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GALVmed workshop: Future of Harmonization for Vaccine Registration Johannesburg, South Africa – November 2010

Setting the Scene- Results of the questionnaire on status of vaccine registration in Africa: Peter Jones

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Who am I ? – Peter Jones


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WALES:- Not a bad place to live!


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What am I?
I am a veterinarian who graduated from the Faculty of Veterinary Science at the University of Liverpool in the United kingdom in 1971, spent several years in practice, then worked in industry in R&D and regulatory affairs, followed by a spell heading up the veterinary department at the European Medicines Agency (EMEA) and finished up in IFAH and am now doing some consulting

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The numbers!

- Number of countries that a Questionnaires was sent: 49
- Number of Questionnaires completed: 35 (71.4%)
- Apologies if your country didn't receive it, or it was not directed to the right person.
- If there has been any misinterpretation, or you would like to modify responses then we can of course fix that
- Thank you very much!

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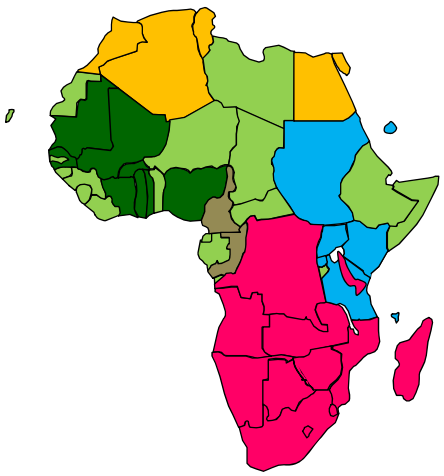
Respondents: 35

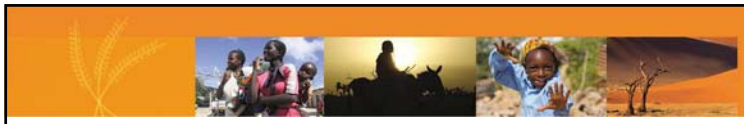


	COUNTRY	Region
1	Algeria	N
2	Egypt	N
3	Morocco	N
4	Tunisia	N
5	Cameroon	C
6	Congo - Brazzavile	C
7	Burkina Faso	W
8	Cote D'Ivoire	W
9	Ghana	W
10	Mali	W
11	Mauritania	W
12	Nigeria	W
13	Senegal	W
14	Togo	W

	COUNTRY	Region
15	Burundi	E
16	Comoros	E
17	Djibouti	E
18	Kenya	E
19	Rwanda	E
20	Seychelles	E
21	Sudan	E
22	Tanzania	E
23	Uganda	E
24	Angola	S
25	Botswana	S
26	Dem Rep Congo	S
27	Lesotho	S
28	Madagascar	S
29	Malawi	S
30	Mozambique	S
31	Namibia	S
32	South Africa	S
33	Swaziland	S
34	Zambia	S
35	Zimbabwe	S

North: 4
Central: 2
West: 8

East: 9
Southern: 12

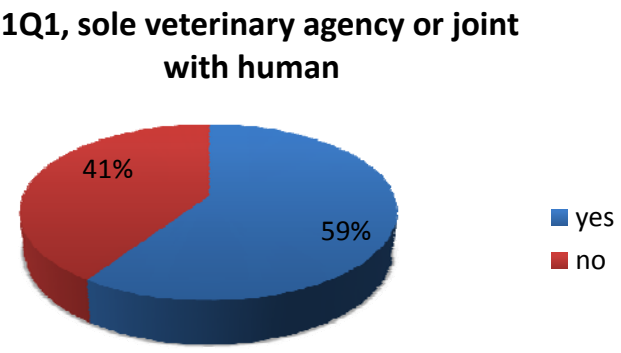


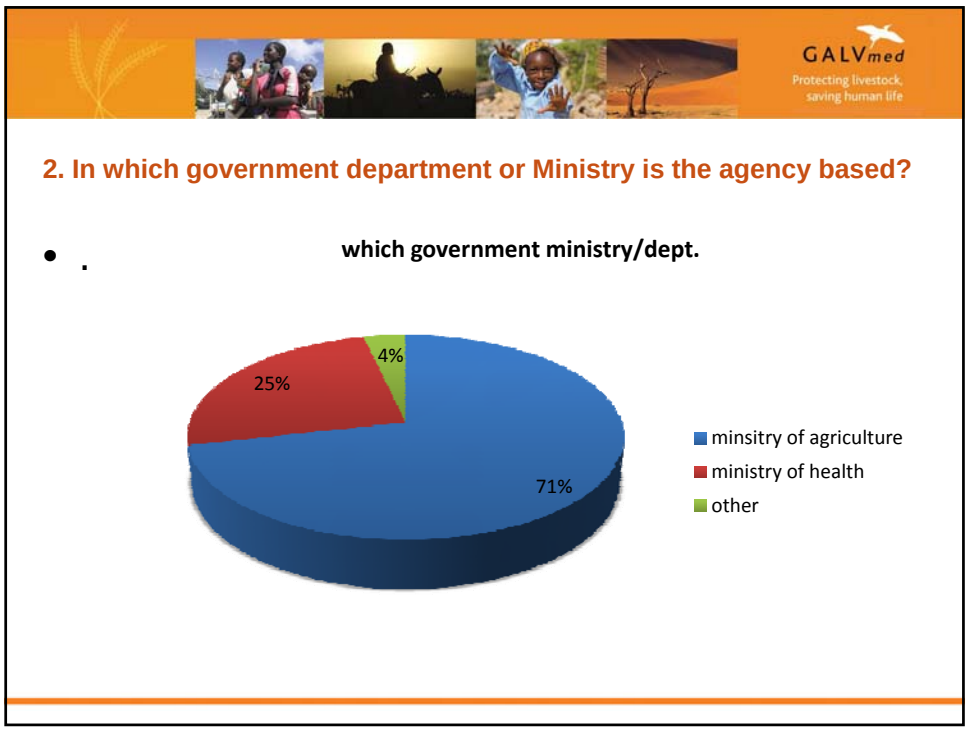
Analysis of GALVmed Questionnaire

Section 1: SCOPE OF REGULATORY SYSTEM IN YOUR COUNTRY

1. Is the agency licensing vaccines just for veterinary products alone or both human and veterinary, i.e joint agency

-

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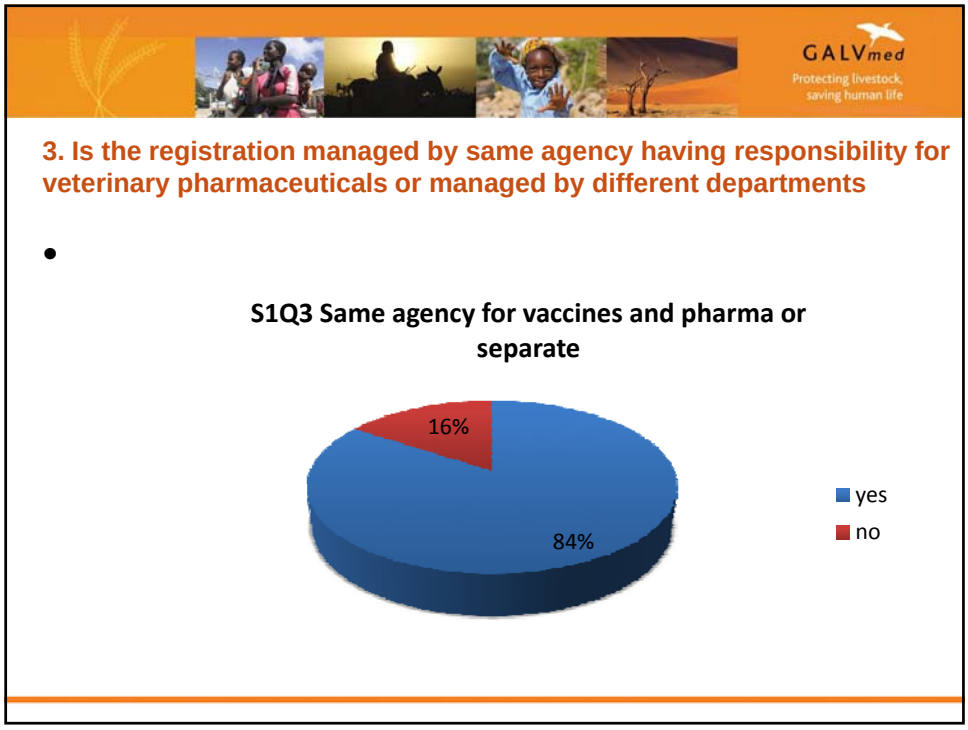
2. In which government department or Ministry is the agency based?
which government ministry/dept.
4%
25%
71%
minsitry of agriculture
ministry of health
other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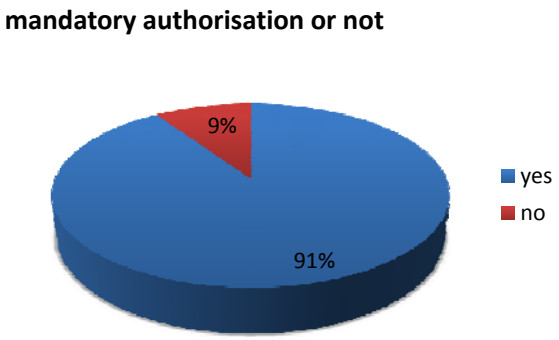
3. Is the registration managed by same agency having responsibility for veterinary pharmaceuticals or managed by different departments
S1Q3 Same agency for vaccines and pharma or separate
16%
84%
yes
no

