LCC Engineering & Trading GmbH
Steinbruchstr 4, CH-4622 Egerkingen, Switzerland
Tel: +41 62 398 52 71, Tel2. +41 79 250 46 02, Fax: +41 62 39852 74
URL: www.chromatographyshop.com, Email : info@chromatographyshop.com-

A revolution is commencing in the post Corona-era

Passion for Professionalism, Precision and Productivity in Drug Discovery

Introduction

In researching Pharmaceutical and Biopharmaceutical companies the job of Drug Discoverer is of **outmost importance**! If Drug Discoverer are not productive employer are forced to acquire bioactive compounds from somewhere else or they must procure a going company with new compounds or close down company.

We like to present you a new and interesting system that is empowering Passion for Professionalism, Precision and Productivity with Drug Discoverer

LCC Engineering & Trading GmbH is since 1995 a globally active engineering and trading company. We sell purification/separation technologies. Furthermore, years back we synthesized intermediates. Today, LCC is focusing on **new tools to improve Passion for Professionalism, Precision and Productivity** (4P Mindset) in pharma research. Unfortunately, most manager do not know what makes a Drug Discoverer productive and successful. They react to it by applying distance and control that strangles creativity. It also requires empathy and relationships with trustworthy and creative external partners. As confidant we were fortunate over many years to talked with thousands of managers and Drug Discoverers in large and small pharma and biotech companies and institutions.

Evolution in Drug Discovery

If one asks Drug Discoverer how they find new drugs then they use the term “serendipity”, - meaning a stroke of luck. For decade’s many researchers try to find laws of nature to convert luck in predictability. They are trying to find rational parameters to increase rate of success. The field is large and complex, and progress is slow.

It is fashionable to believe that artificial intelligence will soon replace human skills in Drug Discovery. However, before we can create a problem solution, we must have a clear definition of the problem. We must know the molecular difference between disease and not a disease?

Research in Genetics, Proteomics and Metabolomics are trying to find clear answers to above question. Once the problem is defined, we must create new products that cure the problem. And finally, we must make sure everything we do is precise and reproducible in every stage of creating the problem solution.

Drug Discoverer are people that create problem solution. So, they must have clear definition of what is” *drug likeness*”. Momentarily we have only a description of the behaviour. https://en.wikipedia.org/wiki/Druglikeness

In small molecules there are the Lipinski Rule of 5 (https://en.wikipedia.org/wiki/Lipinski%27s_rule_of_five) plus some modifications and expansions.

Biopharmaceuticals are being classified (https://en.wikipedia.org/wiki/Biopharmaceutics_Classification_System) to create a kind of focus.

Everything is governed by economic parameters

Managing**/**curing illness/diseases produces costs and revenues, opportunities, and problems. Thus, we need to know the opportunities and its potential.

We divide diseases into three groups

1. Main diseases
2. Orphan diseases
3. Neglected Tropical diseases

There are about 1000 to 1500 Main diseases with more than 200 000 patients' word wide. Large Pharmaceutical/Biopharmaceutical companies invest approx. 15 to 20% of sales into R & D to come up with better solution to address this segment. The cost of developing a new API is approx. USD 4.8 Billion and will take approx. 14 years

There are between 5 000 and 8 000 rare diseases with less than 200 000 patients. Most of them have a genetic basis. A rough estimate is that one out of 15 persons worldwide could be affected by a rare ("orphan") disease – 400 million people worldwide, of whom 30 million are in Europe and 25 million in the United States. there are drugs for about 800 to 1000 orphan diseases. See also:1. https://rarediseases.info.nih.gov/diseases/fda-orphan-drugs 2. https://en.wikipedia.org/wiki/List_of_incurable_diseases

