ICN International Clinical Trial Center Network

NEWSLETTER

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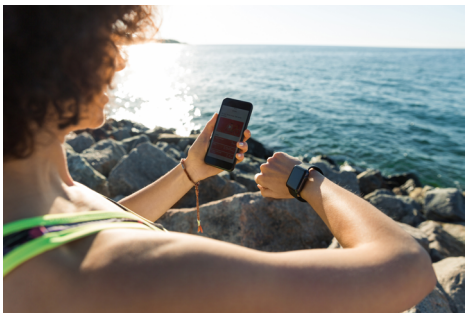
Decentralised Clinical Trials

The outbreak of COVID-19 has disrupted many clinical studies. A separate side-effect of the pandemic has been swift adoption of virtual interactions between physicians and patients to provide continuity of care while maintaining social distancing. Therefore, interest in decentralized clinical trials (DCTs) that use "virtual elements" has grown in parallel with acceptance of "virtual medicine," accelerating shifts in clinical trial design that many feel are long overdue.

University of South Australia

Researchers at University of South Australia recently completed an NHMRC-funded cohort study examining the daily changes in Adelaide adults' physical activity, sitting behaviour, sleep, and weight. They also regularly monitored their diet and well-being eight times throughout the year. They used Fitbits to capture minute-level activity data every day of the year for a full year. Similarly, Fitbit smart scales were used to capture daily weight. They worked with software developers to create custom software that automatically downloaded participants' daily activity and weight data from Fitbit, once they gave one-off permission to share their data. All of the survey data were captured remotely using online surveys. All participants received a single home visit at the start of the study to deliver the Fitbit equipment and help get it set up. After this, all data were collected remotely. Through the custom software, the study team was able to check data completeness on an twice-weekly basis, with participants sent reminder SMS messages and phone calls if activity or weight data were missing for more than three days.



This protocol achieved excellent rates of data completeness, with 90% of participants staying in the study for the full 12 months, and 85 to 90% data completeness for all survey assessments. The approach led to better rates of data completeness than they would expect using traditional research accelerometers, and at considerably less cost, given that Fitbit devices are cheaper to purchase upfront, and they did not need to spend money on repeatedly mailing out and receiving back research accelerometers via the postal service. Study participants were highly satisfied with this study approach, which is likely to have contributed to the high rates of participant retention.

The use of consumer activity wearables (Fitbits), with a custom research dashboard, is likely to be a useful research methodology looking into the future, providing ongoing, high-grain data at low burden. For more information contact Prof Carol Maher (carol.maher@unisa.edu.au).

Decentralised Clinical Trials (cont')

Institute for Advancement of Clinical and Translational Science, Kyoto University and Kyoto University Hospital

According to Ministerial Ordinance on Good Clinical Practice for Drugs, namely Japan GCP, issued by Ministry of Health, Labor and Welfare, the medical organization is responsible for dispensing the investigational drug to subjects and documenting the number of drugs dispensed and returned. With this guideline synchronized as ICH E6 (GCP), Direct-to-Patient (DTP) could be applied. The medical institution could deliver the investigational medicinal products to be delivered from the hospital by a qualified courier (Vendor) to the subject's residence directly.

To apply DTP, the sponsor/sponsor-investigator needs to confirm DTP is well addressed in the protocol and related documents which are then approved by IRB. The hospital needs to assess the courier's qualification. Then the hospital concludes a contract with the qualified courier. The contract contains specified the service scope including temperature and data protection responsibility etc.

After the subject consents to adopt DTP service, the clinical research coordinator (sender) will pack the dispensed drugs and fill in booking form to request DTP service. The trained courier staff will deliver the drug per the contract requirement to the subject's residence at the appointed time and date.

During the DTP process, all the subject information is strictly protected to guard the privacy and data security according to Data Protection Laws and Regulations. All the dispensing procedure and documentation from medical organization to subjects remains the same except the drugs are delivered by a specified courier.

University of South Australia

The University of South Australia, in conjunction with Monash University in Victoria, are currently running a National Health and Medical Research Council (NHMRC) funded project, investigating a range of weight-loss strategies for shift-working populations to try to identify one that may better-suited to their lifestyle.

This research has several virtual elements embedded in its original study design, including using a secure web platform for building and managing the database and questionnaires (REDCap), bluetooth scales and the use of a mobile phone application for participants to record 7-day food diaries. These virtual components provide flexibility to a population that traditionally work hours contrary to traditional data collection periods i.e., outside of 8am-5pm, allowing for greater recruitment and data collection capacity.