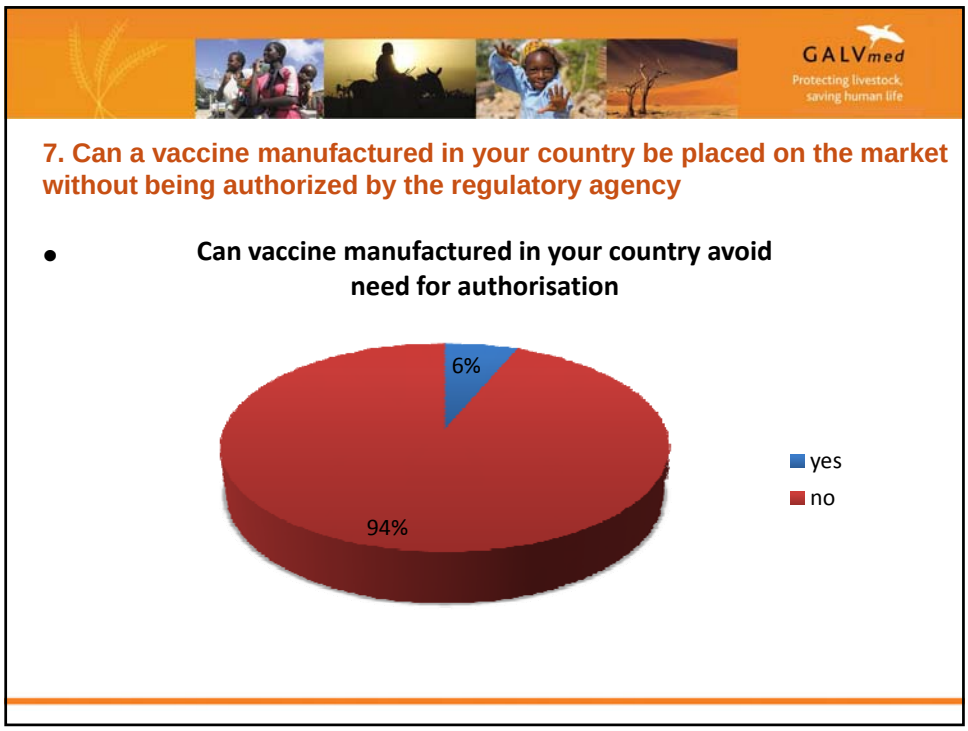
4. Is it mandatory for a vaccine to be authorized by a regulatory procedure in your country, 5 Are there exceptions?



5. Exceptions are very few and far between

6. If your country is in l'UEMOA, please indicate if your agency still operates independently for national registrations in your country

- This question whilst important was confusing in that many respondents chose to answer by stating if they were part of the l'UEMOA or not
- For those countries in l'UEMOA most stated that they still retained their independent systems
- It is therefore difficult from the responses given to draw a conclusion on this point
- A discussion in the break-out groups for those countries in the western region would therefore be very helpful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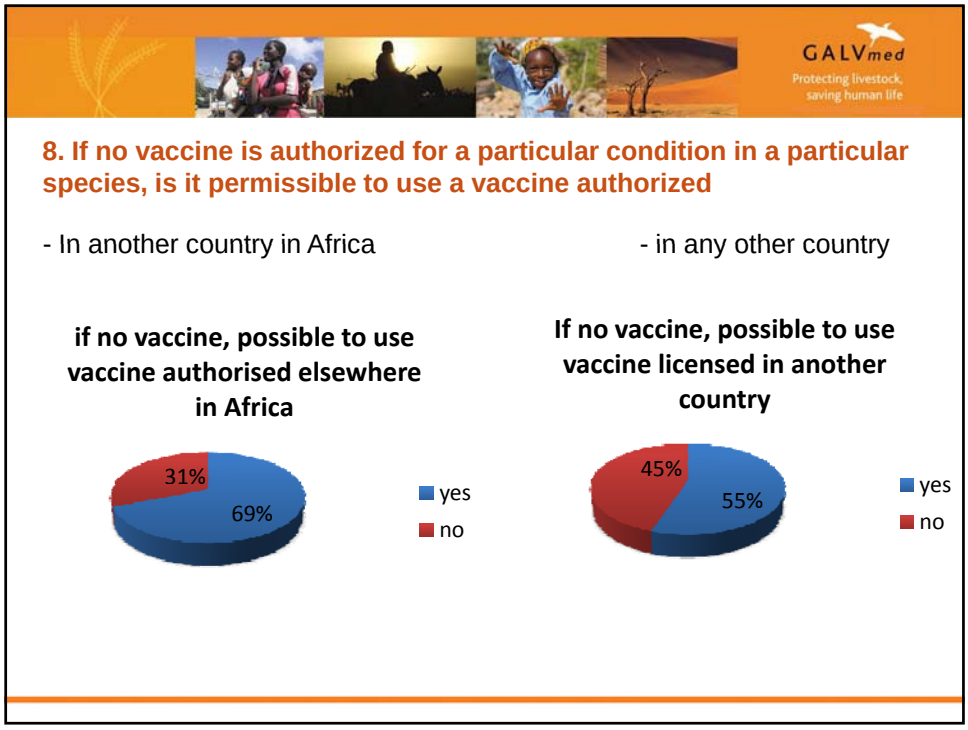
7. Can a vaccine manufactured in your country be placed on the market without being authorized by the regulatory agency
Can vaccine manufactured in your country avoid need for authorisation
6%
94%
yes
no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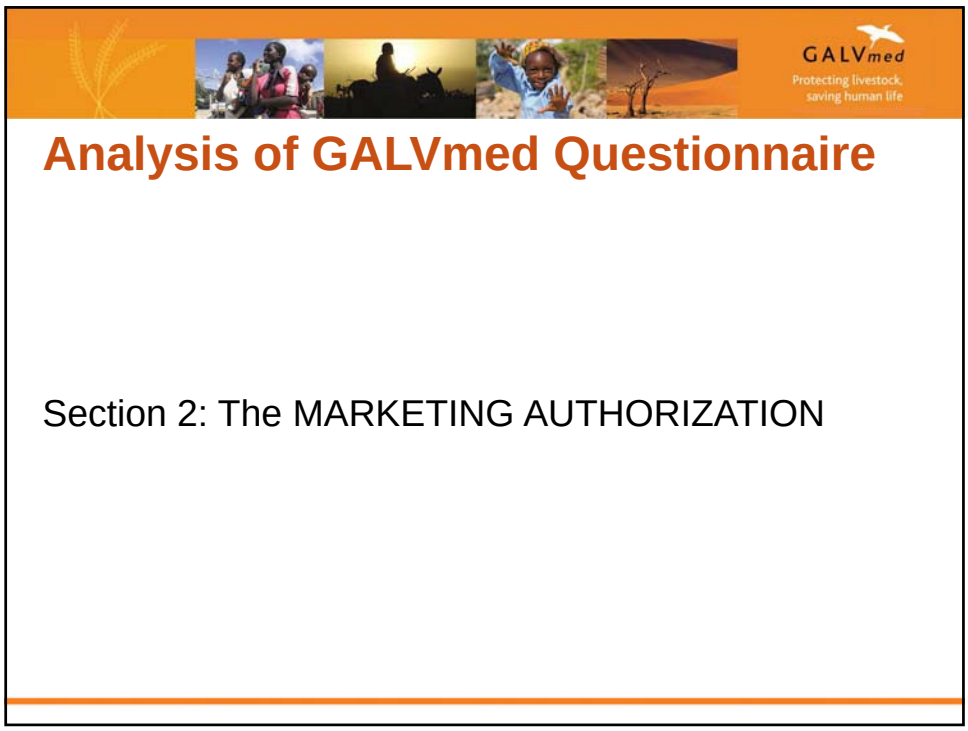
8. If no vaccine is authorized for a particular condition in a particular species, is it permissible to use a vaccine authorized
- In another country in Africa
- in any other country
if no vaccine, possible to use vaccine authorised elsewhere in Africa
31%
69%
yes
no
If no vaccine, possible to use vaccine licensed in another country
45%
55%
yes
no