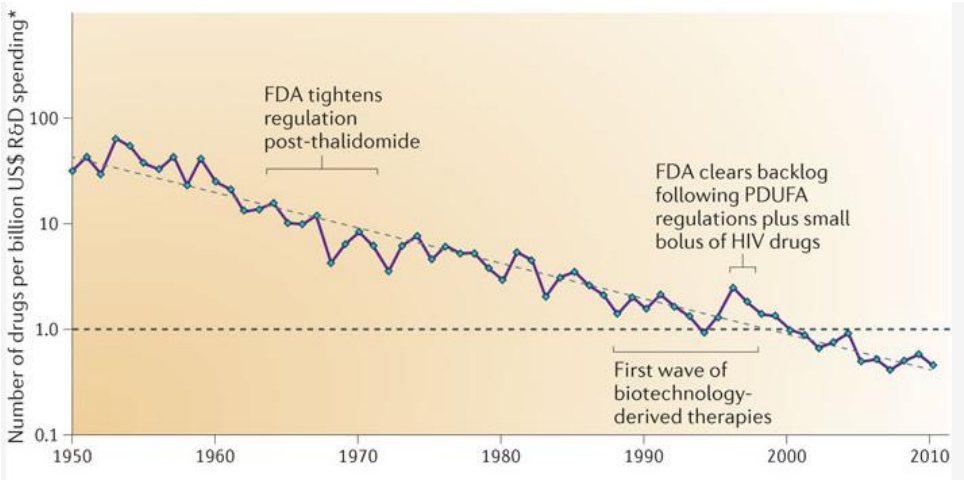
Neglected Tropical Diseases (NTDs) are a group of 20 infectious diseases – caused by parasites, viruses, or bacteria – that disproportionately affect the poor and cause significant health and financial burdens. NTDs are endemic – meaning that they regularly infect humans – in 149 countries, with over 1 billion people infected and 2 billion people at risk. These diseases are largely treatable and preventable through control of the insects that carry these diseases, improved water quality and sanitation, and the efficient delivery of drug treatments already donated by major pharmaceutical companies.

Before we can address above diseases, we have to find new molecules (Chemical or biological entities) that alter the molecule of disease to non-disease without causing any other problems.

By 2015 researcher Jack W. Scannell, Alex Blanckley, Helen Boldon & Brian Warrington investigated the yield of new drugs as a function of R & D investment. They cynically created the term Eroom's law ("Moore" reversed). It depicts that the

number of new drugs approved per billion US dollars spent on R&D has followed a decreasing trend.

Eroom's law indicates the number of new drugs approved per billion US dollars spent on R&D has halved roughly every nine years since 1950.



The graph shows an overall downward trend. However, we also see many short-lived upwards trends followed by a downward trend - this raises Questions?

Indeed, between 1995 and 1998 LCC developed and sold monodisperse Solid Phase Organic Synthesis beads. Migration of molecules into and out of polymeric materials is caused by diffusion – a constant in physics. Our beads provided extremely high reproducibility in solid phase synthesis because they had all the same size, where perfectly round and the polymer network was uniform and swellable. I do not assert that the upwards trend in the graph was caused by our beads. However, I assert that

1. Heterogeneous work in life science is the basis of this graph. Some of the people where directly employed in drug discovery and some were controlling the first group. The graph reveals that growing cost maybe because a expanding amount of people participating in the process.
2. Drug researcher dont extrapolate the gained productivity improvement knowledge forward. The reason for that is either interference from the controllers or nobody is interested to improve productivity.

Humans create data

The best growth potential is in orphan and neglected diseases. Unfortunately, with the current cost and speed of product development there is no chance to continue Drug Development.

Until about 2000 there was a broad group of independent technical specialist that provided Drug Discoverers with innovative tools to create new solutions. After 2000 new managers moved into the large pharmaceutical companies to reduce cost and to improve productivity. The new generation of pharma managers stopped access of the external know how providers. They outsourced research to universities, bought raw

materials and intermediates from India and China and started to collaborate with large ITcompanies to digitalize the industry. After 2008 financial crisis Hedge Funds discovered the lucrative Life science and Health sector. They procured large section of the industry to fix their poor performing investments by transferring profits from the life sciences. To increase profitability, they started to commoditize Health and Life science companies.

At that time LCC conducted custom synthesis of intermediates for researcher in large pharmaceutical companies. We also sold monodisperse Polyethylene Glycols to research laboratories. All recipes for the intermediates came from the pharmaceutical companies and none was reproducible, - **none!** PEGs were used for conjugation with peptides and proteins. Normal PEGs have a broad range of molecular weights and unpredictable kinetics. Monodisperse PEG had one molecular weight and assured reproducible conjugation and QC kinetics. Drug Discoverer were afraid to procure reproducible answers.

