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THERAPEUTIC DRUG MONITORING MARKETS *(SAMPLE COPY, NOT FOR RESALE)*

Trends, Industry Participants, Product Overviews and Market Drivers

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1. Overview

1.1 Statement of Report

This report describes a specific segment of the *in vitro* diagnostics (IVD) market known as the therapeutic drug monitoring (TDM) test market. In the current medical diagnostics market, therapeutic drug testing offers promise for higher than average growth and intense technical innovation. This review analyses the size and growth of the TDM market, including factors that influence the various market segments within it and the dollar volume of sales, both in the U.S. and worldwide.

Also examined are:

- Drug analysis technology platforms
- Clinical applications of therapeutic drug testing
- The market for quantitative diagnostic drug tests
- Companies participating in this sector
- New instrumentation
- Trends in the industry
- The internal structure of the therapeutic drug testing sector

1.2 About This Report

This report includes the following features:

- It examines all of the generally-accepted clinical analytical activities in use today in the therapeutic drug testing sector. It includes the prevalent clinical measurement devices and the accompanying reagents and supplies as utilized in hospitals and large reference laboratories.
- It discusses the potential benefits of the therapeutic drug testing market for various sectors of the medical and scientific communities, and it assesses the market drivers and bottlenecks from the perspective of these communities.
- It establishes the current total market size and future growth of the therapeutic drug testing market and analyzes the current size and growth of various segments.
- It assesses various business models in therapeutic drug testing and provides strategic recommendations for near-term business opportunities.
- It examines the products offered and roles played by companies that have invested significantly in this market, and it provides current and forecasted market shares by these companies.

The main objectives of this analysis are:

- Identifying viable technology drivers through a comprehensive look at platform technologies for therapeutic drug testing, including enzyme immunoassays such as CEDIA and EMIT, high pressure liquid chromatography, gas chromatography and automated laboratory chemistry instruments.
- Obtaining a complete understanding of the chief therapeutic testing assays—*i.e.*, screening, prognostic, monitoring, pharmacogenomic—from their basic principles to their applications.
- Discovering feasible market opportunities by identifying high-growth applications in different clinical diagnostic areas and by focusing on expanding markets.
- Focusing on global industry development through an in-depth analysis of the major world markets for therapeutic drug testing, including growth forecasts.
- Understanding the business issues that go into justifying high end analysis.

1.3 Scope of the Report

The goal of this study is to review the market for therapeutic drug testing equipment and supplies using reagents and instruments for analysis of individual components in body tissues and fluids (particularly blood). This is in contradistinction to analysis of drugs of abuse, the market for which are examined in a separate TriMark report. Toward this goal, this review answers the following key questions:

- Which companies are utilizing cutting-edge technologies to develop, validate and market therapeutic drug testing assays for clinical use?
- Which new therapeutic drug tests show the most promise for approval?
- What are the economic challenges to gaining approval?
- How can regulatory oversight drive approval and adoption of new technologies?
- Which alliances show the greatest synergy in bringing therapeutic drug testing to market?
- Which shared technologies are driving the most encouraging development?

This examination surveys most of the instrument companies known to be currently marketing, manufacturing or developing instruments and reagents for the therapeutic drug testing market, in both the U.S. and the world. Each leading company is discussed in depth, with sections on its history, product line, business and marketing analysis, and a subjective commentary of the company's market position.

This analysis emphasizes the companies that are actively developing and marketing immunoassay clinical laboratory instrumentation, reagents and supplies for performing therapeutic drug testing tests. The emphasis in this report is on the clinical use of therapeutic drug testing tests.

The reader should consult other TriMark Publications reports at <http://www.trimarkpublications.com> for detailed discussions of important individual market segments related to the therapeutic drug testing market, such as clinical chemistry testing, high-growth diagnostic tests markets, and drugs of abuse testing. TriMark provides a separate market report called *Mass Spectroscopy in the Clinical Laboratory Market*, which emphasizes the analytical methods and technology platforms sometimes used in drugs of abuse testing. TriMark's *Drugs of Abuse Testing* report discusses illegal or abusive patient drug testing.

1.4 Objectives

The emphasis in this report is on the clinical use of therapeutic drug testing tests and their development into the instrument mixture of clinical laboratory space.

The principle objective of this study is to review the market for therapeutic drug testing equipment and supplies using reagents and instruments for analysis of individual components in human biological samples. The report also defines the dollar volume of sales, both worldwide and in the U.S., and analyzes the factors that influence the size and the growth of the market segments. The subsections of the therapeutic drug testing market segment are examined in detail, including: major therapeutic drugs requiring monitoring, clinical testing markets, trends, analysis, SWOT, challenges and business decisions.

