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| **Table 2,** Data extraction of results from research articles included in the systematic review (n=13) |
| **S. No.** | **Author** | **Year** | **Country/Region** | **Study Aim/Design** | **Challenge(s)** | **Stakeholder(s)** | **Regulation(s)** | **Impact(s) of Regulation** | **Risk of Bias****(MMAT)** |
|  | Lamy M, Liverani, M  | 2015  | South East Asia-Mekong;Myanmar, Thailand, Lao PDR, Cambodia, Vietnam     |  Highlighting the strengths and weaknesses of past national intervention responses in combatting falsified medicines.   Examination of institutional frameworks that exist to support increased capacity with a focus on Southeast Asian Nations  | Sale of counterfeit medicines in remote, rural communities  Reduced custom controls and increased cross-border exchanges promotes infiltration of falsified medicines.  Lack of general operational and enforcement capacity to monitor supply chains due to inadequate human resources, equipment and infrastructureTransnational nature of falsified medicines Funding shortages and unsustainable financial agreements Trade expansion of pharmaceuticalsOutdated laws and complex pharmaceutical market | Manufacturer   Patient    | National Drug Law (1992, Myanmar),  Law on Pharmacy (2005, Vietnam), Drug Act (2003, Thailand), Law on the Management of Pharmaceuticals (1996, Cambodia), Law on Drugs and Medical Products (2000, Lao PDR)  | Deterrent against falsified medicines Improved case tracking and quality control Movement towards low-cost and easy-to-use quality control detectionAids to strengthen legal frameworks, operational scope, and governance mechanisms | ◼◼◼◼🞎 |
|  | Naughton BD, Roberts L, Dopson S, Chapman S, Brindley D.  | 2016  | United Kingdom  | Identification of the authentication and detection rates of serialised medicines to assess the effectiveness of medicines authentication technology in NHS secondary care   | Difficulties with implementation of FMD-legislated serialisation and authentication technologies in secondary care of some countries  Non-compliance issue due to increased number of guidelines and protocols required to be adhered to by NHS staff.  Detected counterfeit, recalled and/or expired medicines not always quarantined by staff Misinterpretation of alerts due to similar content and colour  | Hospital pharmacy Patient   | Falsified Medicines Directive (FMD)   |  Improved authentication and detection rates  Improved patient safety  Impact on policy and key decision makers- need for effective education and training strategies to achieve successful implementation   | ◼◼◼◼◼ |
|  | Borup R, Kaae S, Minssen T, Traulsen J | 2016 | Denmark | Reviewing the distribution of medicines in Denmark through comparison of legislation before and after Denmark joining the EUAssessing the impact of EU harmonisationEvaluating if drastic increases in mandated Falsified Medicines Directive requirements correlate to a new pharmaceutical supply chain governing approach |  Highly complex legislation now covers the entire supply chain  Little room to allow for interpretation of FMD legislation to fit local settings    Equal compliance with FMD becoming priority as opposed to protection of public health    | ManufacturerWholesalerCommunity pharmacyHospital pharmacyPatient  | Falsified Medicines Directive (FMD)  | New approach to manage the pharmaceutical supply chain- more focus surrounding documentation and increased requirements specificity  Different requirements for individual supply chain actors   Complexity of regulation demands compliance- companies hiring experts in regulatory requirement; additional financial costs  Clear checklist for regulation compliance   | ◼◼◼◼◼ |
|  | Moniveena MG, Pramod Kumar TM. |  2017  | United StatesEuropean UnionFranceJapanIndia  | Inspection of the track and trace regulations in pharmaceutical industryExamining the impact of track and trace regulations to protect drug distribution chains in status regulated countries and India Examining the impact of track and trace regulations on the reverse logistics of medicines  | Establishing the identity of individual medicinal productsSome medicinal products may be classed as prescription pharmaceuticals in one Member state but not in another | Wholesaler  Manufacturer  Patient   | US Federal: Drug Supply Chain Security Act (DSCSA), ‘Track and Trace Act’   California: Epedigree Law Nov.27 2013  European Union: Falsified Medicines Directive (FMD)  France: French CIP13 Coding Legislation   Japan:  Encoding of Pharmaceuticals with Japan Article Number   | Serialisation: electronic methods reduces and/or eliminates human input error Improved accuracy and time efficiencyReduced medication errorsImproved inventory controlIncreased product recall effectivenessDetection of theft, product diversion and parallel trade Tracking systems provide full visibility to chain of custodyElectronic communication helps streamline reverse logistics procedure and reduce cycle time | ◼◼◼◼◼ |