9. For a vaccine for food animals is it mandatory that Maximum Residue Limits (MRL's) are established for any of the active ingredients

- This question was not well structured and hence proved to be confusing
- The question asked if MRL's were required for the active ingredient
- The "active ingredient" in a vaccine is by definition, effectively the antigenic component and hence leaves no residues
- MRL's for the active ingredient cannot therefore be determined
- Question should better have asked if MRL's are required for non-active ingredients e.g preservative, excipient etc.
- If they are pharmacologically active then the answer will likely be in the affirmative

Conclusions from Section 1: Scope of the Regulatory System in your country

- Just over half of countries authorize veterinary vaccines independently of human ones: they have separate agencies
- Over 70% of countries assign the authorization of veterinary vaccines to the Ministry of Agriculture
- Most authorities have joint responsibility for vaccines and veterinary pharmaceuticals
- By far the greatest majority of countries require authorization prior to marketing and there are very few exceptions e.g. special import/crisis management: Same applies even if vaccine is manufactured in the country itself
- If no vaccine authorized for a particular indication, then possible in over 2/3 of countries to use vaccine authorized elsewhere in Africa; in just over half for vaccines authorized outside.
- Consider greater use of a "cascade system"?

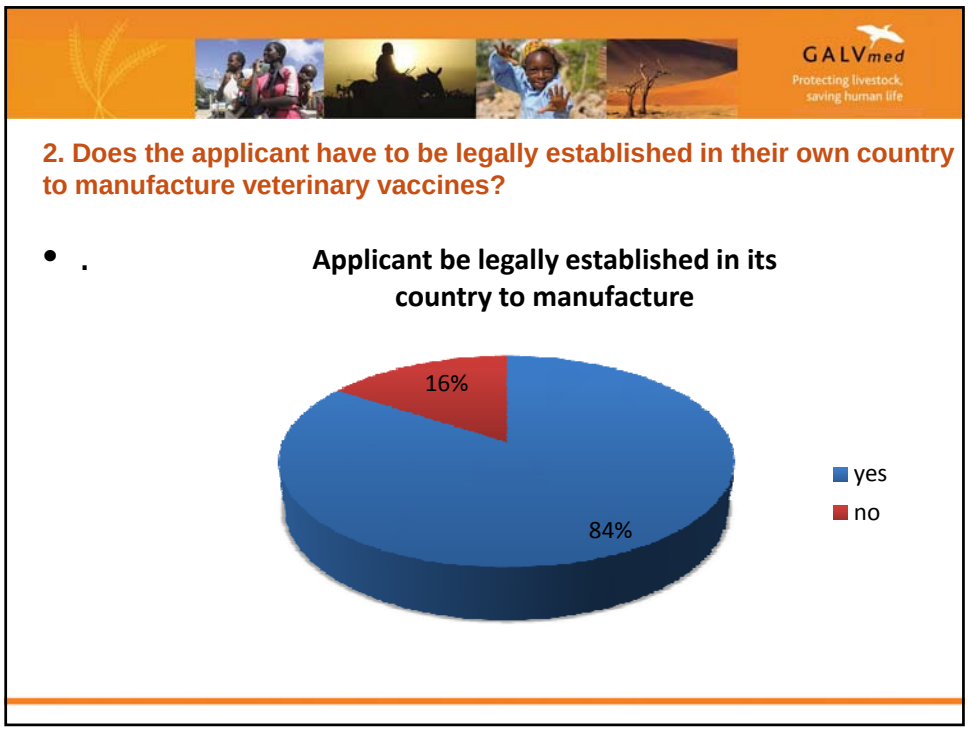


Analysis of GALVmed Questionnaire

Section 2: The MARKETING AUTHORIZATION

1. Does an applicant have to be legally established as a business before being able to apply for registration?

-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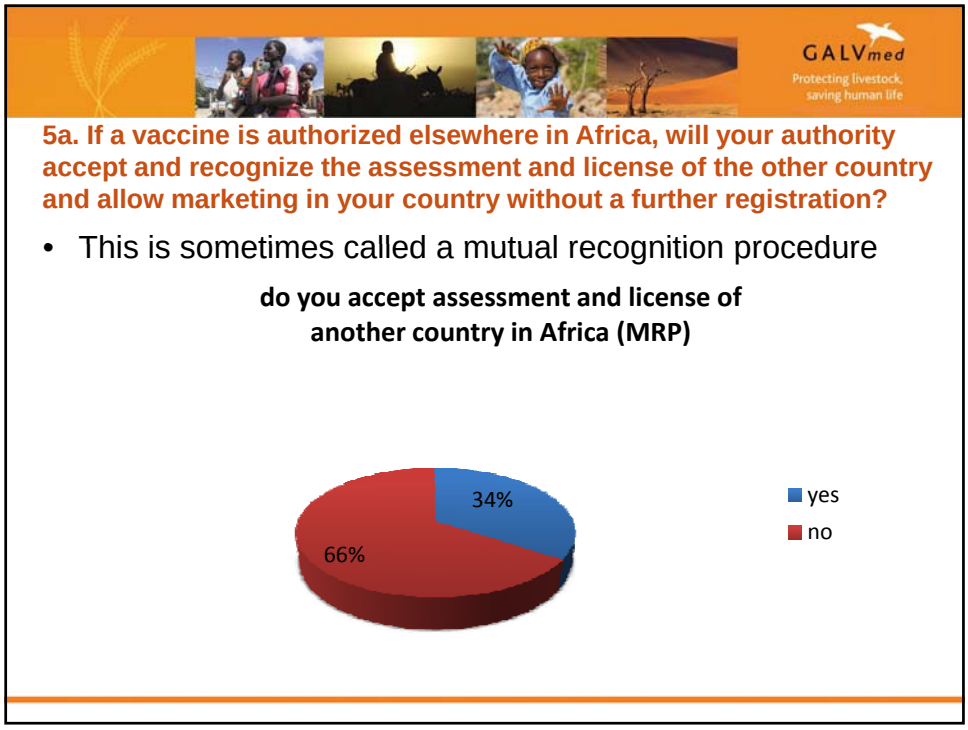
2. Does the applicant have to be legally established in their own country to manufacture veterinary vaccines?
.
Applicant be legally established in its country to manufacture
16%
84%
yes
no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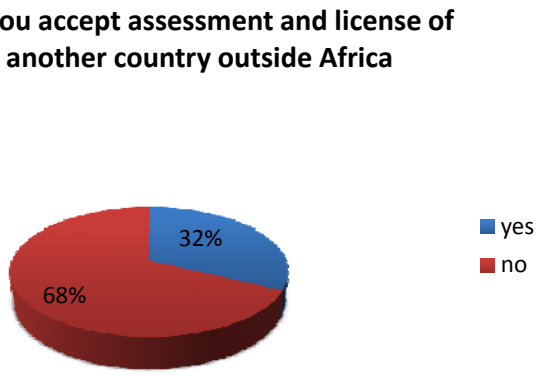
5a. If a vaccine is authorized elsewhere in Africa, will your authority accept and recognize the assessment and license of the other country and allow marketing in your country without a further registration?
This is sometimes called a mutual recognition procedure
do you accept assessment and license of another country in Africa (MRP)
34%
66%
yes
no

5b. If the answer to question 5a is yes how is the process managed and which other African countries does your authority accept?

- For the rather few countries that responded positively the replies were fairly consistent
- Most appear to be countries in eastern and southern communities and having greatest liaison with RSA
- Requirements are fairly consistent with proof of assessment and registration certificates being requested
- "*XXXX is an active member of SADC Harmonisation Programme. Discussions on joint review of dossiers, joint-inspection of manufacturers, information exchange and mutual recognition are being discussed. NO MUTUAL RECOGNITION YET*". No other countries in SADC gave this reply???

6a. If a vaccine is authorized elsewhere outside Africa, will your authority accept and recognize the assessment and license of the other country & allow marketing in your country without further registration?

- .



6b. If the answer to question 6a is yes how is the process managed and which other country registrations does your authority accept?

