THANK YOU
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