Additionally, as the COVID-19 pandemic took control, the study pivoted to virtual dietetic consult sessions, allowing participants to continue to have one-on-one support. Combining these virtual elements with traditional face-to-face components ensured that data collection was able to continue in a timely manner, the primary outcome of weight was protected, whilst maintaining rigor and efficiency, despite challenging circumstances. For more information contact Dr Michelle Headland (michelle.headland@unisa.edu.au).

Updates of ICN

Welcome to ICN: Clinical Trial Center, Research and Innovation Department, Azienda Ospedaliera SS Antonio e Biagio e Cesare Arrigo

Warm welcome to Clinical Trial Center (CTC) of the Research and Innovation Department (DAIRI, Director Dr Antonio Maconi), Azienda Ospedaliera SS Antonio e Biagio e Cesare Arrigo from Alessandria, Italy, for joining ICN as a Regular Member!

The Clinical Trial Center (CTC) of the Research and Innovation Department (DAIRI, Director Dr Antonio Maconi) is a centralized facility working within both the Public Hospital "Azienda Ospedaliera SS Antonio e Biagio e Cesare Arrigo" and the Local Health Authority of Alessandria (Italy). The CTC is focused on designing and conducting high-quality clinical trials: it promotes efficiency during the study activation phase and optimizes study and data management according to the ICH-GCP. The CTC is the designated interface for Sponsors and Contact Research Organizations (CROs) that recognize DAIRI as their partner for testing innovative therapeutic strategies in an effort to offer patients the best quality healthcare available.

Activities include:
- Feasibility and study start-up
- Design and management of clinical trials (profit and no-profit, interventional (phases II-III-IV), observational and medical devices)
- Clinical research census and monitoring
- Education and training

CTC's qualified staff consist mainly in research coordinators and data managers, usually organized according to therapeutic areas (solid tumors and blood cancers, gastrointestinal diseases, infectious diseases, nervous system diseases, cardiovascular diseases, musculoskeletal and connective tissue diseases, and metabolism and nutritional disorders). The CTC is unique in the Piedmont Region for the centralization of its activities and staff.

Publication of Joint Research Paper on *Journal of International Medical Research* "How COVID-19 changed clincial research strategies: a global survey"


Prospective Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

How COVID-19 changed clinical research strategies: a global survey

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We are pleased to announce that the joint research paper titled "How COVID-19 changed clinical research strategies: a global survey" is accepted and published on the Journal of International Medical Research!

A huge thanks to all the members who have contributed to the survey and the valuable inputs. Special thanks to Ms. Annina Bauer, the ICN Operations Officer who is also the PhD student from the University of Zurich, for the coordination and contribution!

If you want to read the whole paper, please click here: https://doi.org/10.1177/03000605221093179.

Global Focuses

Italy: What is issuing authority?

Contributed by Clinical Trial Center, Research and Innovation Department,
Azienda Ospedaliera SS Antonio e Biagio e Cesare Arrigo

In Italy, the issuing authority is The Italian Medicines Agency – AIFA. After the full enforcement of European Regulation n. 536/2014 on 31 January 2022, AIFA published useful information and relevant documents. One is a guidance for the temporary management of pharmacological clinical trials pending the full implementation of the ministerial decrees reforming the ethics committees and the single fee. Others are models about curriculum vitae and declaration of interests of the principal investigator and suitability of the center. All documents have prepared in Italian and approved by The National Coordination Centre of the Ethics Committees, established within AIFA.

European Union: New legislative framework in Europe for clinical trials with medicinal products and medical devices

Contributed by Center for Clinical Trials (ZKS), Hannover Medical School

The new Regulation (EU) No 536/2014 for clinical trials (CT) with medicinal products (Clinical trials regulation, CTR) is applicable from January 31, 2022, and replaces EU Directive 2001/20/EG (Clinical Trials Directive). The Regulation harmonizes the procedures for submission, assessment and supervision of CT in the EU through the Clinical Trials Information System (CTIS). This online platform enables sponsors to submit one online application for CT in multiple EU Member States/EEA countries and thereby fosters innovation and research in the EU.

The European Commission states that if CT are conducted outside the EU, but submitted for marketing authorization in the EU, they have to follow similar principles to the provisions of the Clinical Trials Directive (Annex I, point 8 of the Directive 2001/83/EC).

