World Health Organization

Immunobridging for evaluation of filovirus vaccines

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What is immunobridging?

An inference of effectiveness based on comparing immunological results with a new vaccine/formulation/subgroup with immunological results in a situation with known efficacy

Efficacy of the comparator should be known

Success criteria should account for desired relative efficacy of the new vaccine/formulation/subgroup vs. the comparator, along with various uncertainties

It is implied that some portion of the immune response (most commonly, binding or neutralizing antibodies) will predict other important components of the immune response

How far is an (immuno)bridge too far?

Same vaccine, similar formulation

Same vaccine, different formulation

Same vaccine, different subgroup

Same vaccine, different antigen (how different?)

Similar vaccines (e.g., similar platforms)

Different vaccines

Situations in green are usually well-accepted, others may sometimes be accepted

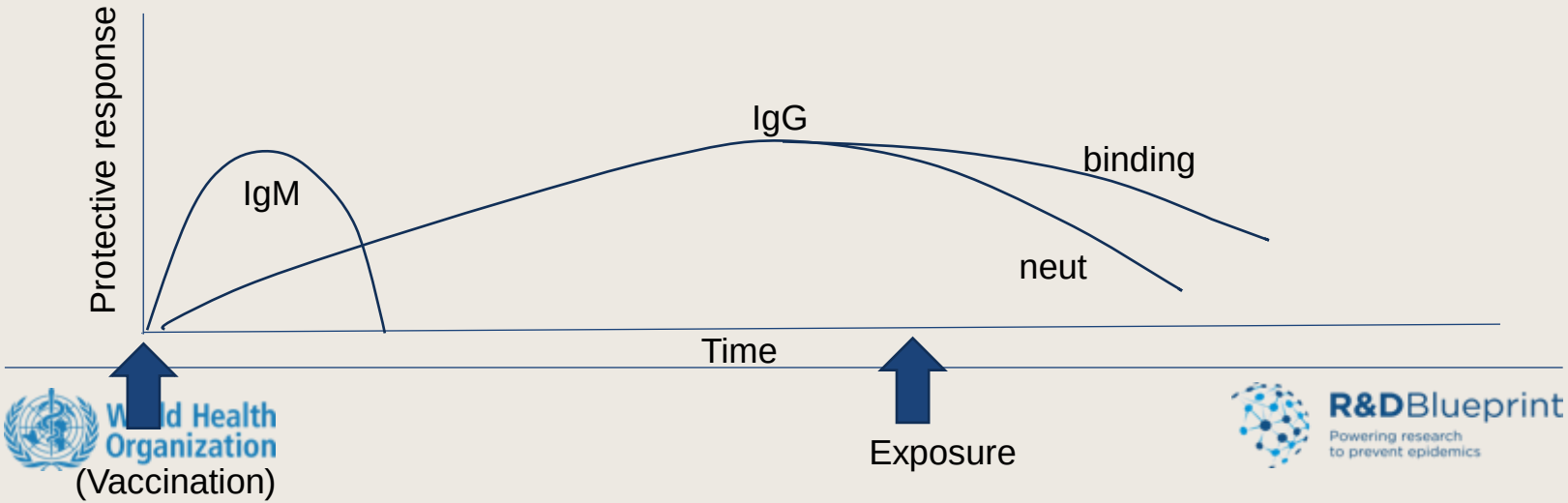
Immunological considerations for immunobridging

What are the protective immune responses likely to be?

Will the chosen immune marker adequately predict the entire protective immune response in both situations?

Memory B cell response leads to rapid increase in antibodies after exposure

CMI may also be important, but role in rapid infections like Ebola is less clear



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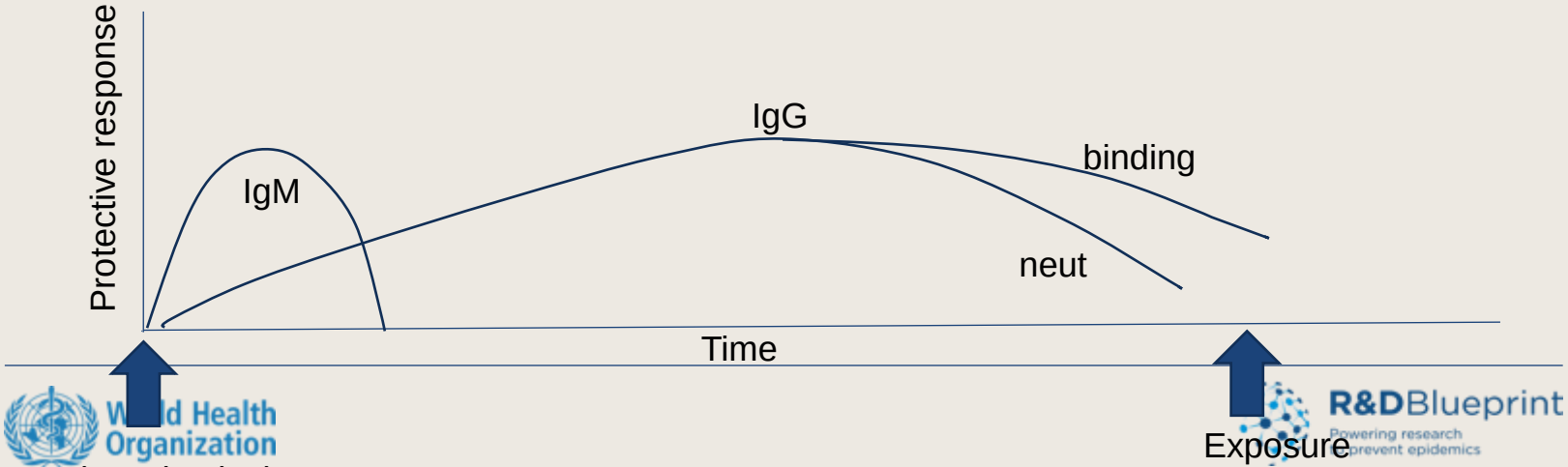

When would immunobridging more likely predict effectiveness of new filovirus antigens in existing vaccines?

Mechanisms of protection are similar

Timing of infection/pathogenesis is similar

Immune evasion abilities of the viruses are similar (or greater for the comparator)

How could animal data help?

Note caveats about animal models for Ebola

Animal models could nonetheless provide support for similarity of protective immune responses across different antigens/viruses

Animal models could provide basic information about protective efficacy of vaccines against different viruses

- Animal models also allow dissection of immune system components, e.g., via transgenic animals and passive transfer studies

While animal data could provide strong support for immunobridging, this likely would not be “animal rule” since the primary data would come from comparisons of human immune responses

Regulatory pathways for demonstrating efficacy

In the US, “traditional approval” can be based on clinical studies or a well-established immune marker that predicts protection

“Animal rule” and “accelerated approval” are based on “reasonable likelihood of clinical benefit” standard in each case

- Additional specific criteria apply
- Additional post-marketing data would be needed

Other countries have similar mechanisms

Conclusions

For platforms with known efficacy against a filovirus, data to support immunobridging to support efficacy of new antigens (within the same platform) against different filoviruses could be obtained

If comparable immune responses could be demonstrated, and if there were data supporting the likelihood that comparable immune responses would lead to comparable efficacy, this likely would (at least) show reasonable likelihood that a new vaccine would be effective

There has been skepticism about immunobridging to new platforms for filoviruses