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Public-Private Partnerships to Promote Biosimilar Access, Affordability, and Patient Safety in Emerging Markets

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Abstract

Biosimilars have tremendous potential to reduce the costs of biologic therapies. Emerging markets may represent a significant fraction of future biosimilar production, development, and consumption. Yet safety concerns, price sensitivity, and lower quality standards represent challenges to public health in emerging markets. Well-crafted public-private partnerships between public health agencies, local biosimilar manufacturers, and global pharmaceutical firms that leverage advantages of each can result in biosimilar production targeted to local public health needs using a safety-focused infrastructure. The key clinical risk for biosimilars—immunogenicity—can be addressed by leveraging patient safety tools and incentivizing local producers to work with global drug firms and local public health departments, while technical expertise in large scale current Good Manufacturing Practices ("cGMP") can be provided by global drug firms. Once this infrastructure is in place, public health departments in partnership with their local and global producers can provide incentives, such as limited market exclusivity, to produce drugs in these emerging markets at higher than required levels (i.e., at or above cGMP). They can also target specific immunotherapies relevant for that particular community's needs. By doing so, global firms, local producers, and local public health departments can provide direction and improved quality and safety so benefits can inure directly to these populations. Moreover, as global populations begin to rely on these emerging market-produced drugs, greater access, sustainability and affordability may also be promoted.

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I. INTRODUCTION

Biologic drugs are complex biotechnology molecules representing the next generation of pharmaceutical treatments and innovation.[1] By 2015, eight of the ten top-selling medications are predicted to be biologics,[2] and global spending for biologics is expected to reach $200 billion.[3] Yet biologic development is expensive, with growth in the number of associated clinical trials but a lack of sufficient corresponding drug approvals.[4] In crucial emerging markets, including Brazil, Russia, India, and China, biologic treatment can be cost-prohibitive to the point of impeding access, including costs greater than $40,000/year due to limited drug manufacturing and coverage.[5]

However, price reductions and increased access can occur with biosimilar development. Biosimilars are biologic products not produced by the original manufacturer but that may be substantially similar to originator products. It is crucial to note, however, that biosimilars are more complex than their "generic" drug counterparts in both molecular and organic structure as well as their manufacturing processes.[6] Hence, biosimilars can only be similar to, not identical

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[1] *What Are "Biologics" Questions and Answers*, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMIN., http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm133077.htm (last updated Apr. 14, 2009).

[2] Ed Silverman, *Drug Pipeline Loses Pressure*, MANAGED CARE (Aug. 2010), http://www.managedcaremag.com/archives/1008/1008.pipeline.html.

[3] Tim K. Mackey & Bryan A. Liang, *Promoting Access to Biosimilars: A Public–Private Partnership Model for Biosimilar Development in Underserved Populations*, 1(2) GENERICS AND BIOSIMILARS INITIATIVE J. 84, 84 (2012), *available at* http://gabi-journal.net/promoting-access-to-biosimilars-a-public%E2%88%92private-partnership-model-for-biosimilar-development-in-underserved-populations.html.

[4] G. R. Woollett, *Innovation in Biotechnology: Current and Future States*, 91(1) CLINICAL PHARMACOLOGY & THERAPEUTICS 17, 19 (2012).

[5] *Biosimilars in Emerging Markets*, BIOSIMILAR NEWS (Sept. 5, 2011, 10:16 AM), http://www.biosimilarnews.com/biosimilars-in-emerging-markets (noting the very high cost of some biologic treatments); Hillary J. Gross & Feffrey Vietri, *Barriers to Biologic Therapy Use for Autoimmune Disorders in Emerging Markets*, INT'L SOC'Y FOR PHARMACOECONOMICS AND OUTCOMES RESEARCH: 16TH ANNUAL EUROPEAN CONFERENCE (Nov. 2-6, 2013), http://www.kantarhealth.com/docs/publications-citations/barriers-to-biologic-therapy-use-for-autoimmune-disorders-in-emerging-markets-.pdf?sfvrsn=4 (linking the high cost of treatment to manufacturing).

