Next Generation Sequencing (NGS)

New interesting technique to detect adventitious agents in biological products

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Disclaimer

- Although I have been a member of the CHMP, my presentation might not be the view of the CHMP, the European Medicines Agency (EMA), the Belgian Medicines Commission, neither of the Vaccine Working Party.

- My presentation is a personal viewpoint and binds in no way the organisations mentioned before.

Declaration of interest

I have signed consultancy contracts with more than 100 organisations and companies under which

- WHO
- B&MGF
- Universities of Antwerp, Ghent, Leuven, Namur, Brussels, Paris, Lausanne, Köln, …
- Big pharma
- Medium pharma
- Small pharma

Vaccine Advice

IABS

Sources

Regulatory guidance documents:

- **ICH Q5A: ICH Guideline Q5A(R2) on viral safety evaluation of biotechnology products derived from cell lines of human or animal origin - Scientific guideline**
  - https://database.ich.org/sites/default/files/Q5A%28R1%29%20Guideline_0.pdf
  - https://www.ema.europa.eu/en/ich-guideline-q5ar2-viral-safety-evaluation-biotechnology-products-derived-cell-lines-human-animal

Sources (2)

A number of interesting articles (open access):

- **Overview of Next-Generation Sequencing Technologies:**
  https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6020069/
- **What is next generation sequencing?**
  https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3841808/
- **Report of the third conference on next-generation sequencing for adventitious virus detection in biologics for humans and animals**
  https://doi.org/10.1016/j.biologicals.2023.101696
- **IABS/DCVMN webinar on next generation sequencing**
  https://doi.org/10.1016/j.biologicals.2022.12.001
- **Report of the second international conference on next generation sequencing for adventitious virus detection in biologics for humans and animals**
  https://doi.org/10.1016/j.biologicals.2020.06.002
- **Report of the international conference on next generation sequencing for adventitious virus detection in biologicals**
  https://doi.org/10.1016/j.biologicals.2018.08.002

Introduction

What is New Generation Sequencing?

Next-generation sequencing (NGS) is a technology for determining the sequence of DNA or RNA to study genetic variation associated with diseases or other biological phenomena.

NGS enables the interrogation of hundreds to thousands of genes at one time in multiple samples, to identify adventitious agents in these samples as well as discovery and analysis of different types of genomic features in a single sequencing run, from single nucleotide variants (SNVs), to copy number and structural variants, and even RNA fusions.

NGS provides the ideal throughput per run, and studies can be performed quickly and cost-effectively.

Some people prefer Whole Genome Sequencing (WGS) or High Throughput Screening (HTS) but most my regulatory colleagues prefer NGS.

Introduction

What is New Generation Sequencing?

- NGS could replace in the near future a number of time consuming and costly viral detection assays in the control of vaccine badges produced in recombinant settings.
- The speed, throughput, and accuracy of NGS has revolutionized genetic analysis and enabled new applications in genomic and clinical research, reproductive health, and environmental, agricultural, and forensic science.
- NGS will become the major way for showing the quality of vaccines in showing the absence of adventitious agents.
- NGS is propagated by US and EU manufacturers and regulators as the technique has become fast, cheap and last but not least highly efficacious: all known adventitious agents will be found, by using NGS.
- As many vaccines are produced in LMIC countries IABS is convinced that this information should not only be discussed with US-EU academia, industries and regulators, but we should involve LMIC regulators, industries as well.

Introduction (2)

What is the program of this session?

- We have 2 presentations on the use of NGS by members of DCVMN
- And we invited 2 regulatory experts from the EU experts in NGS to comment and put remarks and questions to help the audience better understand the pro's and the con's of NGS and where we should go to.
- We of course hope for an active contribution of the audience.

Conclusions

Adaptive design is a major step forward in medicinal product development, but…

- **This technique is based on pro-actively thinking and writing: all possible decisions should be written in the protocol**
- **Time gain lies primarily in defining the right dose**
- **We need experienced people:**
  - **To write the protocol**
  - **To set up the decision criteria**
  - **Take the decisions**
  - **Execute the CTA's**
- **Information exchange with regulators is crucial**
  - **EU & US are on the same page: guidance documents are quite similar.**