In this report, we:

- Assess the therapeutic drug testing market drivers and bottlenecks from the perspective of the medical and scientific communities.
- Discuss the potential benefits of the therapeutic drug testing market for various sectors of the medical and scientific community.
- Establish the current total market size and future growth of the therapeutic drug testing market and analyze the current size and growth of various segments.
- Provide current and forecasted market shares by the company.
- Provide strategic recommendations for near-term business opportunities.
- Assess current commercial uses of the therapeutic drug testing market.

On a more technical level, this report:

- Discuss the problems of using indirect methods such as immunoassays for analyzing complex biological fluids when making diagnostic decisions and their replacement with technology platforms.
- Review the strategies available for sample preparation
- Differentiate the strategies of toxicology analysis to best fit the clinical requirements
- Evaluate the applications of new technologies to the clinical laboratory assessment of therapeutic drugs

This review answers the following key questions:

- Which companies are utilizing cutting-edge technologies to develop, validate and implement drug tests for clinical use?
- What impediments still exist to incorporating promising drug testing tests into clinical practice?
- What are the economic challenges to approval?
- How can regulatory oversight drive approval and adoption of new technologies?
- Which alliances show the greatest synergy in bringing therapeutic drug testing tests to market?
- Which shared technologies are driving the most encouraging development?
- How are businesses entering the clinical lab testing space by leveraging therapeutic drug testing.

1.5 Methodology

The author of this report holds a Ph.D. in medicine/immunology from the Royal College Surgeons of Ireland and has completed post-doctoral studies and lecturing in Trinity College Dublin and University College Cork. The author has many decades of experience in scientific writing and as a medical industry analyst. She has over ten years of experience as a director in laboratory testing and instrument and reagent development technology, as well as extensive experience in senior level positions in biotech and medical service companies. The editor of this report is a Ph.D. in biochemistry from the University of Liverpool and an MBA from Oxford Brookes University with many decades of experience in science writing and as a medical industry analyst. The senior editor holds a Ph.D in biochemistry from the University of Minnesota. He is Board Certified in Laboratory Medicine and is a Fellow of the Society of Clinical Biochemistry. He was a director and has held other senior positions in clinical laboratories as well as in the diagnostic industry.

Company-specific information is obtained mainly from industry trade publications, academic journals, news and research articles, press releases and corporate websites, as well as annual reports for publicly-held firms. Additional sources of information include non-governmental organizations (NGOs) such as the World Health Organization (WHO) and governmental entities such as the Department of Health and Human Services (HHS), the National Institutes of Health (NIH), the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC). Where possible and practicable, the most recent data available have been used.

Some of the statistical information was taken from Biotechnology Associates' databases and from TriMark's private data stores. The information in this study was obtained from sources that we believe to be reliable, but we do not guarantee the accuracy, adequacy or completeness of any information or omission or for the results obtained by the use of such information. Key information from the business literature was used as a basis to conduct dialogue with and obtain expert opinion from market professionals regarding commercial potential and market sizes.

The authors have contacted numerous pharmacos including Roche, Siemens, ThermoFisher, Beckman Coulter, Alere, Bayer, Adnagen, AMDL, BioMerieux and Randox for their professional opinion on the market value. In addition, the editor has contacted Abbott for their estimates of the global TDM market. The authors have also communicated with business and academic contacts and various international associations such as the EDMA, IFCC, BIVDA, IVD Australia and the IATDMCT and also pharmacoeconomic academic specialists for information.

Primary Sources

TriMark collects information from hundreds of Database Tables and many comprehensive multi-client research projects, as well as Sector Snapshots that it publishes annually. TriMark extracts relevant data and analytics from its research as part of this data collection.

Secondary Sources

TriMark uses research publications, journals, magazines, newspapers, newsletters, industry reports, investment research reports, trade and industry association reports, government-affiliated trade releases and other published information as part of its secondary research materials. The information is then analyzed and translated by the Industry Research Group into a TriMark study. The Editorial Group reviews the complete package with product and market forecasts, critical industry trends, threats and opportunities, competitive strategies and market share determinations.

TriMark Publications Report, Research and Data Acquisition Structure

The general sequence of research and analysis activity prior to the publication of every report in TriMark Publications includes the following items:

- Completing an extensive secondary research effort on an important market sector, including gathering all relevant information from corporate reporting, publicly-available data and proprietary databases.
- Formulating a study outline with the assigned writer, including important items, as follows:
 - Market and product segment grouping, and evaluating their relative significance.
 - Key competitors' evaluations, including their relative positions in the business and other relevant facts to prioritize diligence levels and assist in designing a primary research strategy.
 - End-user research to evaluate analytical significance in market estimation.
 - Supply chain research and analysis to identify any factors affecting the market.
 - New technology platforms and cutting-edge applications.
- Identifying the key technology and market trends that drive or affect these markets.
- Assessing the regional significance for each product and market segment for proper emphasis of further regional/national primary and secondary research.
- Completing a confirmatory primary research assessment of the report's findings with the assistance of expert panel partners from the industry being analyzed.