- Despite a positive response by 37%, there is little evidence to suggest any MR agreements in place with countries outside Africa
- One or two countries appear to accept authorizations from France and UK and EU centrally approved products with proof that manufacturing sites are compliant with GMP and regularly inspected
- Others agree to marketing of vaccines endorsed by OIE and PANVAC

8. Indicate which of the particulars below are to be submitted in the application to license vaccines in your country?

- Question 8 responses!
- Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y N Y Y Y N N Y Y
  Y Y N Y Y Y N N Y Y Y Y N Y Y Y N N Y Y Y Y Y Y Y
  Y Y Y Y Y Y Y Y Y Y Y Y
  Y y y y y y y y y y Y Y Y
  Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y N Y Y Y Y
  Y yDespite a positive response by 26%, there is little evidence to suggest any MR agreements in place with countries outside Africa
  y y y y y y y y y Y Y Y Y Y Y Y N Y Y Y Y Y Y Y Y Y Y
  Y N Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y
  Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y
  Y Y Y Y
- It is clear from the responses given to question 8 in section 2 that all those countries with regulatory systems in place are all asking for exactly the same data and all undertaking data assessments which amounts to significant duplication and use of human and financial resources

10. What period of data protection for new vaccines is given by your authority?

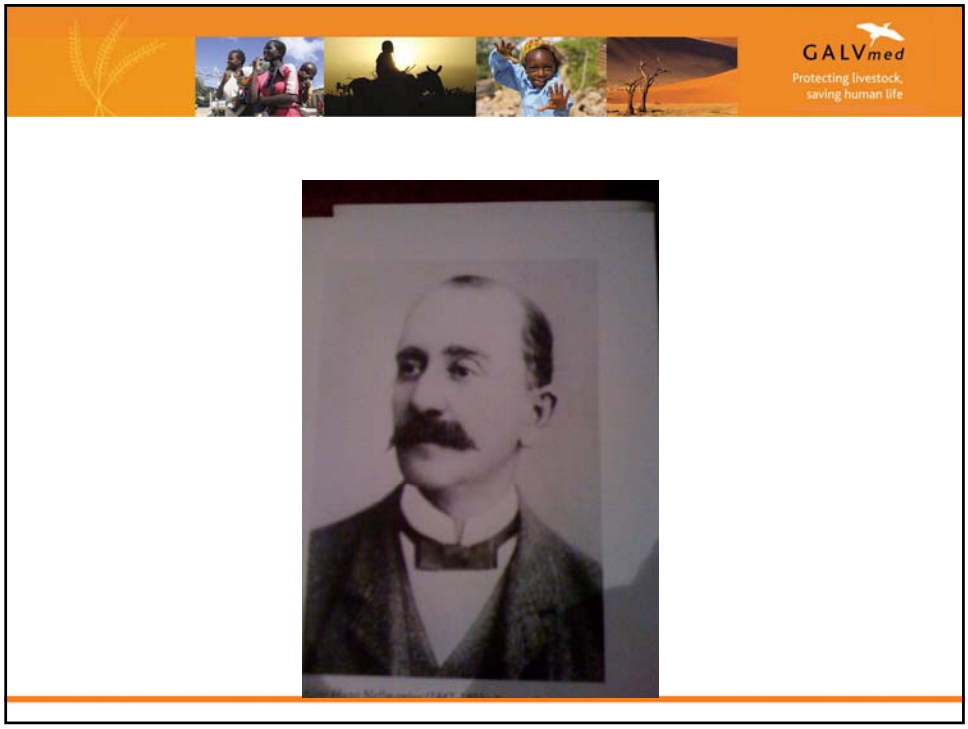
- Data protection in African countries is very variable
- It ranges from 3 months(?) to 5 years maximum
- In some countries there is no protection beyond expiry of the patent period
- This must be a major disincentive to the animal health industry

Conclusions from Section 2: The marketing authorization

- Just over ½ countries require applicants to be established as a business before accepting applications (or agents/distributors)
- Greatest majority of applicants have to be established in own country to manufacture vaccines (other 16% is of concern)
- Only half the countries require vaccines to be authorized in another African country whereas 2/3 require authorization outside Africa
- Some countries undertake full assessment despite assurances that vaccine are fully licensed elsewhere outside Africa

Conclusions from Section 2: The marketing authorization-continued.