|  | Naughton B, Roberts L, Dopson S, Brindley D, Chapman S.  | 2017  | United Kingdom  | Determination of expert opinion and possible improvements in the hospital setting for Falsified Medicines Directive (FMD) authentication technology  | Lack of training and education, contributing to inadequate authentication and detection rates  Unclear differentiation between warning messages leading to misinterpretation of alerts.   | Hospital pharmacy  | Falsified Medicines Directive (FMD)   | Limited impact on daily activity of staff‘Not disruptive’ to daily activity | ◼◼◼◼◼ |
|  | Religioni U, Swieczkowski D, Gawronska A, Kowalczuk A, Drozd M., et al  | 2017  | Poland  | Assess the value of external audits in the context of FMD implementation regulations in the secondary care setting  |  Ensuring products are not authenticated too early in the supply chainDispensing drugs in bulk- better to select products from manufacturers that produce aggregated codes as if not, will increase product authentication time 10-day decommissioning rule Split packs- authentication needed prior to opening package and not transferred to other institution | Hospital Pharmacy  | Falsified Medicines Directive (FMD) Delegated Act (DA)  | FMD impeding workflow in the hospital pharmacy New responsibilities on pharmacists and pharmacy technicians Unused drugs must be returned to hospital pharmacy from the wards within 10 days of product decommission in order to be eligible for transfer to a different institutionExtemporaneously compounded medicines, intravenous and parenteral nutrition products need to be authenticated during assembly before final product is prepared | ◼◼◼◼🞎 |
|  | de Pinto C, Koshkouei M, Jeske M, Zeiler M, Brindley D.   | 2017  | Austria  | Appraise the impact of implementation of FMD legal requirements in an Austrian hospital, using a medicines authentication system (MAS).   | Implementation of MAS could result in significant disruptions and large upheaval for secondary care pharmacy staff when not handled properlyConnectivity issues  | Hospital Pharmacy  | Falsified Medicines Directive (FMD)   | Impact on dispensing operations- to handle the decommissioning, significantly more structure and preparation is required.   Reduction in staff required in FMD environment due to automation.   Increase in operational dispensing time in a FMD environmentIncreased workload - single unique identifier for each product must be decommissioned separately Internet connectivity issues and national repository location can affect response timeIncreased expenditure  | ◼◼◼🞎🞎 |
|  | Naughton BD   | 2019  | United Kingdom  | Investigation of serialised medicines introduction into an operational hospital dispensary and the assessment of technical effectiveness of digital medicine authentication (MA) technology under European Union Falsified Medicines Directive (EU FMD) conditions  | Disruptions to healthcare providers if FMD legislation is poorly implemented- key technical parameters including offline issues, incorrect quarantine, and average response times  Low levels of awareness and understanding of FMD regulation among healthcare providers Inadequately designed technology alerts | Hospital pharmacy  | Falsified Medicines Directive (FMD)   | FMD offline issues may cause significant delays in medicine supply, a backlog of dispensing and cause confusion at point of decommissioning the product- legal and practical impactMA is an additional step that impacts adjacent processes  | ◼◼◼◼🞎 |
|  | Barrett R | 2020  | England  | Assesses the readiness of community pharmacies for the introduction of the Falsified Medicines Directive (FMD)  | Lack of resources, knowledge, competency, training, and confidence in pharmacy personnelLack of compliance with FMD implementation  | Community pharmacy Patient | Falsified Medicines Directive (FMD)    | Negative impact on workload Disruption to normal business flow  Adds to administrative burden Changes in profitability Improves patient safety  | ◼◼◼◼◼ |