1.6 Executive Summary

TDM is an important clinical assessment of drug plasma concentrations that also yields information regarding the efficacy, toxicity levels and potential drug-drug interactions of agents with a narrow therapeutic index. TDM is increasingly important in the healthcare sector as it becomes part of a lifetime regime for patients with chronic conditions such as HIV infection. Ultimately, TDM testing provides clinical information to optimize dosage regimes and prevent adverse reactions and lack of treatment compliance.

Primary research from leading suppliers shows that the global TDM market is estimated to be worth in excess of \$ [REDACTED] in [REDACTED] and that the global market is growing at between [REDACTED]-[REDACTED]% annually. Based on the available evidence, the global TDM market is predicted to be valued at approximately \$ [REDACTED] by [REDACTED] (CAGR [REDACTED]%). Growth rates during the earlier stages of this markets development were higher, while the value of the market was relatively low. As the market value started to increase between [REDACTED] and [REDACTED], the annual growth rate declined slightly, but is expected to increase again as the market expands and the advantages of therapeutic drug monitoring is appreciated in the maturer markets and as the techniques and products appear in the emerging markets.

[REDACTED] percent of the global TDM market has been attributed to the TDM market in the U.S. with the European market accounting for approximately [REDACTED]% of the global market and Japan representing [REDACTED]% and remaining [REDACTED]% scattered around the other countries with more developed healthcare systems.

The U.S. is by far the largest single market and represented revenues sales of approximately \$ [REDACTED] in [REDACTED]. It is predicted that the market is growing rapidly and that, by the end of the forecast period, the market will have increased in value to \$ [REDACTED] (CAGR [REDACTED]%). The European market is estimated to be worth \$ [REDACTED] in [REDACTED] and is estimated to increase in value to \$ [REDACTED] (CAGR [REDACTED]%). Japan and other Asian markets are expected to grow rapidly with a CAGR of [REDACTED] and [REDACTED]% respectively over the forecast period. Similarly the emerging markets of Central and Latin America are also expected to exhibit high growth rates in excess of [REDACTED]% over the forecast period. The Middle East and African TDM markets are small, but expected to reach \$ [REDACTED] by [REDACTED], with a CAGR ([REDACTED]-[REDACTED]) of [REDACTED]%.

The TDM testing market is driven by a number of sub-markets within the IVD industry including:

- Proteomic detection analysis in the HPLC and mass spectrometry markets.
- Immunoassay market.
- Sales of narrow therapeutic range drugs.
- Pharmacogenomic/pharmacogenetic analysis technology.
- Chemical analyzers for ultra-large scale, high scale, mid-volume scale and small scale markets.

TDM market growth is specifically driven by:

- The rise of drug profiling.
- New developments in diagnosis and treatment and the more extensive use of pharmacokinetics.
- Increased use of therapeutic drugs for control of pain.
- The need for screening therapeutic drugs that have a narrow therapeutic index.
- Improved detection levels.
- The use mass spec instrumentation for drug-screening confirmation.
- The development of a wide variety of mass spectrometry and separation based technology platforms.
- The use of computer assisted data analysis and multiplexing.
- Higher than average reimbursement levels.

Growth factors for the overall TDM markets include:

- Increases in consumer driven health care.
- An aging population with better health care services.
- Demand for esoteric testing.
- Demand for genetic testing.
- Increased government and private sector participation in therapeutic markets.

Within the IVD market, there are two main areas that are closely associated with TDM:

- Chemistry/chemical analyzers.
- Immunodiagnostic assays.

The chemistry and clinical automation sector is worth \$ [REDACTED] globally with a CAGR of [REDACTED]%. The immunodiagnostic/immunoassay and molecular diagnostic market is worth \$ [REDACTED] per year globally with a CAGR of [REDACTED]%.

The main weaknesses of the current therapeutic drug testing market include:

- Ongoing problems with reimbursement.
- Retrenchment within the hospital field.
- A weak global economy.

- Fluctuating exchange rates weakens the global market further.

Competition within the TDM market will also intensify with respect to chemical and immunodiagnostic analyzers. As technology within these systems increases, the market will flood with high-specification facilities which could drive sales prices down. Global economic retraction has restricted the number of new-hires to the workplace. This in turn has reduced the number of pre-employment drug tests, specifically for addiction to prescription drugs. Expiration of patents and intellectual property claims also threaten this market place.

The therapeutic drug testing market is dominated by a number of large pharma companies. The main competitors are:

- Roche Diagnostics.
- Abbott Laboratories.
- Alere.
- Siemens.
- Orasure.
- Thermo Fisher.
- Beckman Coulter.
- Bayer.