- Only 1/3 of respondents recognize the assessment and accept authorization of another African country (MRP). Some confusion in that one respondent says that discussion within SADC is ongoing, it is not acknowledged by the others
- About 1/3 (same as above) take the assessments and authorization of countries outside Africa; mainly UK, France and EU (centralized) and endorsements by OIE and Panvac
- Only centralized initiative is l'UEMOA
- Data requirements for applicants to file for authorization are very consistent throughout, with little if any derogations (**generally all asking for the same thing)**
- Data protection is very limited/variable and a likely disincentive to many R&D companies
- Independent expert reports are required by mostly all countries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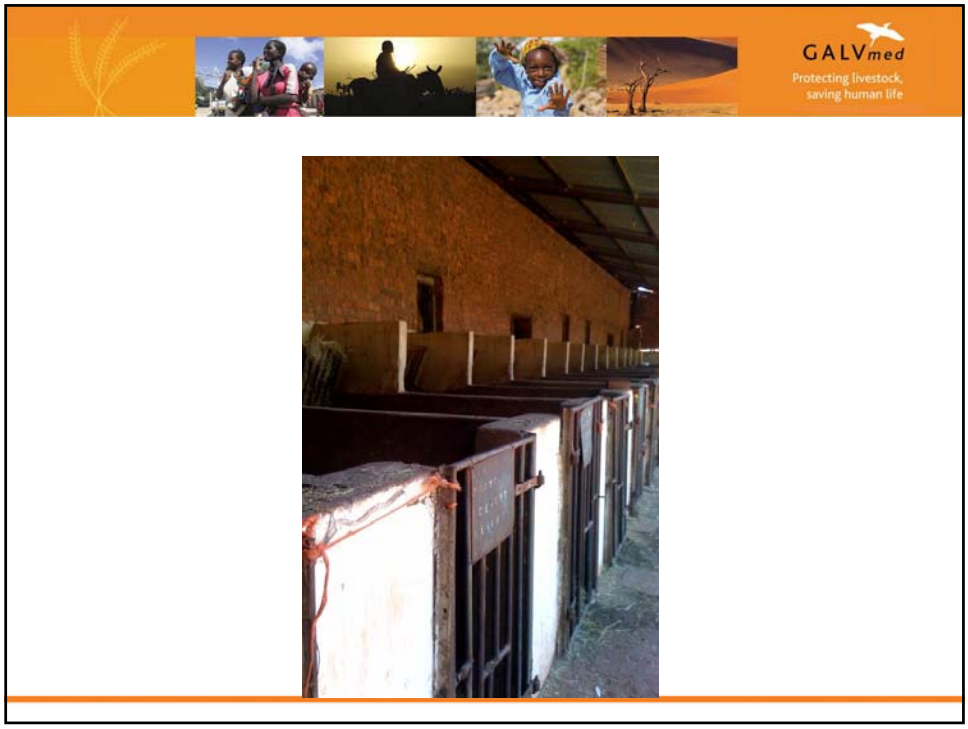
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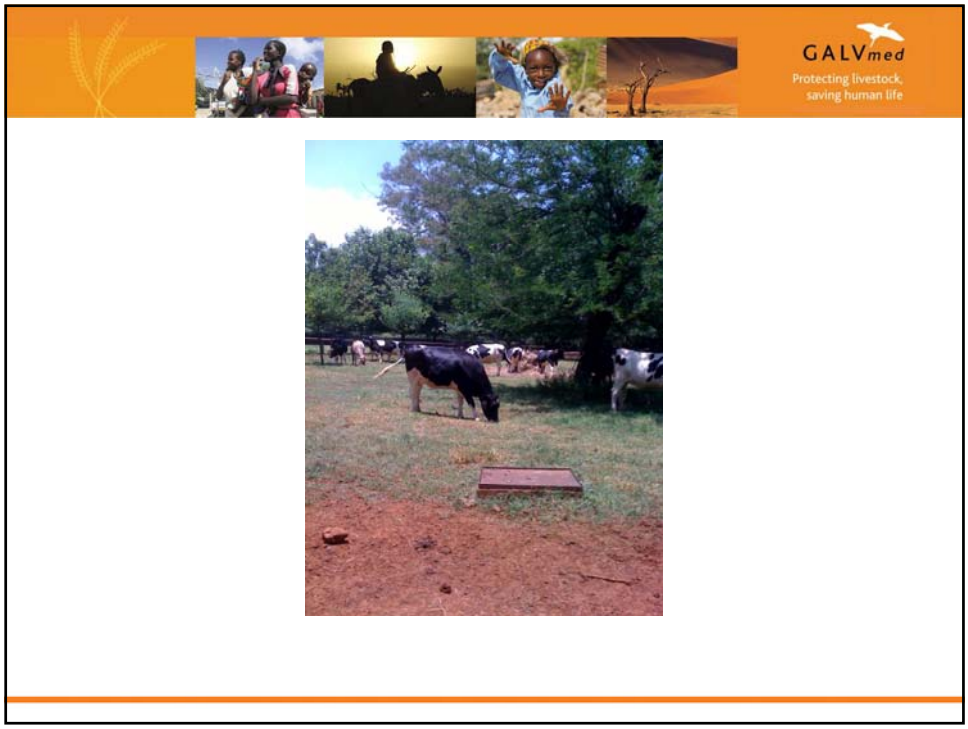
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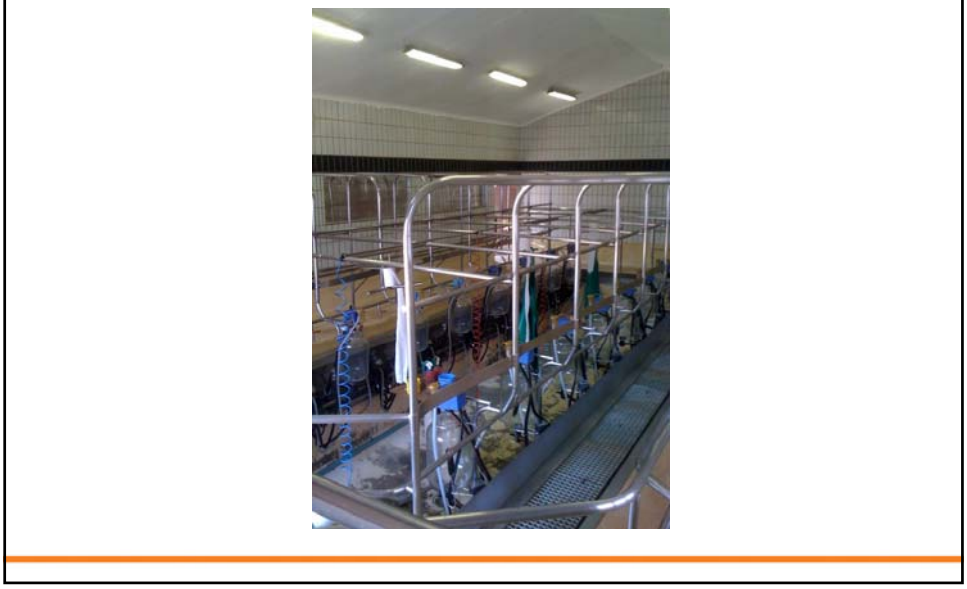
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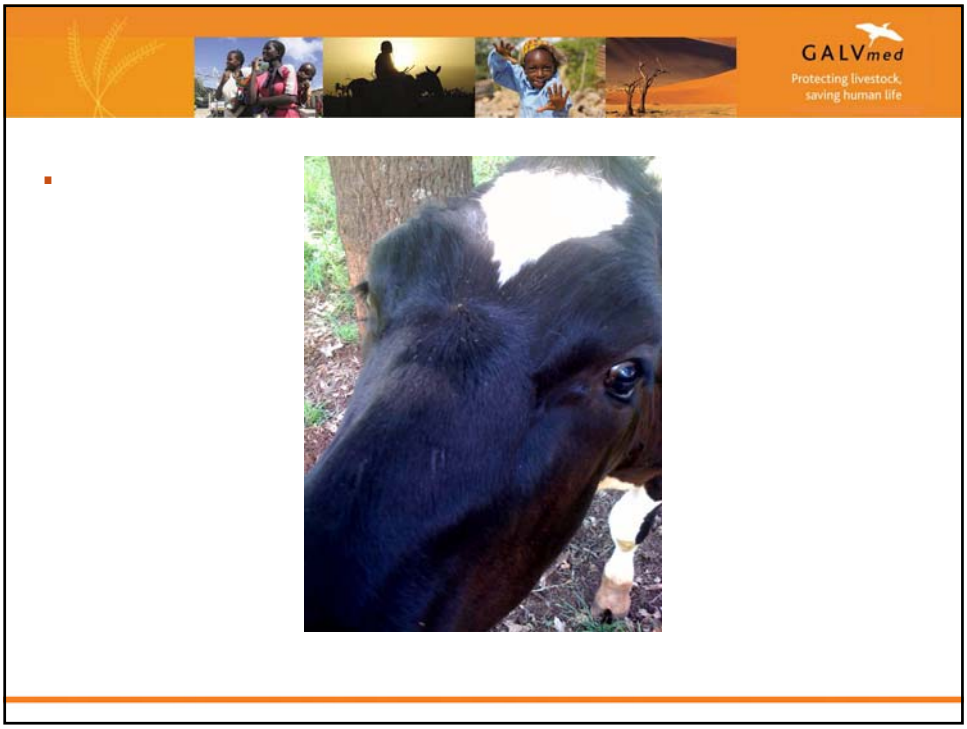
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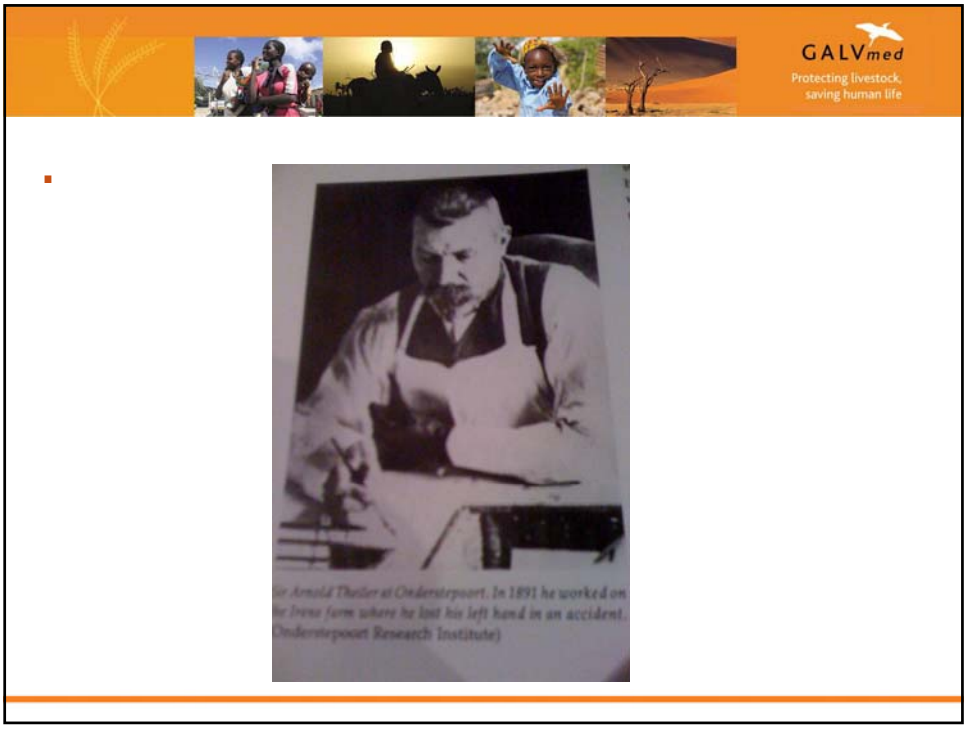


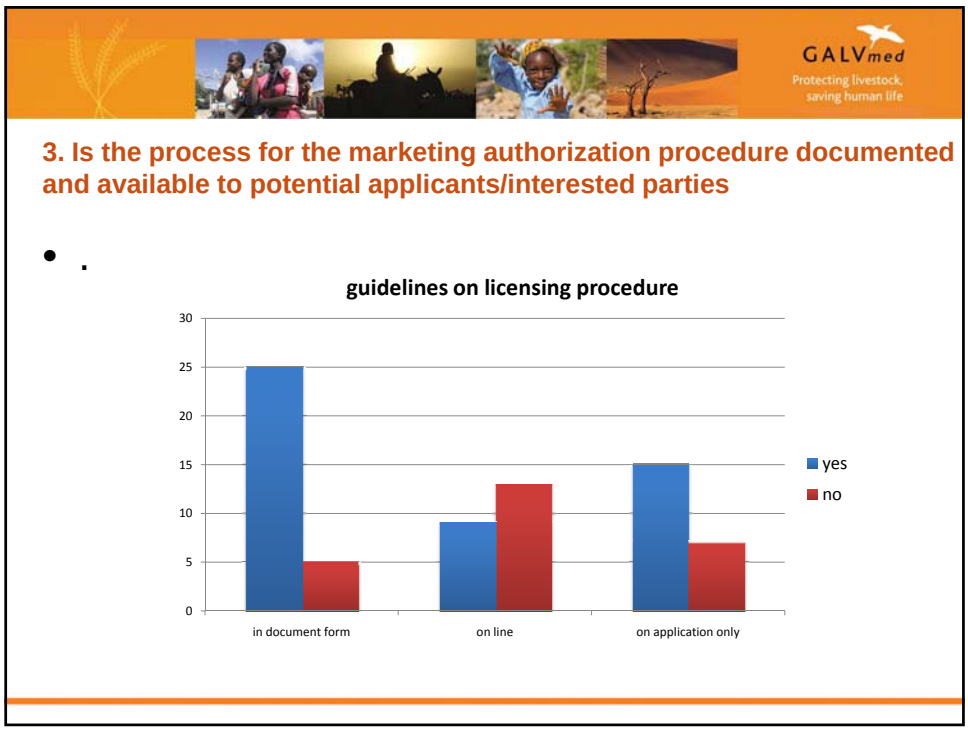
Sir Arnold Theiler at Onderstepoort. In 1891 he worked on
his Irene farm where he lost his left hand in an accident.
(Onderstepoort Research Institute)