EU Regulation 2017/745 for medical devices (Medical Device Regulation, MDR) is mandatory in all EU member states from May 26, 2021. The Medical Devices Implementation Act (Medizinprodukterecht-Durchführungsgesetz, MPDG) serves to implement and supplement Regulation (EU) 2017/745 in Germany. The MDR replaces the existing Directives for medical devices (93/42/EEC and 90/385/EEC). Annex I of the MDR defines the General Safety and Performance Requirements which need to be met if a medical device shall be placed on the European market.

European Union: IVDR – In Vitro Diagnostic Medical Devices Regulation (EU) 2017/746

Contributed by Clinical Trials Center,
University of Zurich and University Hospital Zurich

After a transition period of 5 years, the Regulation (EU) 2017/746 (IVDR) became fully applicable on May 26, 2022. IVDR sets a new milestone in the regulation of in-vitro diagnostic medical devices. In 113 articles and 15 annexes, the IVDR confronts manufacturers with massive changes compared to the previous IVDD.

Manufacturers of in vitro diagnostics must completely revise their quality management system and technical documentation for all products. New procedures must be introduced to meet the increased requirements. The greatest differences in content lie for example in:

- The classification system with new risk classes. Here, the majority of products will be grouped in higher risk classes thus needing a Notified Body to remain in compliance.
- Performance evaluation, where the corresponding documents will be subject to increased scrutiny.

IVDR Compliance Process in brief:

1. Appoint your European Authorized Representative
2. Identify all EU Directives/Regulations applicable to your product
3. Select and perform the conformity assessment procedure applicable to your product
4. Check your device against the General Safety and Performance Requirements (annex I)
5. Identify the applicable harmonized standards for your product
6. Prepare a Technical File (annex II and III) and implement a Quality Management System
7. Select a Notified Body (except for class A) and sign your Declaration of Conformity

Members' Snapshots

DACH-Symposia for Clinical Trials 2022, May 30/31

Contributed by Clinical Trials Center,
University of Zurich and University Hospital Zurich

After a pandemic-dependent longer interim period, the DACH this year took place in Salzburg, Austria. DACH was organized by members of the Austrian, German and Swiss networks of clinical trial centres and is directed to clinical study personnel of academia, industry and other interested stakeholder. A comprehensive update of actual developments in clinical research was presented in more than 30 sessions to 650 participants (including ICN members of Freiburg, Graz, Munich and Zurich) accompanied by an industrial exhibition and many opportunities for networking and exchange.

Several sessions focussed on new regulatory requirements including the European Clinical Trial- and Medical Device-Regulations as well as the In Vitro Diagnostic Regulation. Actually, worldwide clinical research is awaiting the revision of the ICH E6(R2) Guideline "Good Clinical Practice" (GCP). Interestingly, a double session with four presentations was dedicated to the theme of this newsletter, „Decentralised Trials", with views and experiences from regulatory / ethic bodies and industry. The next DACH will take place 2024 in Berlin.

Newly Constituted Center for Clinical Trials (ZKS), Hannover Medical School

Contributed by Center for Clinical Trials (ZKS),
Hannover Medical School

With the establishment of a central unit, Hannover Medical School (MHH) has taken a major step in terms of support for the planning and implementation of clinical trials. The Center for Clinical Trials (ZKS) was newly constituted in 2021 and combines four already existing supporting pillars for the conduct of clinical studies under one roof. Clinical Trial Services (CTS) delivers all services of an academic CRO, the Financial Risk Management Unit (FRMU) provides commercial / calculative competence for study budgets, and the Operational Structure Management (OSM) supports the ZKS with a joint structural and quality management system. The Early Clinical Trial Unit (ECTU) is the central point of contact for conduction of early clinical trials. With this, ZKS will serve all needs of clinician scientists as well as pharmaceutical and medical device companies with respect to the planning, regulatory submission and conduction of clinical trials of sponsors, PIs and investigators at MHH. Prof. Christoph Schindler, executive head of the ZKS, and his team look forward with confidence and motivation to tasks ahead and the cooperation within the ICN.

Prof. Dr. Christoph Schindler; Executive Head of the ZKS in Hannover

Patient and Public Involvement at CTC Zurich

Contributed by Clinical Trials Center,
University of Zurich and University Hospital Zurich

After a successful symposium on patient and public involvement (PPI) in clinical research at the end of 2021, the CTC Zurich got down to business with its own PPI project. Two dedicated patient representatives support the CTC in this project, which focuses on lay summaries, patient-centered General Consent and aims at enhanced communication between researchers and patients and the public. In May, we conducted a first workshop open to the public where we gained valuable input for the continuation of our project.