|  | Vajda P, Richter K, Bodrogi Z, et al.  | 2021  | Hungary  | Evaluation of the current practices, cost, and workload implications of FMD implementation in Hungarian hospitals within the stabilisation period | Implementation and maintenance costs of verification and decommissioning   Staff resource issues Pharmacists struggle with different codes and false alarms   | Hospital pharmacy  | Falsified Medicines Directive (FMD)   | Tightens the legal drug supply chain High implementation and operational costs- IT and infrastructure investment Additional human resources required in hospitals  Impedes workflowPrice increase in serialised medicationsDrug supply issues under FMDIncreased storage capacity requirements- differences in product packaging size under FMDIncreased pharmacist and pharmacy technician workloadIncrease in FMD related premises- financial burden | ◼◼◼◼◼ |
|  |  Merks P, Religioni U,  Pinto De Castro N, Drozd M, Mack C,  Świeczkowski D,  Zerhau M, Gawrońska A, Kowalczuk A,  Jaguszewski M, Brindley D, Hug M.  |  2021  |  Germany  | Determination of additional operating time for internal workflow to comply with FMD and establishment of suitable areas to conduct efficient medicine packaging scanning  | Establishing the optimal operational procedure for decommissioningDetermining when scanning requires the least operational timeProduct packaging- inability to scan through plastic covering, barcode printed at different points of package depending on manufacturer leading to inaccessibility and delaysType of scanning equipment- wired vs mobile scannerArticle 13, 10-day decommissioning rule | Hospital pharmacy  | Falsified Medicines Directive (FMD)  Delegated Regulation (DR)  | Additional workload on hospital pharmacy staff Point of decommission and its impact on workflow (optimal point is authentication of products before sending to the ward)Scanning and location of barcode increases operational time on daily basis 10-day decommissioning rule limits emergency loans and supply to other hospitals | ◼◼◼🞎🞎 |
|  | Dalton, K, Connery C, Murphy KD, O’Neill D |  2022  | Ireland  | Examination of community pharmacists’ views on how FMD has affected their practice.  | Lack of regulation compliance- belief that manufacturers should be responsible for the verification steps Hardware and software issues- add variation and unpredictability  Busy work periods- reduced priority of decommissioning products Scanner location- constrained dispensary staff positioning and space Increased product packaging size due to 2D barcode - storage issues, less information on packaging when pharmacist checking medicine  | Community Pharmacy  Patient  | Falsified Medicines Directive (FMD)  | Significant disruption to dispensing process  Loss in staff productivity  Additional implementation costs- training, software, and equipment  Time consuming distraction to clinical checks, leading to increased risk of dispensing and/or near miss errors Reduced patient interaction time  Increased prescription turnaround time for patients  Increased workload Increased technical support requirement Easier full pack dispensingIncreased patient safety- advantage to track medicines at batch recalls and expiry date check Benefits stock control process | ◼◼◼◼◼ |
|  | Fedalto M, Stumpf Tonin F, Borba H, Lins Ferreira V, Correr C, Fernandez-Llimos F, Pontarolo R | 2022 | Brazil | Investigating the practice of pharmacists relating to pharmacovigilance activities Identifying difficulties and possible stimuli to improve these activities in pharmacies and drugstores | Low numbers of pharmacists reporting suspected substandard medicines to NotivisaLack of motivation to notify the system Pharmacists unsure of the cause of the problemPharmacists unconvinced by the confidential handling of reported informationDifficult for pharmacists to admit that patients have been harmed Insufficient clinical and technological medicines knowledge Pharmacists fear being legally responsible for the issuesVaried knowledge regarding Notivisa- association between education level and Notivisa knowledge, better knowledge associated with a master’s degree to post-doctorate level, specialization, and professional residencyComplexity of making a Notivisa notification Lack of access to the system at workNot knowing the email address to send a report to Unaware of how to notify the system  | Community pharmacyPatient | National Health Surveillance Notification System (Notivisa) | Pharmacists agree with pharmacovigilance importance in protecting public and patient healthReporting services recognized as part of pharmacist duties and pharmaceutical careMaking a notification is a time-consuming task– impedes workflow and increases turnaround time  Need for additional material, education, courses, and training surrounding the system- requires both time and funds | ◼◼◼◼◼ |