Analysis of GALVmed Questionnaire

Section 3: PROCESS FOR THE REGULATORY PROCEDURE

1. Please describe the arrangements for submitting an application in your country for authorization of a veterinary vaccine

- The responses are vary variable depending on the existing processes for authorization
- In some countries it appears to be the simple completion of a form
- Countries relying on licenses issued elsewhere generally have a standard procedure in place for deposit of essential documents
- Those countries with a full regulatory process, operate to a standard operating procedure requiring full data packages for quality, safety and efficacy with time clock in place.
- For genetically modified organisms separate legislation exists in some countries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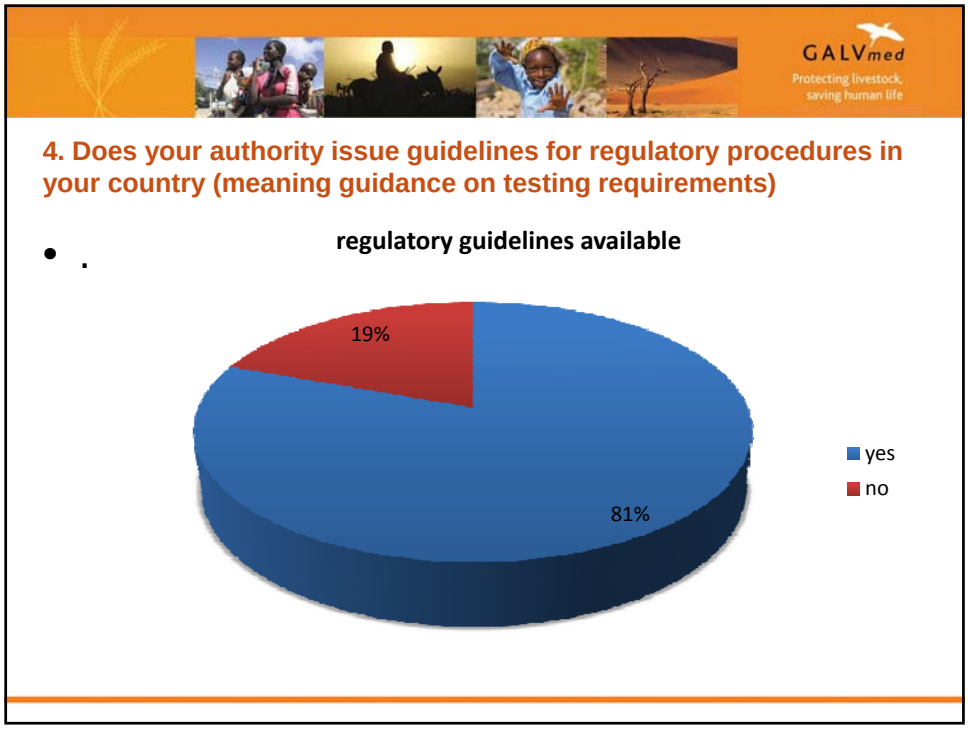
3. Is the process for the marketing authorization procedure documented and available to potential applicants/interested parties
guidelines on licensing procedure
30
25
20
15
10
5
0
in document form
on line
on application only
yes
no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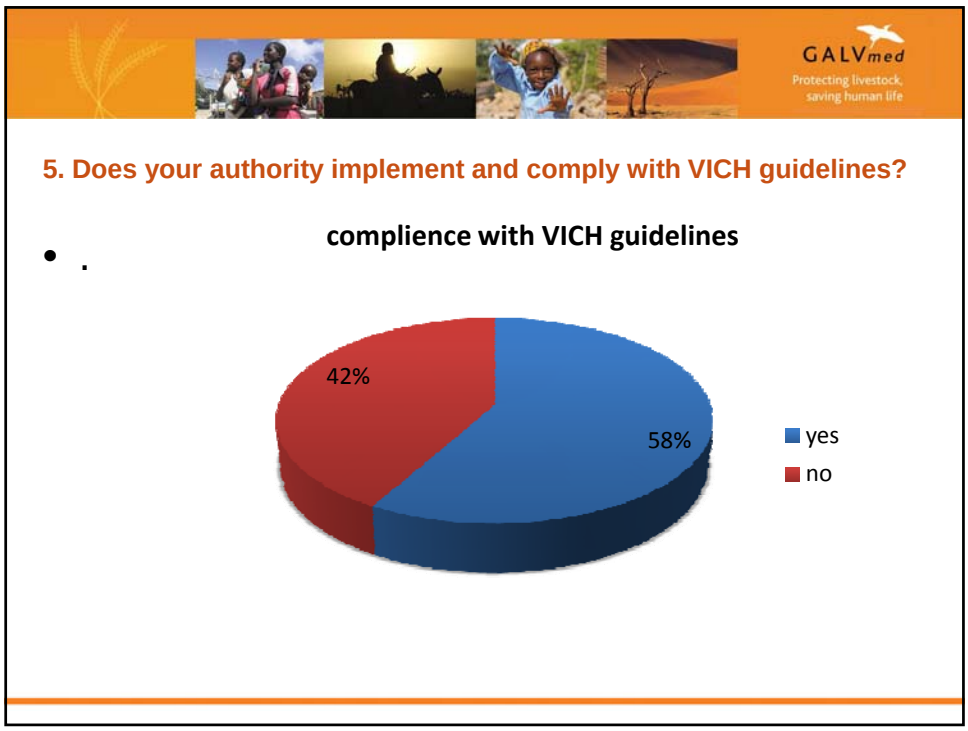
4. Does your authority issue guidelines for regulatory procedures in your country (meaning guidance on testing requirements)
regulatory guidelines available
19%
81%
yes
no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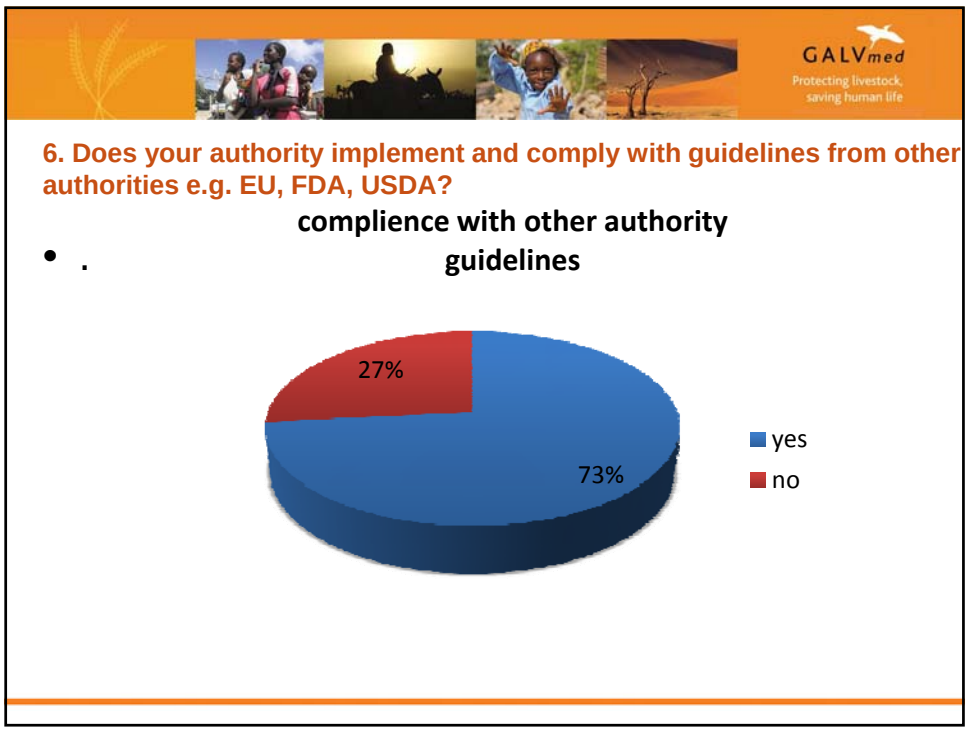
5. Does your authority implement and comply with VICH guidelines?
complience with VICH guidelines
.
42%
58%
yes
no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6. Does your authority implement and comply with guidelines from other authorities e.g. EU, FDA, USDA?
complience with other authority guidelines
.
27%
73%
yes
no

Conclusions from Section 3: Process for the regulatory procedure

- Application procedure and processes involved depend on the type of authorization in place
- In smaller countries generally it is an administrative procedure requiring document submission plus samples e.g. import certificate, GMP compliance certificate etc. and can take between 2/3 weeks to 2 months
- In larger countries there is often a full regulatory procedure in place requiring submission of complete regulatory dossier with quality, safety and efficacy sections, and this procedure can take between 180 days to a full year; certificates and samples also needed
- Information on reg. processes generally available mostly in hard copy and on application only; on line information is available in few countries
- Many countries state that guidelines are available but this in unclear and may have been confused with guidance on procedures

Conclusions from Section 3: Process for the regulatory procedure – continued.