We also attended complaints from Chemistry and Biolabs in Universities. They asserted that our chromatography columns were bleeding. A quick visit to the labs proved the same problem – we always found cells in the buffer tanks that produced new molecules.

Students, Docs and Post docs must deal with a growing number of variables and subprocesses that influence outcome. We all remember what we did in synthetic chemistry lab during our student times! Nobody worried about yield and productivity. The focus was on «prove of concept», passing exams and getting a paid job as quickly as possible. Many of the reactions did not start, we newer investigated why – we just threw them away. We rationally reasoned that “Not enough time and research funds did force us to procrastinate and to focus on what is expected from the superiors».

The same problem in industry. To do things cheaply was much more important than to do things precisely and reproducibly. Unfortunately, with such a data basis we can’t extrapolate forward the gathered knowledge and we can’t build a basis for artificial intelligence. It is the bull dust in and bull dust out black box system.

The real problem is much larger! The Drug Discoverer or Researcher have never learned and understood that they produce **value**. And so, the administrators perceived them as gamblers that destroy money.

Already in the late nineties we offered top managers in pharmaceutical companies to find new application for those compounds that were unsuccessful in the assays. Instead of creating value the highly payed managers trained the creative Drug Discoverer to become procrastinators and to create mainly unusable garbage.

After 2008 large Hedge Funds started to tighten control in Life sciences and Health sector. They bought laboratory supply companies. With the support of the top managers they installed them as sole purchaser in the companies they controlled. They outsourced basic research to taxpayer financed universities with the promise to

adsorb the graduates. To increase profitability the operations were commoditized. With the growing influence of Biotech, diversity of people was increased. At the same time external training courses and workshops were exchanged with Webinars. Diversity of tool was reduced while complexity of Compounds grew. Fishing around for low cost materials eliminated IPR and with that billions of additional revenues. The gap between top managers and staff grew. Instead of motivating staff they used their given power to coerce people. *"You were hired to do that and this, if you can't do it efficiently you should leave".*

Staff turnover and apathy grew.

And suddenly there was COVID-19

With the arrival of COVID19 the broad public suddenly realized that many tools to cope with diseases and pandemics were missing. Many people experienced how some of their friends and relatives suffered and died because of lack of appropriate equipment. Lock downs slowed down most economic activities. Many governments were not able or interested to stop unemployment with salary bridging. Suddenly the anaemic assembly line workers in companies and institution woke-up and interacted with colleagues and neighbours to offer help and collaboration, worldwide.

In all previous recessions Entrepreneurs and Government felt responsible to battle growing economic problems. However, it was always the entrepreneurs that quickly started to evolve problem solutions. They started to employ people and the recession eased.

As techno-entrepreneurial company we have witnesses that the life science and health sector have a huge growth potential provided, we focus on curing more diseases and managing more illness. The race for a vaccine has created a huge technology revolution in the life sciences. It is time to bring Drug Discoverer into this revolution! They must be the creator of effective and efficient problem solutions (Diagnostics and Drugs) and they must be in power to use productivity tool such as Robotics and AI. Today, there are too many hangers-on that want to share success if the Drug Discoverer succeed.

Currently they are producing "prove of concept" and nobody cares about it. We hope to get their involvement in the revolution. That will evolve Passion and drive for Professionalism, Productivity and Precision. Drug Discoverer know that with false data it is impossible to create algorithm that design and produce novel bioactive compounds.

Let's liberate and reactivate Drug Discoverer

To reverse the EROOM Law we must motivate Drug Discoverers to get passioned about their work. Chromatography has the potential to create precise and reproducible data. With precise and reproducible data, we can evolve pattern and create algorithms that may be used for designing rational molecular synthesis. It is a

fact, proud and passioned people work harder, they reject being commoditized and they are simply more productive.

Most Drug Discoverer are currently in a competitive and aggressive environment. If manager us competition to make employees more productive, they must enable them to design their own path to success!