[6] *Biosimilars in Emerging Markets*, *supra* note 5.

with, originator biologic drug formulations due to the complexity, large size, and cell origin of biologic drugs.[7]

Being a nascent market, the European Union ("EU") has only approved biosimilars since 2006; the United States has only released guidelines and recently approved biosimilars as investigational new drug applications.[8] Other countries such as Australia, Japan, Canada, and South Africa are developing biosimilar pathways, as is the World Health Organization.[9] Ultimately, emerging markets are anticipated to drive and dominate biosimilar development due to drug price sensitivity, double-digit annual market expansion, and significantly lower development costs.[10] Indeed, bringing a biosimilar to market in India does not require current good manufacturing practices ("cGMP") as mandated in developed country markets.[11] In addition, multinational pharmaceutical firms have not focused efforts in emerging markets nor on these products: only 3.8% of the fifteen largest global drug firms' revenues are derived from sales in Brazil, Russia, India, and China, and these revenues are from blockbuster drug sales efforts, not biosimilar or other generic formulation entry.[12]

The social potential for biosimilars is thus significant. There is, however, a fundamental and difficult safety issue associated with biologics and biosimilar development: immunogenicity, which arises when a drug induces unwanted, life threatening immune reactions.[13] Although these reactions can represent a major medical emergency, they are notoriously difficult to predict.[14] For example, an EU-licensed version of erythropoietin developed in the United States caused severe immunogenicity reactions due to a processing change though no reactions were ever observed by patients in the United States.[15] For some of these patients, the processing change resulted in death, permanent dependency on transfusion, and/or renal transplant.[16] However, where consistent and appropriate scientifically-based regulatory standards are applied,

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[7] *Id.*

[8] Alexander Gaffney, *FDA Releases Fourth Biosimilar Guidance Outlining New Types of Meetings,* REGULATORY FOCUS (Apr. 1, 2013), https://www.raps.org/focus-online/news/news-article-view/article/3106/fda-releases-fourth-biosimilar-guidance-outlining-new-types-of-meetings.aspx.

[9] *European Union*, ALLIANCE FOR SAFE BIOLOGIC MEDICINES, http://safebiologics.org/european-union.php (last visited Mar. 4, 2014).

[10] *See Pharmaceuticals & Biotech Industry Global Report*, IMAP HEALTHCARE REP. (IMAP), 2011, at 6-7 [hereinafter IMAP], *available at* http://www.imap.com/imap/media/resources/IMAP_PharmaReport_8_272B8752E0FB3.pdf (noting largest global markets are emerging markets and China).

[11] S.D. Roger & D. Goldsmith, *Biosimilars: It's Not as Simple as Cost Alone*, 33(5) J. CLINICAL PHARMACY & THERAPEUTICS 459, 461 (2008).

[12] *See* IMAP, *supra* note 10, at 6-7.

[13] CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMIN., IMMUNOGENICITY ASSESSMENT FOR THERAPEUTIC PROTEIN PRODUCTS 2 (2013), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM338856.pdf.

[14] *See* Paul Chamberlain, *Immunogenicity of Therapeutic Proteins: Part I: Causes and Clinical Manifestations of Immunogenicity*, 5 REG. REV. 4, 4 (2002).

[15] Bryan A Liang & Timothy Mackey, *Emerging Patient Safety Issues Under Health Care Reform: Follow-On Biologics and Immunogenicity*, 7 THERAPEUTICS & CLINICAL RISK MGMT. 489, 490 (2011); *see also* Charles L. Bennett et al., *Long-Term Outcome of Individuals with Pure Red Cell Aplasia and Antierythropoietin Antibodies in Patients Treated with Recombinant Epoetin: A Follow-Up Report from the Research on Adverse Drug Events and Reports (RADAR) Project*, 106(10) BLOOD 3343, 3343-44 (2005), *available at* http://bloodjournal.hematologylibrary.org/content/106/10/3343.full.pdf (discussing reports of pure red cell aplasia in patients receiving erythropoeitin).

[16] Liang & Mackey, *supra* note 15, at 490.

biosimilar development can be safely achieved alongside the attendant cost savings and improved access, which has been recently demonstrated in Europe.[17]

Emerging markets are consequently at a watershed moment. Emerging market needs are shifting from developing country concerns (e.g., infectious and other communicable diseases) to developed country needs (e.g., cancer treatment and other non-communicable diseases).[18] Hence, emerging market populations increasingly require expensive, complex biologic drugs at reduced prices while their governments simultaneously attempt to promote access and increase investment in infrastructures that address the accompanying safety concerns. Lack of access to these therapies may postpone treatment of otherwise treatable diseases, and preclude access to unmet health needs for many populations while also raising treatment costs.[19]

