AGENZIA ITALIANA DEL FARMACO

WMA Conference
on the Revision of the Declaration of Helsinki
- focused on research in resource-poor settings -
18-19 January 2024
Vatican City

Session 4: Experiences of conducting medical research in low-resourced settings under the DoH (B)

….through the lens of Sickle cell disease and the regulatory perspective…

Enrico Costa
Head of International Affairs Department – AIFA
Member of the Committee for Orphan Medicinal Products - EMA

1

Public Declaration of transparency/interests*

The view and opinions expressed are those of the individual presenter and should not be attributed to AIFA

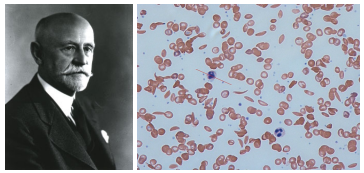
Interests in pharmaceutical industry	NO	Current	From 0 to 3 previous years	Over 3 preavious years
DIRECT INTERESTS:				
1.1 Employment with a company: pharmaceutical company in an executive role	x	☐	☐	☐ mandatory
1.2 Employment with a company: in a lead role in the development of a medicinal product	x	☐	☐	☐ mandatory
1.3 Employment with a company: other activities	x	☐	☐	☐ optional
2. Consultancy for a company	x	☐	☐	☐ optional
3. Strategic advisory role for a company	x	☐	☐	☐ optional
4. Financial interests	x	☐	☐	☐ optional
5. Ownership of a patent	x	☐	☐	☐ optional
INDIRECT INTERESTS:				
6. Principal investigator	x	☐	☐	☐ optional
7. Investigator	x	☐	☐	☐ optional
8. Grant or other funding	x	☐	☐	☐ optional
9. Family members interests	x	☐	☐	☐ optional

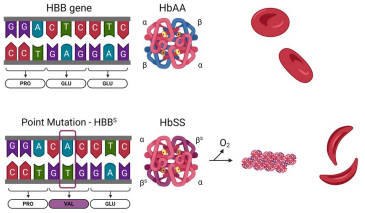
*Enrico Costa, in accordance with the Conflict of Interest Regulations approved by AIFA Board of Directors (Resolution n. 37 dated 13/10/2020).

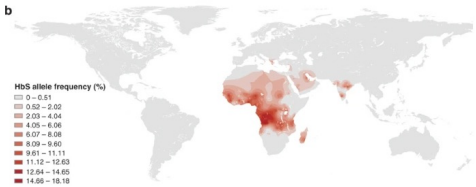
N.B. I am not receiving any compensation

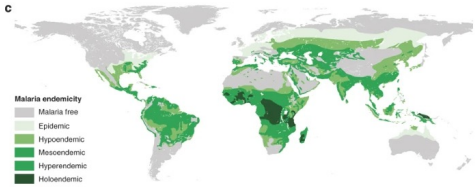
2

Sickle cell disease, a brief introduction





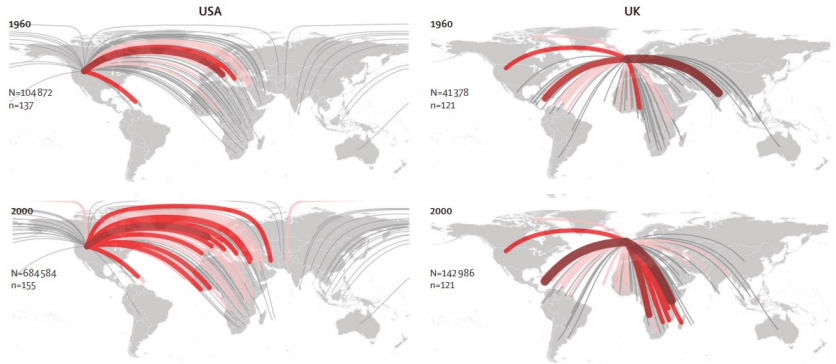




3

Global migration and the changing distribution of sickle haemoglobin: a quantitative study of temporal trends between 1960 and 2000

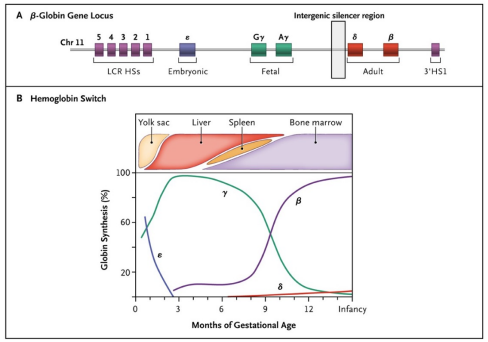
Frédéric B Piel, Andrew J Tatem, Zhuojie Huang, Sunetra Gupta, Thomas N Williams, David J Weatherall