Experienced Drug Discoverer know that one can't create new to the world molecules with commodity raw materials and tools. We must give them the freedom to chose and to procure tools they can use creatively.

Drug Discoverers know that they must create new unique, IPR protectable drugs. They get cynical when they learn that purchasing officer don't respect the IPR law and invite competition by fishing around for low cost material.

Experienced Drug Discoverer know that they require new intermediate and tools to create «new to the world» molecules. They also know that finance investors priority is to substitute new tools with low cost commodities. Nevertheless, if Discoverer succeed in creating more new compounds this will increase profitability many times more than what the Hedge Funds people save by using commodities. Furthermore, they build a future for the company. Drug Discoverer will give much more of themselves if they are regarded and treated as specialists. They work in a difficult and lonely world of serendipity. However, producing reproducible data is tangible knowledge that can be extrapolated forward. Consequently, productivity will be moving gradually upwards. Drug Discoverer must be able to chose trustworthy and creative partners to supply the required tools.

Let's try to create better drugs more productively.

At LCC, we invite Drug Discoverer to join us trying to make the discovery process much more productive. Managers claim to be productive, why dont they empower Drug Discoverer also to become productive?

We believe Drug Discoverer require compact multifunctional tools, comparable with a Swiss army knife that enable them to perform many creative tasks. A Swiss army knife has no application guidelines. The user decides when and when not to use it.

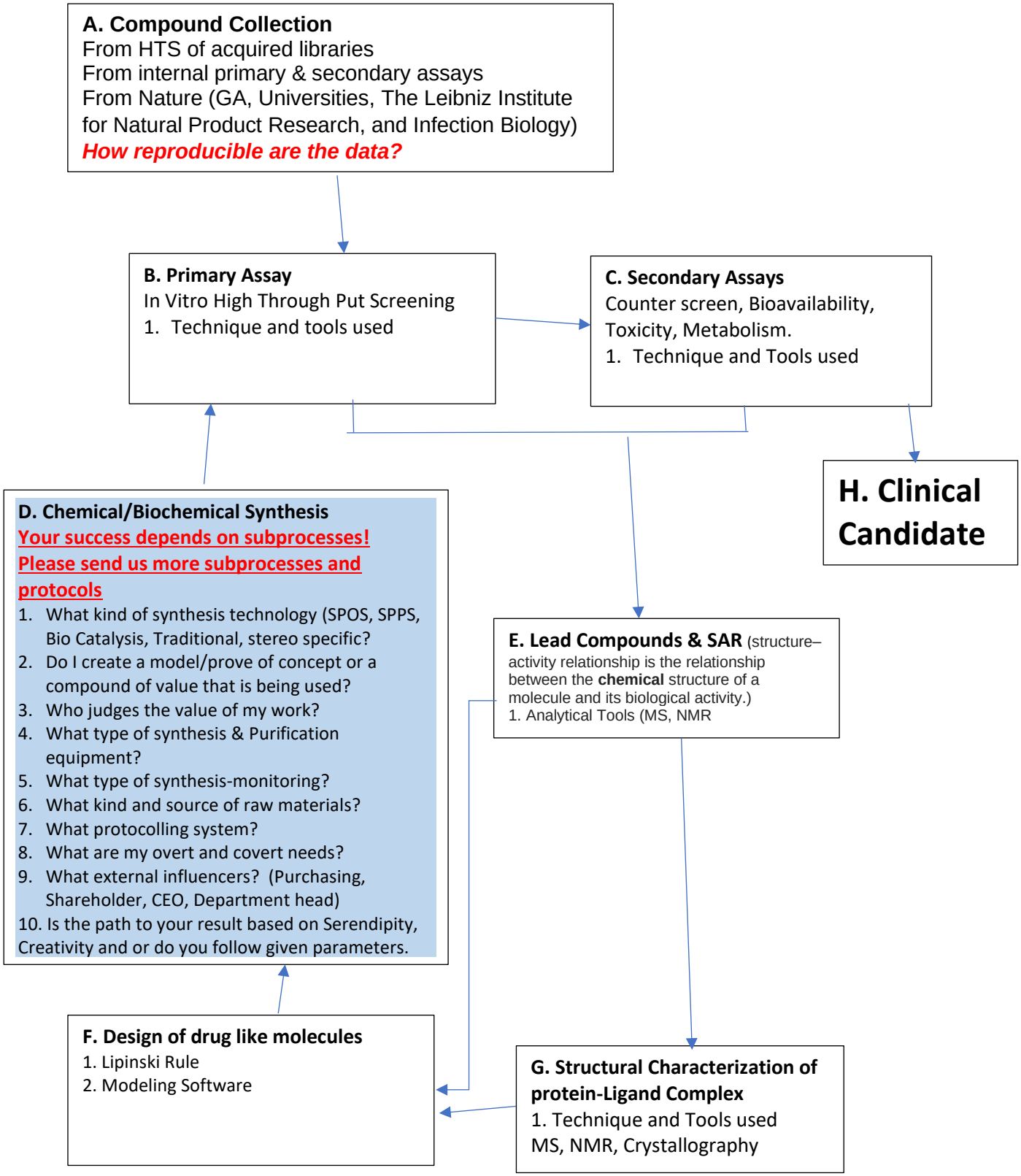
We also believe that Drug Discoverer should own their tool. They can than decide to share it or not with other. Having your own equipment will provide freedom - it is almost like driving your own Harley Davidson. In the next pandemic Drug Discoverer can take the instrument home to continue discovery. However, with freedom also comes responsibilities – as Drug Discoverer you must look after your equipment.