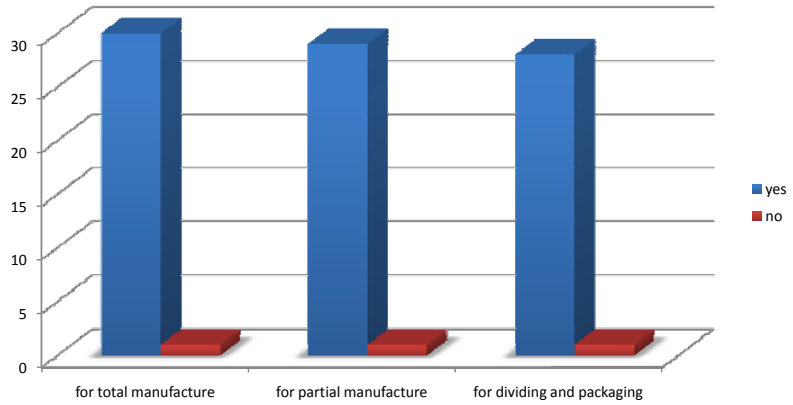
- 58% of responses declare implementation of, and compliance with VICH guidelines
- Well over two thirds of respondents say that guidelines on testing requirements from overseas regulatory agencies are applied
- Samples of finished product are often required by most authorities
- Duration of authorization depends on type: an administrative procedure may only be valid for one year whereas a full product license is valid for between 3 and 5 years (mostly the latter), and renewal applications are the norm

Analysis of GALVmed Questionnaire

Section 4: MANUFACTURE AND IMPORTS

1. If a company wishes to manufacture a veterinary vaccine in your country, is it necessary to obtain an authorization

- .

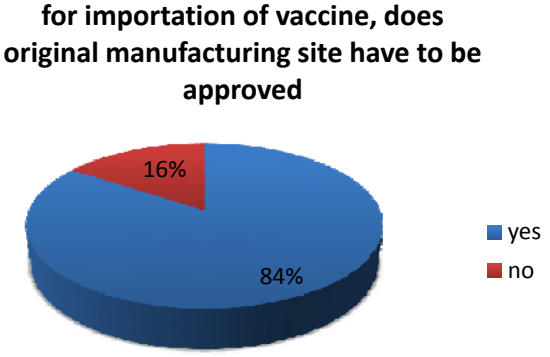


2. What requirements are there to obtain such a manufacturing authorization?

- The responses to this question were the most varied of all and confirm that the requirements and very heterogeneous
- Some countries just require a paper application to be lodged
- Applications to a number of Ministries are often required
- The more sophisticated require: evidence of conformance with GMP, that the facilities are satisfactory, the presence of qualified personnel (pharmacist or vet usually)
- Guidelines are available in some countries

3. If a company wishes to import a vaccine form outside your country is it necessary for the site of manufacture in the other country approved by the authorities there?

- .

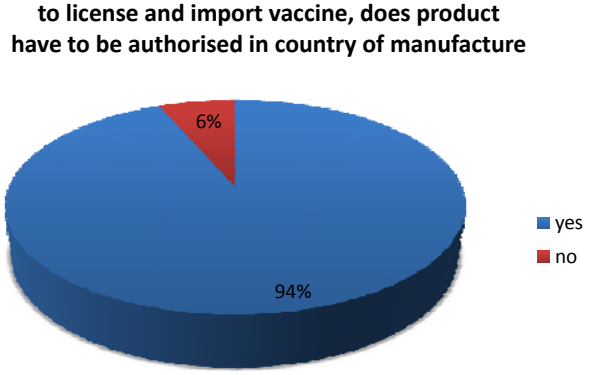


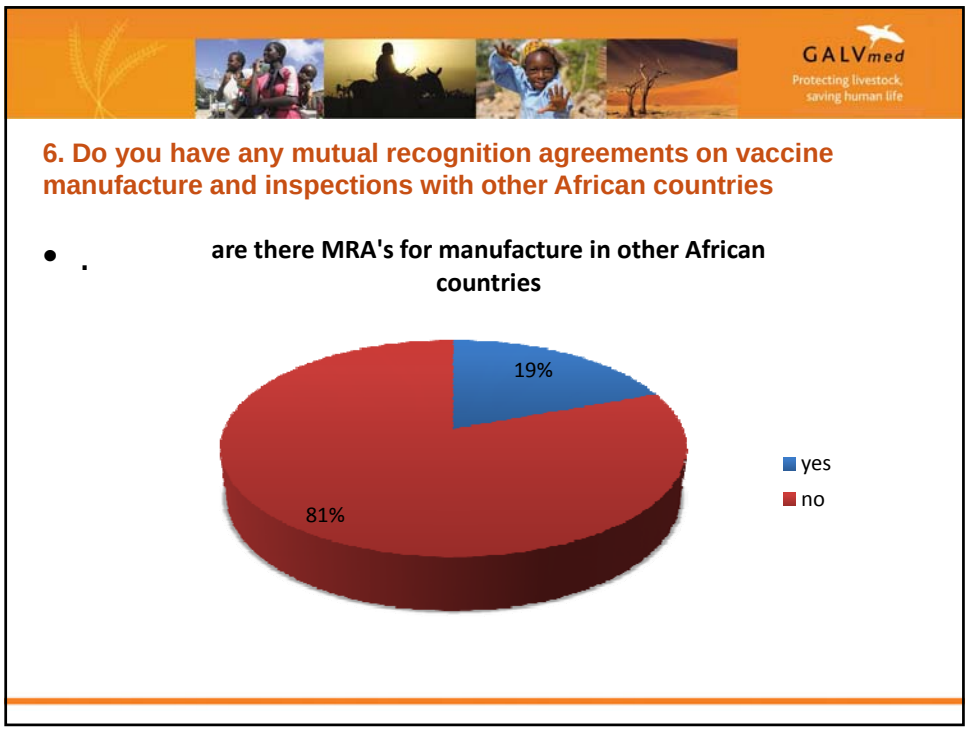
3. If a company wishes to import a vaccine form outside your country is it necessary for the site of manufacture in the other country approved by the authorities there? *And what documentation required*

- More consistency in this response and requirements seem more demanding than for domestic facilities
- Manufacturing authorizations and GMP certificate
- Certificat de produit pharmaceutique (World Health Organization model)
- Evidence of appropriate facilities, and qualified personnel
- Certificate of authorization

4. If a company wishes to import & license a vaccine manufactured in another country, must it be licensed in the country of manufacture

- .