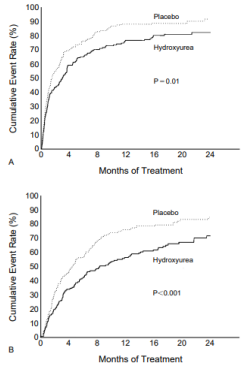
Lancet Glob Health 2014; 2: e80–89

4

Foetal Haemoglobin (HbF) and Hydroxyurea



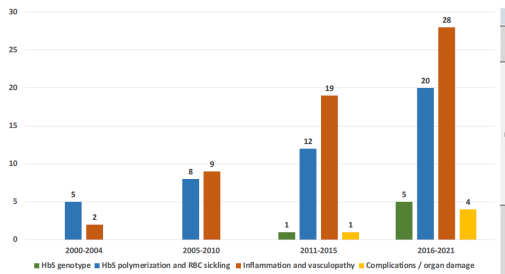
N Engl J Med 2011



Charache et al. N Engl J Med 1995

5

Successes and pitfalls in orphan drug development for SCD



- 20 years of sickle cell orphan drug development has ~12% success rate, with highest rates when targeting early pathophysiological steps.
- Failure rates for lack of efficacy were highest in late stages of drug development when vaso-occlusive crisis was the key clinical endpoint.

Costa et al. (under revision)

6

Protections for clinical trials in low and middle income countries need strengthening

Revision of Helsinki declaration aims to prevent exploitation of study participants (*BMJ* 2013;347:f6401)

Table 1 | Changes relating to benefits for clinical trial participants and communities in Declaration of Helsinki, 2000 to 2013

Edinburgh, 2000[1]	Note for clarification, 2004[2]	Seoul, 2008[3]	Fortaleza, 2013[4]
	Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review	14. The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits	22. In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions
		17. Medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research	20. Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research
30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study	It is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care	33. At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it—for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits	34. In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial

***BMJ* 2014;349:g4254**

7

Pivotal clinical trials of medicines approved for SCD in the US and the EU

Costa et al. *in submission*

8

The Meaning of Informed Consent: Genome Editing Clinical Trials for Sickle Cell Disease

Stacy Desine[a], Brittany M. Hollister[a], Khadijah E. Abdallah[a], Anitra Persaud[a], Sara Chandros Hull[b,c], and Vence L. Bonham[a]

The **objective** of this study was to investigate the views of adults with SCD, parents, and healthcare providers on what information is required to sufficiently understand the risks and benefits of consenting to participate in a genome editing clinical trial.

The general goal of informed consent for genome editing trials is the same as for other clinical trials: ensuring the participant understands the aims of the trial; procedures, risks and benefits;

Understanding genome editing trials is especially complex, however, due to the nature of the treatment and potential for misunderstanding the treatment, its goal, and its process

- Desired information about CRISPR genome editing
- Concerns about side effects of treatment
- Mechanism of action: How does it work?
- Inclusion criteria for being a study participant
- Impact on quality of life

9

Advance the African Medicines Agency to benefit health and economic development

The African Medicines Agency can enable African people to live the healthier lives they deserve while boosting continental trade and economic development, write **Michel Sidibé and colleagues**

Michel Sidibé, [1] Abdoul Dieng, [2] Kent Buse[3]

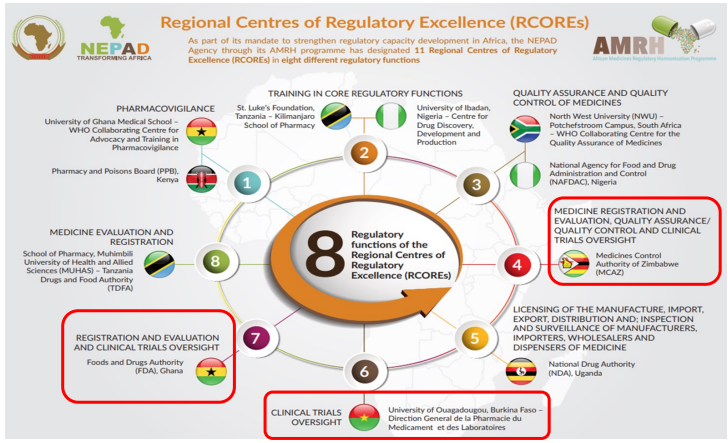
The aim is to **improve access to safe, effective, affordable, and quality medical products** across African countries by **creating and enabling regulatory environment.**

Developing **common standards and regulations**, **coordinating reviews of clinical trial applications**, **coordinating the evaluation** of medical products and pharmaceutical ingredient manufacturing sites, and **sharing information** about products authorised for marketing

The **entry** of new products into the healthcare system can be **accelerated**, the **costs of medicines can be decreased**, **access to medicines will be increased**, and that **fake, substandard, and harmful products will be crowded out**.

BMJ 2023;380:p386 | doi: 10.1136/bmj.p386

10



11

Conclusions

Globalization and complexity of clinical research in the regulatory space have been increasing

Global movements of people: north-to-south and south-to-north trajectories

The implementation of the AMA can improve the reliability of the whole pharmaceutical ecosystem including clinical trials, so protecting the most vulnerable communities

12