The global TDM market is dominated by eight major suppliers: Roche Diagnostics, Abbott Laboratories, Alere/Inverness Medical Innovations, Siemens Healthcare, Orasure, Thermo Fisher, Beckman Coulter and Bayer AG. The market leader is Roche Diagnostics accounting for █% of the market or the equivalent of \$ █ in revenues. Abbott Laboratories is recognized as the second largest supplier of TDM products with an estimated █% of the global market or the equivalent of sales valued at \$ █. The third largest supplier of TDM products with an estimated █% of the global market or the equivalent of sales valued at \$155 █ is Alere/Inverness Medical Innovations.

These top eight suppliers account for an estimated █% of the global market in █ with the market leader Roche Diagnostics accounting for █% of the market or the equivalent of \$ █ in revenues..

The most commonly monitored therapeutic drugs include:

- Antiepileptics.
- Antiarrhythmics.
- Antibiotics.
- Antineoplastics.
- Bronchodilators.
- Immunosuppressives.
- HIV/AIDS drugs.

Future Perspective

In the future, TDM will concentrate more on improving the patients' quality of life as well as assessing toxicity effects. The objective will be not only to reduce side effects, but also to reduce the number of drug administrations and length of hospital stays. TDM is not just a concentration detection assay, but a way in which to provide individualized therapy. This analysis system requires not only clinical expertise and interpretation, but the integration of pharmacokinetics, pharmacogenetics and pharmacodynamics. During the next decade, the TDM market will undergo significant transformation. These changes will be caused by convergence of new and more stringent regulations; and intensifying competition.

It is possible that, in the future, TDM will involve not the mere measurement and interpretation of drug concentrations, but will include both traditional TDM and pharmacogenetics-oriented TDM. In contrast to traditional TDM, which cannot be performed until after a drug is administered to the patient, pharmacogenetics-oriented TDM can be conducted even before treatment begins.

Other advantages of genotyping over traditional TDM include, but are not limited to, the following: (1) it does not require the assumption of steady-state conditions (or patient compliance) for the interpretation of results; (2) it can often be performed less invasively (with saliva, hair root or buccal swab samples); (3) it can provide predictive value for multiple drugs (*e.g.*, a number of cytochrome P450 (CYP) 2D6, CYP2C 19 or CYP2C9 substrates) rather than a single drug; (4) it provides mechanistic, instead of merely descriptive, information; and (5) it is constant over an individual's lifetime (and not influenced by concurrent drug administration, alteration in hormonal levels or disease states).

Pharmacogenetic information can be applied a priori for initial dose stratification and identification of cases where certain drugs are simply not effective. However, traditional TDM will still be required for all of the reasons that we use it now. In current clinical practice, pharmacogenetic testing is performed for only a few drugs (*e.g.* mercaptopurine, thioguanine, azathioprine, trastuzumab and tacrine) and in a limited number of teaching hospitals and specialist academic centers. It has been proposed that a variety of other drugs (*e.g.* warfarin, phenytoin, codeine, oral hypoglycaemics, tricyclic antidepressants, aminoglycosides, digoxin, cyclosporin, cyclophosphamide, ifosfamide, theophylline and clozapine) are potential candidates for pharmacogenetics-oriented TDM. However, prospective studies of pharmacogenetics-oriented TDM must be performed to determine its efficacy and cost effectiveness in optimising therapeutic effects while minimising toxicity. In the future, in addition to targeting a patient's drug concentrations within a therapeutic range, pharmacists are likely to be making dosage recommendations for individual drugs on the basis of the individual patient's genotype.

Other applications for TDM include antiretroviral (ARV) therapy for the treatment of HIV infection. This position arises because clinicians and pharmacologists are increasingly recognizing:

- The clinical/virological consequences of therapeutic failure.
- That there is a considerable amount of data demonstrating a great deal of inter-individual variability in the concentrations of ARVs among patients.
- That there is a considerable amount of data demonstrating relationships between drug concentrations and responses, either virological or toxicological.

Currently TDM as a method of determining the effect of different patient drug concentrations has been based on the measurement of the plasma concentration of parent drugs. In the future a variety of other methods have been identified that will be used to determine the therapeutic concentration of a particular drug on a patient. These will include:

- The measurement of dose-limiting toxicity of metabolites arising from the exposure to a particular drug.
- The emergence of new analytical methods, such as liquid chromatography combined with mass spectrometry or tandem mass spectrometry as a method of providing major improvements in specificity and sensitivity.
- The development of non-invasive methods such as nuclear magnetic resonance (MRI) for the determination of drugs and active metabolite concentration and/or effects on targeted tissues
- The creation of innovative, highly specific and easier to use software as well as a better knowledge of pharmacokinetic-pharmacodynamic methodology among clinical pharmacist.