Bulgaria is the 14th country as surface from Europe (110.994 km²) being located between Romania at North, Serbia and Macedonia at West, Greece and Turkey at South and Black Sea at Est, with a population of 7.364.570 inhabitants and a distribution between ethnic groups of 84.4% Bulgarians, 8.8% Turkish, Gypsies 4.9% and 1.9% other. Bulgaria is divided in 24 regions and has one metropolitan area surrounding the capital Sofia.

In March 2013 a number of 847 studies are developed in Bulgaria, some of them completed already, some of them ongoing, recruiting patients.

Bulgaria has a medical system financially supported by taxes and contributions to the National Found for Health Insurance (NHIF), which supports the greatest part of medical services for primary care. Between 2002-2004, 4.3% from national budget was spent for health sector and NHIF contributed with over 60% to this annual spendings. Almost 4.2% from gross national income (GNI) was distributed in 2010 for health expenditure (approx. 1.3 billions euro). The number of medical doctors is 181:100.000 inhabitants (over European average) even there is an acute need of medical personnel (especially general nurses and medical administrative staff) in the hospitals. Life expectancy is below European average, with 73.6 years old and principal death causes are the same as for the rest of Western countries: cardiac disease, cancer and respiratory diseases.

If we talk about the past in clinical trials, the beginning is dated in 1995 with 10 approved studies and has grown significantly in the last years.

Clinical Trials developed in Bulgaria aimed a diverse pathology, the most common being the projects of oncology specialty, clinical pharmacology, cardiology,
By far the center of attraction is the Capital Sofia, university center with a population of inhabitants over 1,200,000. For this reason you can find in Sofia either representatives of pharma sponsors as: Roche, Glaxo SmithKline, Novartis, Merck Serono, Jansen Cilag, Sanofi, Bayer, Johnson & Johnson, Servier, Lilly, Boehringer Ingelheim or local CROs. Two-three pharma sponsors or representatives of international big CROs with small teams have opened their offices in Sofia in the past (e.g. Quintiles 1997, Astra-Zeneca in 2000), now there are more pharma and many CROs from all sizes and coverage.

At the legislative level, the development of clinical trials was done under Drug Law auspices, adopted in 1995, having more than 20 articles reflecting GCP and which had many revisions until 2005. In 2007, the new Drug Law was adopted, chapter 3 comprising 67 articles being dedicated to clinical trials and fully reflecting EU directives requirements. This is the reason why the number of clinical trials has expanded very much since 2007 (i.e. 153 applications to National Drug Agency and 41 approvals in 2007 reached at 230 applications with 221 approvals in 2011). If in 1990’s a consecutive submission to EC and RA was requested for each clinical study, this is not needed anymore, nowadays a simultaneous submission to EC and RA is done and the approval process takes 60 days instead of 90 days as it was in the past. Also, if in the past any SAE should have been reported to the RA, in years of 2000’s only SUSAR must be reported to RA.

Regarding the profile of clinical trials developed in Bulgaria, first studies developed in 90’s were bioequivalence/bioavailability studies, but in the present phase III is the great majority, together with phase II and I and non-interventional studies.

The participating sites are from large university hospitals, oncology specialized hospitals as far as private hospitals and outpatients clinics (almost 200 institutions in the present). It as a true fact that infrastructure was poor at the beginning at the developing CT in Bulgaria, very often investigative centers needed additional equipment such as fax, PC, centrifuges, spirometer,
ECG, fact rarely found in the present, more and more high technology studies being able to be developed in this country. Investigator teams are much more experienced these days than in the past, with many young co-investigators with very good English knowledge, but extremely overloaded and unable to look into details. The quality of data is a good one, Bulgaria served many times like “rescue” country for different studies where the patient population was difficult to be reached in the planned time. No FDA inspection took place until 2004, but today more and more FDA and European authorities inspections are performed.

As for the costs, if we compare with western countries, investigator and hospital “per patient” fees are still low, not as low as they were in 90’, but much more comparable with developed countries requirements in this respect. The investigators are accommodated and use on daily basis the e-CRF and e-diaries, thing which was not possible to use in the past, when data collection had been done only on paper. Patients are more informed, but the patient consent is still very much depending of the “patient-physician” relation.

As for the future, there are few challenges to take into account by the companies which look into enrolling patients for their studies in Bulgaria:

- Saturation with studies in highly competitive areas like oncology, rheumatology
- Overload with studies in some centers
- Increasing costs in “Patient fees”
- Delays in contract management
- Competition with emerging countries/regions
- Loosing competitive advantage in speed and cost

As a conclusion is to say that the development of the clinical trials in this country is very promising, the existing legislative framework is suitable for any pharmaceutical company to direct its actions to Bulgarian patients and the fact that Bulgaria is part of European emerging countries has to be seriously taken into account.

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