Furthermore, a spectrum of stakeholders are involved in biosimilar development, many of whom may be leveraged to promote safe biosimilar access and development. Private sector manufacturers and global pharmaceutical firms as well as local public health agencies all have important needs to promote high quality, competitive biosimilars. Each has important capacities that can be leveraged through well-structured public-private partnerships ("PPPs").[20] These PPPs can promote safety and cheaper biosimilar development through lower labor costs and technology transfer, and subsequently provide access to therapies relevant to the particular country's specific public health needs.[21] Building on strengths and shared interests of public health agencies, local manufacturers, and global pharmaceutical firms, these PPPs can drive competition for higher quality, essential biosimilars beyond in-country mandated levels, and can incentivize development of drugs relevant to the public health needs of that community.

In Part II, we describe medication patient safety systems, and how extant tools are available that can be applied to biosimilars. These include designation of biosimilars as high-alert medications, use of local manufacturer communication infrastructures for patient outreach and education, and use of local public health agency knowledge of community needs and communication systems to develop additional education and dissemination, both for providers and patients.

In Part III, we describe integration of the extant biologic patient safety tools with additional safety policies to promote higher-level quality production. This includes focusing upon a single identified biosimilar for rapid immunogenicity source determination. In addition, PPPs can be developed that incentivize local manufacturers to produce at higher quality levels in exchange for government-based limited exclusivity, procurement contracts, and other benefits that can be coordinated and made available with public health agencies and hospitals.

In Part IV, we make a proposal to integrate local production for targeted therapies at cGMP levels—the standard for highly regulated, developed markets—into emerging market production of biosimilars. Incentivizing the identification of priority disease states and therapies by public health agencies can promote local high quality treatments, improve needed access to essential treatments, and promote product use in developed markets. This strategy has the

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[17] Mark McCamish & Gillian Woollett, *The State of the Art in the Development of Biosimilars*, 91(3) CLINICAL PHARMACOLOGY & THERAPEUTICS 405, 405 (2012).
[18] Rachel Nugent, *Chronic Diseases in Developing Countries: Health and Economic Burdens*, 1136 ANN. N.Y. ACAD. SCI. 70, 70 (2008).
[19] McCamish & Woollett, *supra* note 17, at 405.
[20] Sania Nishtar, *Public-Private 'Partnerships' in Health – A Global Call to Action*, 2 HEALTH RES. POL'Y & SYS. 5, 7 (2004); Mackey & Liang, *supra* note 3, at 85.
[21] Nishtar, *supra* note 20, at 7; *see also* Liang & Mackey, *supra* note 15, at 491-92.

potential to increase the cost savings from, and simultaneously enhance access to, biosimilars globally.

II. BIOLOGIC PATIENT SAFETY SYSTEMS AND PUBLIC-PRIVATE PARTNERSHIPS

A. *Immunogenicity*

The paramount issue in biosimilar integration into emerging market delivery systems is addressing the threat of immunogenicity. Because manufacturers without the benefit of originator information and data will largely produce biosimilars,[22] immunogenicity issues may be magnified in emerging markets.

This situation is exacerbated by the fact that there is no uniform method of biosimilar naming, which makes rapid identification of the manufacturing source highly challenging.[23] In addition, varying laws and regional and bilateral trade agreements protect exclusivity of biologic clinical test data, increasing the opportunity for safety failure from a lack of necessary data.[24] Such exclusivity grants may complicate attempts to develop safe and uniform biologic products.[25] Moreover, emerging market public health agencies and local manufacturers likely lack the experience or necessary infrastructure to address emerging immunogenicity challenges, adding to the vulnerability of emerging markets to immunogenicity events.

B. *Addressing Immunogenicity with Public-Private Partnerships*

1. High Alert Medications: Providers

Public-private partnerships could reduce immunogenicity risks by promoting patient safety standards. For example, public health agencies could create "high-alert medication" warnings similar to those established by the United States Institute for Safe Medication Practices ("ISMP").[26] Local public health departments would use established provider communications systems to disseminate information deeming biosimilars high-alert medications. This information would be accompanied by publicly-available ISMP tools and recommendations, such as sign out sheets, warnings in prescriber areas, and relevant trainings.