In return our promise to you is:

1. Our technology is easy to drive by touch-screen menu.
2. We offer you a low-cost and multifunctional equipment.
3. The primary function of the tool is to perform high-quality purification and separation operations to assure that all recipes are reproducible

4. We help you to find secondary functions so that you can perform with the instrument unique subprocesses (e.g. SPOS or to reinforce IPR)
5. We endeavour to link Pride of Drug Discovery users with other Pride of Drug Discovery users, provided you desire to be linked

Drug Discovery Cycle



The drug discovery cycle is fundamentally a simple process. Unfortunately, talking about subprocesses that are necessary to be done to create a unique and pure hit or lead is taboo.

Pride of Drug Discovery™ – is our answer to the problem

Pride of Drug Discovery™ is a compact and competitively priced purification/separation instrument, a bit like a Swiss army knife.

It can be used to purify new compounds, to fractionate by-products and target-product to obtain high purity.

It is easy to handle and is touch menu driven.

You should collect all fraction because they tell a lot about raw material purity and reaction quality.

The Pride of Drug Discovery™ is a personal device of the Drug Discoverer.

The instrument doesn't care whether you are male, female, black or white, what title or socio-economic background you have. It is your personal assistant that has only one purpose, to make you more successful.

You can do with it what you consider best for achieving your goal. The instrument should convey to your superiors: "Trust me I will be productive!".

In collaboration with LCC we will propose to apply new subprocesses and process tricks.

The Pride of Drug Discovery™ can be used to purify solvents or intermediates.

It doesn't make sense to perform data mining with recipes that are not reproducible. Pride of Drug Discovery™ changes this game.

You can use the instrument competitively. Show your superiors or colleagues that you understand purification/separation technology as you understand chemical/biochemical synthesis. Show them your chromatographs and column you are using

A set of spare part are supplied. We will show you how to maintain and optimize your instrument. Your competitors will depend on maintenance contract – but you are different and competent to solve problems.

In a homogenized world people are controlled by people with ulterior motives. It is important that Pride of Drug Discovery™ is a personal device. You don't need to be controlled – You have decided to be productive, precise, and successful, values that make you different.

In the post Corona world technically, skilled peoples will have to create economic activity to ease unemployment. The Asians are already changing the path of life sciences. It is time to reinvent and revitalize the path to success applying

professionalism, precision and productivity. We hope that the Pride of Drug Discovery™ system will be used in many Industries and universities

We endeavour to build a community of innovative and creative individuals that have developed new workable tricks to evolve novel bio active compounds.

Please visit our website and click Pride of Drug Discoverer in the section Advanced Chromatography Systems