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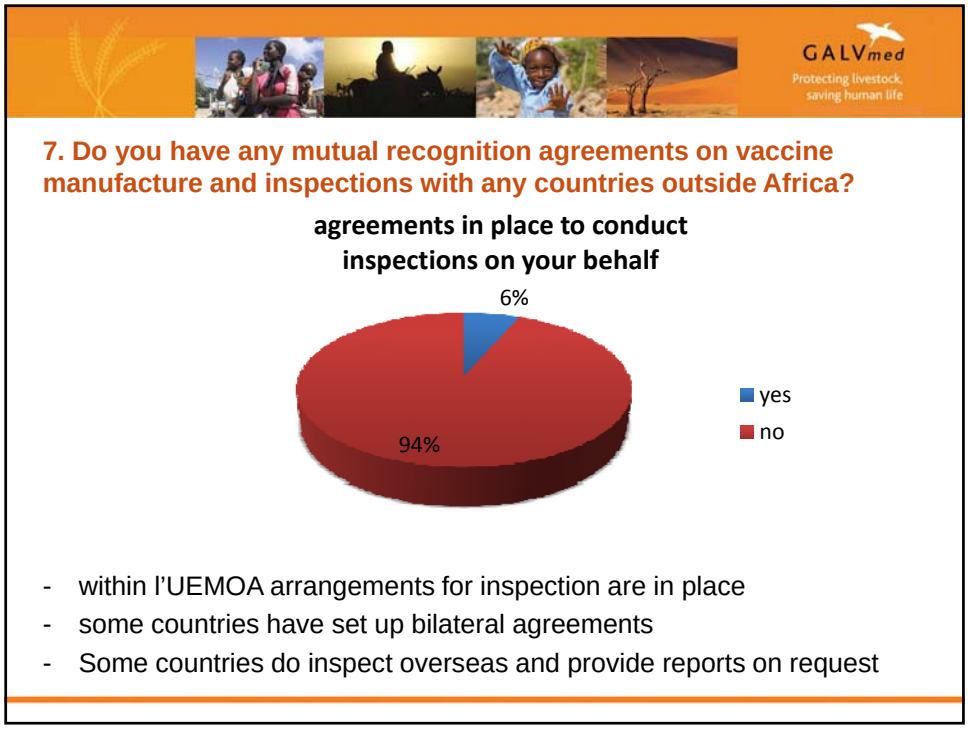
6. Do you have any mutual recognition agreements on vaccine manufacture and inspections with other African countries
are there MRA's for manufacture in other African countries
19%
81%
yes
no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7. Do you have any mutual recognition agreements on vaccine manufacture and inspections with any countries outside Africa?
agreements in place to conduct inspections on your behalf
6%
94%
yes
no
- within l'UEMOA arrangements for inspection are in place
- some countries have set up bilateral agreements
- Some countries do inspect overseas and provide reports on request

8. For imported vaccines what analyses and testing of finished product is required pre authorization being granted? 9. What records needed?

- Whilst there are surprisingly a few countries that ask for **no** data on testing of final product, those that do are very consistent in their requirements
- Certificates of analysis for ? batches to include data on impurities, pyrogens, stability, sterility, potency, impurities in the manufacturing process
- Mostly all require results of batch testing on all batches being imported with the relevant documentation being provided

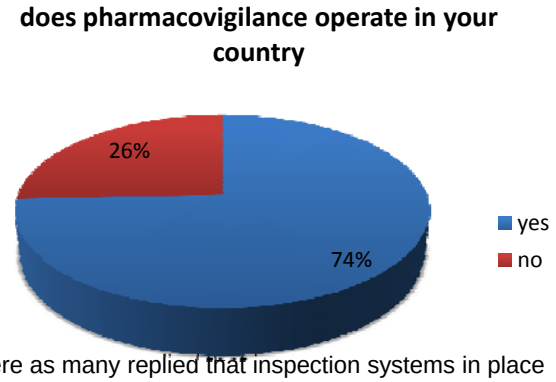
Conclusions from Section 4: Manufacture and Imports

- With the exception of one or two countries responses indicate that manufacture in Africa requires authorization
- Requirements for local manufacture are very varied from a simple written request to more sophisticated demands with applications to a number of ministries often needed
- Rules for evidence of good manufacturing standards for imported vaccines are more demanding and all such sites have to be approved by authorities in the foreign country
- Documentary evidence is consistent and in most cases the vaccine must be authorized for sale in exporting country
- Testing requirements for imported vaccines very similar for all countries, but one or two countries require nothing

Analysis of GALVmed Questionnaire

Section 5: SUPERVISION AND SANCTIONS

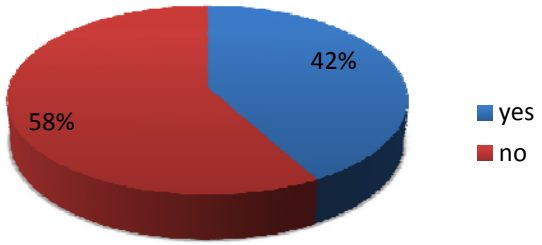
1. Are there arrangements in place for post-marketing safety monitioring in your country (pharmacovigilance). 2. If yes please provide details



- Some confusion here as many replied that inspection systems in place
- One or two of the larger countries have reporting systems
- Post marketing surveillance is currently very heterogeneous

5. Does your authority undertake routine batch testing of vaccines

- .



Conclusions from section 5: supervision and sanctions

- ¾ of countries state that there is a pharmacovigilance system in operation
- Very large majority of countries carry out inspections of manufacturing sites and or distributor operations\
- Less than half the countries undertake batch testing to underpin quality control
- Vaccines are removed form the market for a variety of reasons mostly as a result of adverse reactions with concerns about safety or lack of efficacy as well as manufacturing problems

Analysis of GALVmed Questionnaire

Section 6: LABELLING

Conclusions form Section 6: Labeling

- Main languages required on labeling are as follows:

  French in northern, western and central regions
  English in southern and eastern regions
  Arabic with French in many northern countries
  Portuguese in Mozambique and Angola
  Some other official languages in a few countries

- Mandatory text on labels, outer packaging and ampoules varies somewhat but is mostly consistent

Analysis of GALVmed Questionnaire

Section 7: GENERAL PROVISIONS

1. Are there any arrangements in place for regular communication with other countries

- in Africa

- outside Africa

- Responses are quite variable and show that within regions there is ongoing dialogue between some countries
- In addition there are bilateral arrangements in place between e.g. French speaking countries and the French authorities and English speaking countries and the UK
- Little or no evidence of any structured mechanisms in place to advance harmonization with the exception of l'UEMOA where significant progress has been made

So What?

1. Evidence suggests that we have the basis for advancing greater harmonization
2. The building blocks are in place
3. If l'UEMOA can do it why not elsewhere?
4. Go carefully at first; mutual recognition prior to centralized systems are preferred
5. This can happen if we commit to moving forward working together in partnership
6. Let's go work at it?

Thank you for you support ,commitment and response to the initiative so far and for moving forward to the next steps

Working groups:

1) Split in 3 groups based in yesterday's lists
2) Each group to work on the same 5 questions for about 50 minutes:
   - Back in this room at 15:45
3) Group presentations:
   - 10 minutes per group
4) Discussion and Conclusions

Working groups:

1

	COUNTRY	Region
1	Algeria	N
2	Morocco	N
3	Tunisia	N
4	Cameroon	C
5	Congo - Brazzavile	C
6	Cote D'Ivoire	W
7	Ghana	W
8	Mali	W
9	Mauritania	W
10	Nigeria	W
11	Senegal	W

Chair: Cameroon
Rapporteurs: Nigeria & Algeria

2

	COUNTRY	Region
12	Burundi	E
13	Kenya	E
14	Rwanda	E
15	Seychelles	E
16	Sudan	E
17	Tanzania	E
18	Uganda	E

Chair: Kenya
Rapporteur: Tanzania

3

	COUNTRY	Region
19	Angola	S
20	Botswana	S
21	Dem Rep Congo	S
22	Lesotho	S
23	Madagascar	S
24	Malawi	S
25	Mauritius	S
26	South Africa	S
27	Swaziland	S
28	Zambia	S
29	Zimbabwe	S

Chair: Botswana
Rapporteur: Zambia

Working groups:

1

	COUNTRY	Region
1	Algeria	N
2	Morocco	N
3	Tunisia	N
4	Cameroon	C
5	Congo - Brazzavile	C
6	Cote D'Ivoire	W
7	Ghana	W
8	Mali	W
9	Mauritania	W
10	Nigeria	W
11	Senegal	W

This room (back)

2

	COUNTRY	Region
12	Burundi	E
13	Kenya	E
14	Rwanda	E
15	Seychelles	E
16	Sudan	E
17	Tanzania	E
18	Uganda	E

This room (front)

3

	COUNTRY	Region
19	Angola	S
20	Botswana	S
21	Dem Rep Congo	S
22	Lesotho	S
23	Madagascar	S
24	Malawi	S
25	Mauritius	S
26	South Africa	S
27	Swaziland	S
28	Zambia	S
29	Zimbabwe	S

Boardroom

Working groups - Questions

1) What do you think are the benefits and advantages of the mutual recognition system for your country, and can you suggest some initiatives to investigate how to progress such a system?

2) Would your country be willing to participate in a Regional Forum of Regulatory Authorities to continue to work on the way forward for mutual recognition and harmonisation (if not doing so already)?

3) Now that PANVAC is fully operational as a “Centre of Excellence” for veterinary vaccines on the African continent, how do you see its role in progressing such an initiative (mutual recognition) with the support of the OIE?

4) a- If Regional Forums were set up, how the group see the progress and achievements of the Regional Forum, and what milestones would you like to see in place to meet these achievements in 5 years time?

   b- What would you think will be the challenges to achieve this, and possible mitigation actions?

5) If certain members of your group are not convinced that the time is right to progress just yet such a proposal; what more needs to be done before further consideration can apply?

CONCLUSIONS