In addition, local manufacturers could coordinate and partner with public health departments to ensure uniform biosimilar packaging and labeling to reinforce this messaging, and ensure that immunogenicity risks are communicated to providers and staff. For example, a simple, inexpensive paper tape label or other standard packaging common to all biosimilars can be announced, designated by local public health agencies, and used by local manufacturers. Uniform packaging and labeling efforts create greater opportunities for coordination between public health agencies, providers, and local manufacturers, allowing more effective and efficient dissemination of biosimilar warnings and general information.

Beyond benefiting clinicians, such a provider education approach would be of tremendous benefit to manufacturers. By participating with public health agencies,

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[22] Bryan A. Liang, Regulating Follow-On Biologics, 44 HARV. J. ON LEGIS. 363, 371 (2007).
[23] Liang & Mackey, *supra* note 15, at 490.
[24] *Test Data Protection for Medical Inventions*, KNOWLEDGE ECOLOGY INT'L, http://keionline.org/testdata (last visited Mar. 4, 2014).
[25] See generally, Henry Grabowski et al., Data Exclusivity for Biologics, 10(1) NATURE REV. DRUG DISCOVERY 15 (2011), *available at* http://fds.duke.edu/db/attachment/1592 (discussing exclusivity and challenges to innovation rather than focusing upon safety).
[26] *ISMP's List of* High-Alert Medications, INST. FOR SAFE MEDICATION PRAC. (2012), http://www.ismp.org/Tools/highalertmedications.pdf; Liang & Mackey, supra note 15, at 491-92.

manufacturers would have lower dissemination costs regarding their drug, show their public concern regarding their product, and provide safety information and marketing simultaneously for their specific product. Public health entities would also benefit significantly. With PPPs, public health authorities can ensure that communication is accurate using manufacturer clinical data, while ensuring that information is balanced and transparent without the use of traditional and questionable aggressive marketing campaigns that have plagued drug marketing in the past.[27]

Ideally, such safety communication systems should be co-developed between the public and private sector to ensure the benefits listed above. This could potentially include development of technical labeling and safety communication details by industry, with final decision-making on form and content by the in-country public health agency and drug regulatory agency. This would allow sharing of firm drug-specific expertise and ensure conformity with national drug labeling and marketing requirements.

2. High Alert Medications: Patients

Building upon provider efforts, patient educational efforts are also critically needed to ensure safe access to biosimilars made available in emerging country markets. PPPs should leverage public health agency knowledge of local needs and existing infrastructure to reach patients, as well as provide easily recognizable information on biosimilars, immunogenicity, and safety through labeling. In addition, local manufacturers should also employ their own community marketing outreach systems, again in coordination with public health messages, to disseminate biosimilar risk information to potential patients.

Global private-sector pharmaceutical partners and manufacturers can contribute to patient-centered immunogenicity information by providing content tailored to a specific biosimilar product used in other markets. This includes particular drug immunogenicity causes related to packaging, storage, administration, and type of patient. Drawing upon the technical experience of complying with labeling and safety warning mandates from drug regulatory agencies when producing previous biosimilar (and biologic) drugs, global pharmaceutical firms can jointly assist with local manufacturers and public health agencies in crafting culturally sensitive and appropriate communications for maximum patient impact and comprehension. In this manner, patients are provided with locally-vetted biosimilar communications that build upon global firm expertise, local manufacturer presence, and public health agency knowledge and dissemination infrastructures.

3. Rapid Reporting and Surveillance

Early detection and surveillance systems are imperative to ensure pharmacovigilance for high-risk drugs such as biosimilars because of the potential for severe and sometimes life-threatening immunogenicity reactions. These rapid reporting and immunogenicity surveillance systems used to establish robust pharmacovigilance can also be jointly created through PPPs.

Global firms have extensive experience developing and using adverse event reporting systems and can provide comparative assessments for emerging markets. Local manufacturers can leverage the foundation of global pharmaceutical firm knowledge regarding reporting and surveillance to provide insights into extant reporting systems and processes being considered, while still remaining sensitive to their specific production environments in the particular

[27] See generally Bryan A. Liang & Tim Mackey, Direct-to-Consumer Advertising with Interactive Internet Media: Global Regulation and Public Health Issues, 305(8) J. AM. MED. ASS'N 824 (2011) (discussing issues with pharmaceutical company marketing and penalties associated with off label marketing).

emerging market. Public health agencies can contribute perspectives on the practical workings of current adverse event detection and surveillance systems and on the potential for integration. This can also include exploration of resources that can be allocated to jointly crafted systems, and it can provide opportunities to identify immunogenicity target strategies within these PPPs.

In combination, a proactively designed, comparatively assessed, and locally sensitive safety structure can result. The system may be built upon emerging technology solutions, including use of electronic auxiliary labels and automated alerts as local health information technology systems develop, as well as social media, mobile handset technology for safety communications, and other technological approaches to address biosimilar immunogenicity where available in emerging markets.

Functionally, the system can also be expanded beyond immunogenicity concerns. A wide array of public health issues implicating a spectrum of communication needs—including drug recalls, other post-market surveillance, counterfeit drugs, food safety, pandemic warnings, and other concerns—can be rapidly communicated using the immunogenicity safety infrastructure. The result can be a jointly-designed, culturally-competent biosimilars education and communication system that maximizes detection of biosimilar patient care concerns and is flexible to permit integration of additional components and to be used for other public health communication goals.

III. PROMOTING QUALITY TO HIGHER LEVELS THROUGH SAFETY POLICY

A. *Using Purchasing Power to Accomplish Safety Goals*

As a safety matter,[28] standardization of purchase and use of biosimilars is crucial. Because of biosimilar naming challenges, governments and facilities using biosimilars should consider purchasing only one authorized version to permit prompt identification and forensic analysis of any product that results in immunogenicity and related adverse patient safety events, avoiding delays in determining which specific biosimilar was used.

Leveraging this need for safety, PPPs that incentivize local producers to manufacture at higher-quality levels can create an infrastructure that results in joint safety engagement. Through PPPs, public health agencies can grant longer term and/or limited exclusive biosimilar supply and procurement arrangements with local firm partners that commit to manufacturing biosimilars at cGMP levels and at agreed-upon prices that ensure domestic access.[29] Global firm partners clearly can contribute in this area due to their extensive technical experience in cGMP production as well as by providing capital investment and potential technology transfer and licensing for the shared effort of creating higher quality biosimilars beyond that level required by the emerging market's domestic laws.

This leveraging of cGMP quality level production is important. Harmonized good manufacturing and science practices in these environments vary, and concerns have been raised

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[28] *See id.* (discussing immunogenicity risks for biosimilars). Note that the "stock out" issue, where medicine availability may be at risk if one producer has a temporary or permanent reduction/cessation in production, can be addressed by having the exclusive manufacturer reserve an estimated 3 month supply as a deposit to the government for use in the event of such supply challenges. This should be coupled with mandated notification requirements for any anticipated shortages, similar to USA efforts. *See* Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, §§ 1001-1008, 126 Stat. 993 (2012) (mandating companies report changes likely to reduce production of life-saving drugs that could lead to a shortage to the secretary of Health and Human Services).

[29] Mackey & Liang, *supra* note 3, at 86.

regarding quality of produced biologics in many emerging economies.[30] Local producers committing to cGMP can consequently obtain local market benefits from higher-level quality production.

Other inducements and benefits for cGMP production can also be considered. Facilitated national formulary inclusion into public hospitals as well as expedited drug regulatory approval and review are both readily available and can serve as persuasive motivators for these quality partnerships.[31] Continued opportunities for leveraging economic benefits with increased quality can be identified, and the PPP strategy can also be utilized when these arise.

B. *Benefits*

Through this approach, both public health and emerging market patients can benefit from local development and manufacturing of essential biologic drugs. This includes potentially lower priced biosimilars to improve access and higher quality products delivered within a vigorous, cooperative, stakeholder-designed drug safety system.[32]

Local manufacturers gain access to manufacturing capacity and the ability to serve the local market. Local manufacturers also gain from capacity strengthening, investment, technical assistance from global innovator firms, and revenue generation from product sales.[33] Global pharmaceutical firms receive an increased market share and ensure appropriate cGMP standards for their associated products while simultaneously serving a market where there may be market or regulatory barriers to entry requiring local expertise. Furthermore, global firm partners can benefit through lower cost biosimilar development at cGMP levels that may ultimately be accessible and reach highly-regulated markets that lack sufficient coverage. This system hence potentially opens up large, developed-country markets that may be crucial for economic viability of biosimilar production by local emerging market manufacturers in the future.

Such combinations could be facilitated through equitable technology transfer arrangements using voluntary or "out" licensing agreements, as well as through potential joint venture efforts with the primary mission of making biosimilars more accessible to populations where such treatments may not be currently available. This can be modeled using offset agreements, as primarily used in defense contracts, whereby a global firm agrees to buy products/services from the national government seeking access to biosimilars in the PPP in order to "offset" some or all of the national government's outlay for the transaction.[34] In this case, a national government through the PPP could request direct offsets (such as co-production with a local manufacturer) or indirect offsets (such as export or marketing assistance or foreign direct investments in infrastructure) to offset the cost of voluntary license fees for technology transfers associated with production of the biosimilar. Either can create important incentives for assessing

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[30] *See* Simon D. Roger, *Biosimilars: How Similar or Dissimilar Are They?*, 11 NEPHROLOGY 341, 344 (2006) (noting less stringent safety requirements in South-East Asian countries); *see also* Roger & Goldsmith, *supra* note 11, at 462 (discussing increased adverse reactions due to small changes in formulation of EPREX).

[31] *See* Mackey & Liang, *supra* note 3, at 86 (noting that drug regulatory agencies will offer expedited review and approval in exchange for agreement to meet cGMP standards).

[32] *Id.* at 86-87.

[33] *Id.* at 87.

[34] An offset agreement is an agreement between two parties whereby a supplier agrees to buy products from the party to whom it is selling, in order to win the buyer as a customer and offset the buyer's outlay. Generally the seller is a foreign company and the buyer is a government that stipulates that the seller must then agree to buy products from companies within their country. *See 76th Annual Report*, 76 BANK FOR INT'L SETTLEMENTS 1, 28 (2006), *available at* http://www.bis.org/publ/arpdf/ar2006e.pdf (describing offset agreements and their use).

markets, technology, and entry points as well as financial relationships that can meet local needs while also providing for expanded uses and commercial opportunities in greater market spheres.

IV. LEVERAGING CGMP SAFETY POLICY FOR TARGETED DEVELOPMENT

PPPs can promote not only high quality biosimilars, they can also result in targeted therapy development sensitive to the localized public health needs of emerging market communities. For example, China has a greater need for liver cancer treatments than does Brazil,[35] and hence would require treatments focused on these disease states to specifically address priority public health needs that remain underserved. As emerging markets and other countries begin to engage and require clinical trials for biosimilar development and approval, PPPs formed for cGMP production can play a significant role in ensuring this public health-targeted product development.

To do so, public health agency PPP partners can identify priority biosimilar candidates that reflect local public health needs, such as the aforementioned example of liver disease in China. In this situation, they can also engage their public health relationships with providers and the community to assist in recruiting participants for multisite clinical trials.[36]

Local producers can leverage their production infrastructure and manufacturing to produce biosimilar candidates at cGMP levels, while also coordinating their own contacts with the provider and patient community to support necessary biosimilar testing. Global firm partners, with their extensive experience in clinical trials design, can assist in guiding these efforts in underserved markets while also providing needed technical and financial capital to promote such work.

These PPPs can consequently accelerate market entry of safe, priority biosimilar drugs produced at levels beyond minimum regulatory standards within a proactive safety structure. Further, this PPP cooperative approach for quality enhancement and targeted public health-sensitive therapies, adopted and adapted, can result in a global health model, as increasing numbers of countries join the "pharmerging" markets and face similar safety, cost, and access concerns.

It should also be noted that benefits from expansion of cGMP manufacturing to a broader array of biosimilar treatments and manufacturing sources will not only inure to emerging markets, but also to highly-regulated markets by providing additional manufacturing sources of high quality drugs. This can increase access and lower costs in these developed markets.

V. CONCLUSION

Overall, stakeholders in emerging markets have significant opportunities to work together and invest in PPP strategies for present and future mutual benefits in biosimilar production. By promoting cooperation and competitive advantages of each stakeholder, PPPs can advance local and global health by ensuring safe and affordable access to essential biosimilar pharmaceuticals.

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[35] *See, e.g.*, *Liver Cancer Statistics*, WORLD CANCER RESEARCH FUND, http://www.wcrf.org/cancer_statistics/data_specific_cancers/liver_cancer_statistics.php (last visited Dec. 30, 2013) (reporting top 19 countries with liver cancer including China and not including Brazil).

[36] Bryan A. Liang & Timothy Mackey, *Tipping Point: Biosimilars, Emerging Markets, and Public-Private Engagement to Promote Global Public Health*, 18(4) J. COM. BIOTECH. 65, 71-72 (2013).